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Treatment of COVID-19 Patients during Second Wave in a Tertiary Care Center of Nepal

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ABSTRACT

Introduction
The second wave of the COVID-19 pandemic was confirmed in Nepal in April 2021. It was caused by genetic variants of SARS-CoV2. The objective of the study was to find out severity of patients, their treatment and approximate drug cost for the treatment of COVID-19 in the second wave.

Methods
In this retrospective, cross-sectional study, data of all patients who tested positive and were admitted in KIST Medical College and Teaching Hospital between April 2021 – July 2021 was collected for the study. A total of 215 patients were included.

Results
Among the cases admitted, 190 (88.4%) patients were symptomatic. ICU/HDU admission was done in 113 (52.5%) cases, among which 33 (29.2%) patients received ventilator support. The patients treated in isolation unit were 102 (47.4%). Among the patients admitted, 23 (10.7%) were vaccinated. Severe cases were 80 (37%), moderate cases were 71 (33%) and mild cases were 49 (23%). Antibiotics were used in 190 (88.4%) cases. More than one antibiotics were used in 141 (65.6%) cases. Antifungals were used in 39 (18.1%) cases. Other drugs like corticosteroids were used in 185 (86%), proton-pump inhibitors in 179 (84.3%), antihistaminics in 169 (78.4%) and anticoagulants in 165 (76.7%), Vitamin C in 153 (71.2%), Vitamin D in 152 (70.7%) and zinc in 140 (65.1%) cases. The number of patients discharged after recovery was 151 (70.2%) and 41 (19.5%) patients died. The average drug cost was NPR. 3,246 in mild, 27,645 in moderate and 76,420 in severe cases.

Conclusion
Majority of patients were treated in ICU/HDU. Most commonly used drugs were antibiotics, corticosteroids and anticoagulants. Mortality was high in the second wave.

Keywords
Cost, COVID-19, drugs

INTRODUCTION

The second wave of the COVID-19 pandemic was confirmed in Nepal with an exponential rise in the number of cases in April 2021.[1,2]

Some variants of SARS-Cov2, considered as variants of concern (VOCs) are α (B.1.1.7 lineage), β (B.1.351 lineage), γ (P.1 lineage) and δ (B.1.617.2 lineage).[3] The first wave of Covid-19 occurred due to SARS-CoV-2, whereas the second wave is considered to be due to its genetic variants.[3]

Though various national and international guidelines have been developed for the treatment of COVID-19, no single drug has been proven effective against COVID-19 even after the occurrence of the second wave of the pandemic.[4-7] Our study aims to find out the clinical features of COVID-19, pharmacological measures and approximate drug cost for the treatment of COVID-19 in a tertiary care center in Nepal.

METHODS

The study was designed as a retrospective cross-sectional study. The study was conducted after ethical approval from the Institutional Review Committee of KIST Medical College and Teaching Hospital (Ref no.:2078/79/13). The data of all patients admitted at KIST Medical College and Teaching Hospital, Nepal between the time period of April 2021 to July 2021 was collected for the study. The patients who tested positive for COVID-19 by RT-PCR (Reverse transcriptase-polymerase chain reaction) and were admitted in the hospital were our study population. A total of 215 patients were included in the study.

The data was collected in a structured study proforma. The study proforma contained demographic information of the patients, signs and symptoms on admission, disease severity, treatment and treatment outcomes. The data of drugs administered to the patients for the treatment of COVID-19 was collected and their cost was calculated. The unit price of the drugs was collected from the hospital pharmacy. The cost did not include the cost of the drugs taken by the patients for their comorbidities. The collected data were entered and analyzed using SPSS version of 26.0 for Windows. The results are presented using descriptive statistics.

RESULTS

The total number of COVID-19 patients admitted in the second wave was 215. All patients were included in the study. Among them, 114 (53%) patients were male and 101 (47%) were female. The patients from age group 15 – 91 were admitted to the hospital. Patients of age group up to 40 years were 51 (23.7%). Patients with age group 41 – 50 and 51 – 60 were 45 (20.9%) each and patients from age group 61 – 70 were 42 (19.5%). The least number of patients represented extreme age groups with 2 (0.9%) patients from age group less than 20 and 14 (6.5 %) patients from age group above 71 years (Table 1).

Table 1. Demographic details of the patients

Characteristics	Number (%)
Age, Years	
Less than 20	2 (0.9)
21-30	23(10.7)
31-40	28 (13.0)
41-50	45 (20.9)
51-60	45 (20.9)
61-70	42 (19.5)
Above 71	14 (6.5)
Gender	
Male	114 (53.0)
Female	101 (47.0)

Table 2. Comorbidities, clinical features and admission of the patients

Characteristics	Number (%)
Comorbidities	
Overall comorbidities	117 (54.4)
Hypertension	72 (33.5)
Diabetes	43 (20.0)
Hypothyroidism	27 (12.6)
Respiratory Disease	18 (8.4)
Others*	40 (18.6)
Symptoms on admission	
Overall Symptoms	190 (88.4)
Fever	141 (65.6)
Cough	119 (55.6)
Shortness of breath	86 (40.0)
Myalgia	36 (16.7)
Headache	17 (7.9)
Chest pain	10 (4.7)
Others**	13 (6.0)
More than one symptoms	132 (69.5)
Admission on Unit/s during hospital stay	
Isolation Unit	102 (47.4)
ICU	28 (12.0)
ICU with ventilator	5 (2.3)
Isolation Unit and ICU	52 (24.2)
Isolation Unit and ICU with ventilator	6 (2.8)
ICU and ICU with ventilator	13 (6.0)
Isolation Unit, ICU and ICU with ventilator support	9 (4.2)

Comorbidities were present in 117 (54.4%) patients, of which 72 (33.5%) had hypertension, 43 (20%) had diabetes, 27 (12.6%) patients had hypothyroidism and 18 (8.4%) patients had preexisting respiratory diseases like COPD and asthma. Patients were symptomatic in 190 (88.4%) cases. The common symptoms were fever, cough and shortness of breath seen in 141 (65.6%), 119 (55.6%) and 86 (40%) cases respectively. Patients presented with more than one symptom in 132 (69.5%) cases.

Among the patients admitted to the hospital, 102 (47.4%) were treated in an isolation unit, 113 (46.5%) required ICU admission and 33 (15.4%) patients received ventilator support (Table 2).

Out of the 215 COVID-19 patients, 23 (10.7%) were vaccinated, 172 (80%) were not vaccinated and vaccination data of 20 (9.3%) patients was not available. The vaccines included Covishield in 16 (69.6% of vaccinated), Vero cell in 3 (13%) and J&J in 1 (4.3%) patients. Among the vaccinated, 10 (43.5%) patients received a single dose and 9 (39.1%) patients received double doses of the respective vaccines (Table 3).

Table 3. Vaccination profile

Characteristics	Number (%)
Vaccination Status	
Vaccinated	23 (10.7)
Non-Vaccinated	172 (80.0)
Not mentioned	20 (9.3)
Type of Vaccines	
Covishield	16 (69.6)
Vero cell	3 (13.0)
J&J	1 (4.3)
Not mentioned	3 (13.0)
Number of Doses of Vaccine	
Single	10 (43.5)
Double	9 (39.1)
Not mentioned	4 (17.4)

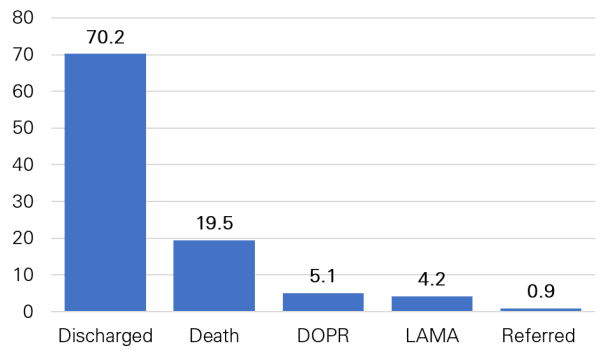

Figure 1. Outcomes of patients admitted in the hospital

In the second wave, severe cases were 80 (37%), moderate cases were 71 (33%), mild were 49 (23%) and the severity of 15 (7%) patients was not mentioned.

The mortality was seen in 42 (19.5%) cases, 151 (70.2%) patients were discharged after recovery and 2 (0.9%) patients were referred to another center (Figure 1).

Antibiotics were used for the treatment of COVID-19 in 190 (88.4%) patients. The antibiotics used were ceftriaxone in 132 (61.4%), azithromycin in 96 (44.7%), piperacillin-tazobactam combination 38 (17.7%), moxymycin in 25 (11.6%), meropenem in 16 (7.4%) and others in 79 (36.7%) cases. Other antibiotics included cefixime, clindamycin, amoxicillin-clavulanic acid combination, cefoperazone-sulbactam combination, cefepime, ciprofloxacin, levofloxacin, metronidazole,

Table 4. Common therapies in the treatment of COVID-19 patients during hospital stay (n = 215)

Therapy	Number (%)
Antibiotic treatment	190 (88.4)
Ceftriaxone	132 (61.4)
Azithromycin	96 (44.7)
Piperacillin + Tazobactam	38 (17.7)
Moxymycin	25 (11.6)
Meropenem	16 (7.4)
Others	79 (36.7)
>1 antibiotic used	141 (65.6)
Antifungal treatment	39 (18.1)
Fluconazole	22 (10.2)
Voriconazole	22 (10.2)
Others*	6 (2.7)
>1 antifungal used	11 (5.1)
Anticoagulant therapy	165 (76.7)
Enoxaparin	153 (71.2)
Dalteparin	27 (12.6)
Rivaroxaban	10 (4.7)
Dabigatran	1 (0.5)
>1 anticoagulants used	25 (11.6)
Other commonly used drugs	
Corticosteroids	185 (86.0)
Remdesivir	81 (37.7)
Proton pump inhibitors	179 (84.3)
Antihistamines	169 (78.6)
Vitamin C	153 (71.2)
Vitamin D	152 (70.7)
Zinc	140 (65.1)
Vitamin B Complex	28 (13.0)
Anti-cough	85 (39.5)
Paracetamol	113 (52.6)
Codeine	16 (7.4)
Codeine and Paracetamol	16 (7.4)

cefuroxime-sulbactam combination, amikacin, colistin, tigecycline, teicoplanin and erythromycin. In 141 (65.6%) cases, more than one antibioitcs were used. Antifungals were used in 39 (18.1%) cases, with fluconazole was used in 22 (10.2%) and voriconazole in 22 (10.2%) cases. More than one antifungals were used in 11 (5%) cases (Table 4).

Use of anticoagulants was a common therapeutic intervention in COVID-19 patients in the second wave. Enoxaparin was the most common anticoagulant and was used in 153 (71.2%) cases. Dalteparin was used in 27 (12.6%), rivaroxaban in 10 (4.7%) and dabigatran in 1 (0.5%) patients. More than one anticoagulants were used in 11.6% cases. Other commonly used drugs in second were corticosteroids (86%), remdesivir (37.7%), proton pump inhibitors (84.3%), antihistamines (78.4%), Vitamin C (71.2%), Vitamin D (70.7%), zinc (65.1%), vitamin B complex (13%), anti-cough drugs (39.5%), paracetamol (52.6%), codeine (7.4%) and codeine-paracetamol combination (7.4%) (Table 4).

The approximate average drug cost was NPR. 3246 in mild, 27644.5 in moderate and 76420 in severe cases (Table 5).

Table 5. Average drug cost during hospital stay

Disease severity	Cost (NPR)
Mild	3,246
Moderate	27,645
Severe	76,420

DISCUSSION

In our study, there were more males (53%) than females (47%). This finding is similar to a recent study done in Bangladesh by Ali et al., in which male patients were 60.1% and females were 39.9%.[8] A review study done by Pradhan and Olsson has also shown the predominance of males in severity and mortality and has mentioned that the reason might be due to a decrease in immunity in males by testosterone, whereas estrogen increases the immunity.[9]

Chief complaints of covid-19 patients in our study were fever (65.6%), cough (55.6%), shortness of breath (40%), myalgia (16.7%) and headache (7.9%). Fever, cough and shortness of breath were common symptoms in another study done by Hu et al., as well.[10] COVID-19 disease severity classification was done according to WHO guidelines.[11] In our study severe cases were more (37%), followed by moderate (33%) and mild (23%), these findings are in contrast to the findings of the study done in the same institute in the first wave of covid-19, where majority cases were mild (74.3%), followed by moderate (20.6%) and severe (5.1%).[12]

Antibiotics are commonly prescribed in COVID-19 cases. A Point Prevalence Survey (PPS) done by Seaton et al., in Scotland among hospitalized adults with COVID-19, prevalence of antibiotic prescribing in the two weeks prior to admission was 29.2% and 62.4% on the day of admission.[13] In a meta-analysis done by Langford et al., antibiotic prescribing in Europe was 63.1%, in North America 64.8%, in China 76.2%, in Middle East 86.0% and in East/Southeast Asia (excluding China) 87.5%. In our study, antibiotics were the most common group of drugs prescribed and were prescribed in 88.4 % of cases.[14] The five most commonly used antibiotics in COVID-19 cases were Ceftriaxone (88.4), Azithromycin (44.7), Piperacillin/Tazobactam (17.7%), Moximycin (11.6%) and Meropenem (7.4%), all of which are watch group of drugs from WHO AWaRe Classification of antibiotics. Watch group of antibiotics include most of the highest-priority critically important antimicrobials for human medicine and veterinary use. These Watch groups of antibiotics are recommended only for specific, limited indications and have high potential of resistance.[15]

Corticosteroids were used in 185 (86%) of cases in our study. Nepal Medical Council clinical guidelines has recommended starting corticosteroids like dexamethasone, hydrocortisone, prednisolone and methylprednisolone early when SpO_2 is less than 93% on room air in outpatient settings.[16] A meta-analysis of randomized control trial done by Pasin et al. in 2019, has shown that overall mortality of patients treated with corticosteroids was slightly but significantly lower than mortality of patients in the control group.[17] As studies have shown that thromboembolic disorders are among the common extra-pulmonary manifestations of COVID-19, anticoagulants are the commonly prescribed drugs in COVID-19.[18] In a retrospective cross-sectional study done by Bastola et al., a total of 62% patients received therapeutic anticoagulation, whereas the use of anticoagulants was more in our study, which was 76.7%.[19] Vitamin C was used in the majority of cases (71.2%) in our study. A systemic review and meta-analysis done by Rawat et al., has failed to show any benefits of Vitamin C in terms of mortality, ICU stay, hospital length of stay, need for invasive mechanical ventilation and severity of illness.[20]

The vaccinated population in the second wave was 10.7% indicating that the risk of acquiring infection after vaccination is reduced. A case-control study done in a large teaching hospital in Southern India has also shown a decreased risk of COVID-19 in vaccinated patients, and if infection occurred a lesser number of moderately severe cases needed hospital care.[21]

The vaccines administered were covishield, verocell and J&J. Covishield vaccine is a recombinant,

replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein, verocell vaccine an inactivated SARS-CoV-2 vector and J&J vaccine is a recombinant, a human adenoviral vector encoding the SARS-CoV-2 Spike (S) glycoprotein.[22,23] In Nepal, vaccination for COVID-19 started in 3rd January 2021.[24]

Mortality was found higher (23.2%) in the first wave compared to that in the second wave (12.3%) in a study done in USA, which is in contrast to finding in our study where mortality is higher in second wave.[25] Such finding can be attributed to a lack of preparedness specifically human resources, inadequate logistics management and laboratory facilities in Nepal compared to that in developed countries.[26] Adding to that, higher transmissibility demonstrated for the δ variant, indicated by a higher reproduction number and shorter latent and incubation periods and higher viral loads in infected cases compared with the wild-type SARS-CoV-2 might have a significant role in increasing the mortality in the second wave.[27]

COVID-19 had a huge economic impact as well. Drug cost is of major concern in low and middle income countries (LMICs) like Nepal.[28] The average drug cost was NPR 3,246 (~$ 26) in mild, NPR 27,645 (~ $ 224) in moderate and NPR 76,420 (~ $615) in severe cases. These cost only represent cost of drugs used for the treatment of COVID-19 during hospital stay. The real scenario is much different and overwhelming as these cost did not include the cost of drug used for the treatment of comorbidities, cost for laboratory and other investigations, cost for hospital admission and ward charges, where majority of patients were managed in ICU/HDU and many required ventilator support.

CONCLUSION

Common presenting symptoms were fever, cough and shortness of breath. Majority of patients had severe SARS-CoV2 infection. Patients required ICU/HDU treatment in most of the cases. Use of antibiotics, corticosteroids and anticoagulants were significantly higher. Drug cost was high, particularly in severe case. Mortality was high in the second wave.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Ministry of Health and Population, Nepal. Responding to COVID-19: Health sector preparedness, response and lessons learnt. Kathmandu, 2021.
2. Dahal S, Luo R, Subedi RK et al. Transmission Dynamics and Short-Term Forecasts of COVID-19: Nepal 2020/2021. Epidemiologia. 2021 Dec 16;2(4):639–59.
3. Aleem A, Akbar Samad AB, Slenker AK. Emerging Variants of SARS-CoV-2 And Novel Therapeutics Against Coronavirus (COVID-19). In: StatPearls. Treasure Island (FL); 2022 Feb.
4. World Health Organization. Clinical management of COVID-19 Interim guidance, 2020.
5. World Health Organization. Infection prevention and control guidance for long-term care facilities in the context of COVID-19: interim guidance, 21 March 2020.
6. Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease, (COVID-19), 2021.
7. Ministry of Health and Population, Nepal. Interim pocket book of clinical management of COVID-19 in Healthcare setting, 2020.
8. Ali MR, Hasan MA, Rahman MS et al. Clinical manifestations and socio-demographic status of COVID-19 patients during the second-wave of pandemic: a Bangladeshi experience. J. Infect. Public Health. 2021 Oct 1;14(10):1367-74.
9. Pradhan A, Olsson PE. Sex differences in severity and mortality from COVID-19: are males more vulnerable? Biol. Sex Differ. 2020 Dec;11(1):1-1.
10. Hu B, Guo H, Zhou P et al. Characteristics of SARS-CoV-2 and COVID-19. Nat. Rev. Microbiol.. 2021 Mar;19(3):141-54.
11. Son KB, Lee TJ, Hwang SS. Disease severity classification and COVID-19 outcomes, Republic of Korea. Bull World Health Organ. 2021 Jan 1;99(1):62-66.
12. Manandhar T, Devkota P, Kafle S et al. COVID-19 patients and their management in a tertiary care center in Nepal. JKISTMC. 2021 Oct. 12;3(2):1-6.
13. Seaton RA, Gibbons CL, Cooper L et al. Survey of antibiotic and antifungal prescribing in patients with suspected and confirmed COVID-19 in Scottish hospitals. J. Infect. 2020 Dec 1;81(6):952-60.
14. Langford BJ, So M, Raybardhan S et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clin Microbiol Infect. 2021 Apr 1;27(4):520-31.
15. Adekoya I, Maraj D, Steiner L et al. Comparison of antibiotics included in national essential medicines lists of 138 countries using the WHO Access, Watch, Reserve (AWaRe) classification: a cross-sectional study. Lancet Infect Dis. 2021 Oct 1;21(10):1429-40.
16. Dhakal N, Siwakoti S, Shakya U et al. Pharmacological Effort and Medication Approaches for the Management of COVID-19 Pandemic in Nepal. Int J Med Biomed Sci. 2021 Dec 29;5(2):5-12.
17. Pasin L, Navalesi P, Zangrillo A et al. Corticosteroids for patients with coronavirus disease 2019 (COVID-19) with different disease severity: a meta-analysis of randomized clinical trials. J. Cardiothorac. Vasc. Anesth.. 2021 Feb 1;35(2):578-84.
18. Chandra A, Chakraborty U, Ghosh S et al. Anticoagulation in COVID-19: current concepts and controversies. Postgrad. Med. J.. 2022 May;98(1159):395-402.
19. Bastola A, Shrestha S, Nepal R et al. Clinical mortality review of COVID-19 patients at Sukraraj tropical and infectious disease hospital, Nepal; A retrospective study. Trop. Med. Infect. Dis.. 2021 Sep;6(3):137.
20. Rawat D, Roy A, Maitra S et al. Vitamin C and COVID-19 treatment: A systematic review and meta-analysis of randomized controlled trials. Diabetes Metab. Syndr.: Clin. Res. Rev.. 2021 Nov 1;15(6):102324.
21. Pramod S, Govindan D, Ramasubramani P et al. Effectiveness of

Covishield vaccine in preventing Covid-19–A test-negative case-control study. Vaccine. 2022 Feb 9;40(24):3294–7.

22. Zahid MN, Moosa MS, Perna S et al. A review on COVID-19 vaccines: stages of clinical trials, mode of actions and efficacy. Arab J. Basic Appl. Sci. 2021 Jan 1;28(1):225-33.
23. Ndwandwe D, Wiysonge CS. COVID-19 vaccines. Curr. Opin. Immunol.. 2021 Aug 1;71:111-6.
24. Sah R, Khatiwada AP, Shrestha S, Bhuvan KC et al. COVID-19 vaccination campaign in Nepal, emerging UK variant and futuristic vaccination strategies to combat the ongoing pandemic. Travel Medicine and Infectious Disease. 2021 May 1;41:102037.
25. Oladunjoye O, Gallagher M, Wasser T et al. Mortality due to COVID-19 infection: A comparison of first and second waves. J. Community Hosp. Intern. Med. Perspect.. 2021 Nov 2;11(6):747-52.
26. Shrestha N, Mishra SR, Ghimire S et al. Health system preparedness for COVID-19 and its impacts on frontline health-care workers in Nepal: A qualitative study among frontline health-care workers and policy-makers. Disaster Med. Public Health Prep.. 2021 Jun 18:1-9.
27. Kang M, Xin H, Yuan J et al. Transmission dynamics and epidemiological characteristics of SARS-CoV-2 Delta variant infections in Guangdong, China, May to June 2021. Euro Surveill.. 2022 Mar 10;27(10):2100815.
28. Murshed SM. In Covid-19 and international development Springer Verlag; 2022 Chapter 5, Consequences of the Covid-19 pandemic for economic inequality. p. 59-70.