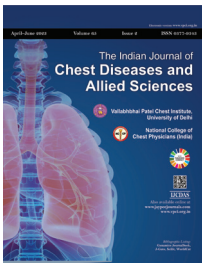
RESEARCH ARTICLE

Comparative Analysis of First, Second, and Third Waves of COVID-19 Infection in Himachal Pradesh – North India: A Retrospective Study



This article is available on www.vpci.org.in

Manisha Bhardwaj[1], Pratibha Himral[2], Rajesh Bhawani[3]

Received on: 11 August 2023; *Accepted on:* 05 September 2023; *Published on:* 31 October 2023

Abstract

With the evolving coronavirus disease-2019 (COVID-19) pandemic, India witnessed multiple peaks with dissimilarities at various levels. We conducted a cross-sectional study on COVID-19 patients admitted at a tertiary care hospital in Himachal Pradesh, India, during the peak of the first wave (from 1 November 2020 to 20 November 2020), the second wave (from 20 April 2021 to 10 May 2021), and the third wave (from 15 January 2022 to 15 February 2022) to evaluate differences in the clinico-demographic profile and treatment outcomes. A total of 300 confirmed cases of COVID-19 were included in the analysis, 100 from each wave. The mean age (in years) of study participants during the first, second, and third waves was [mean ± standard deviation (SD)] 56.94 ± 14.80, 54.92 ± 14.98, and 61.29 ± 18.69, respectively; $p = 0.16$. Males outnumbered females in all three waves. The hospital stay was maximum during the second wave (mean ± SD; 12.22 ± 8.81 days) when compared to the first (5.21 ± 3.43 days) and third waves (3.71 ± 2.74 days); $p = 0.008$. Fever and cough were primarily reported in the first wave (with $p < 0.001$ and $p = 0.001$, respectively). Gastrointestinal symptoms were more common in the second and third waves ($p < 0.001$). Diabetes, hypertension, and cardiovascular diseases were common underlying diseases among admitted patients in three waves. Total leukocyte count, neutrophil-to-lymphocyte ratio, and erythrocyte sedimentation rate were higher in the second wave ($p = 0.004$; $p < 0.001$; and $p < 0.001$, respectively). The incidence of liver dysfunction was more common in the second wave. The second wave was deadly both in terms of severity and mortality as compared to the first and third waves. The younger age-group (18–40 years) was largely affected during the second wave while the elderly age-group was primarily affected during the third wave.

Keywords: Coronavirus disease-2019, Differences, Mortality, Waves.

The Indian Journal of Chest Diseases and Allied Sciences (2023): 10.5005/jp-journals-11007-0070

Abbreviations used in this Article

ALP = Alkaline phosphatase; ALT = Alanine transaminase levels; AST = Aspartate transaminase levels; CI = Confidence interval; CAD = Coronary artery disease; CKD = Chronic kidney disease; COVID-19 = Coronavirus disease-2019; CRP = C-reactive protein; DCH = Dedicated COVID-19 hospital; ESR = Erythrocyte sedimentation rate; IL-6 = Interleukin-6; LDH = Lactate dehydrogenase; LFTs = Liver function tests; LMWH = Low molecular weight heparin; NLR = Neutrophil-to-lymphocyte ratio; RBS = Random blood glucose; RAT = Rapid amplification test; Rt = Real-time reproduction number; RTPCR = Reverse transcriptase polymerase chain reaction; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus; SD = Standard deviation; SOB = Shortness of breath; SSPS = Statistical Package for the Social Sciences; TLC = Total leukocyte count; WHO = World Health Organization.

[1]Department of Pulmonary Medicine, Shri Lal Bahadur Shastri Medical College and Hospital, Ner Chowk, Mandi, Himachal Pradesh, India

[2,3]Department of General Medicine, Shri Lal Bahadur Shastri Medical College and Hospital, Ner Chowk, Mandi, Himachal Pradesh, India

Corresponding Author: Manisha Bhardwaj, Department of Pulmonary Medicine, Shri Lal Bahadur Shastri Medical College and Hospital, Ner Chowk, Mandi, Himachal Pradesh, India, Phone: +91 9988636983, e-mail: mbgmch@gmail.com

How to cite this article: Bhardwaj M, Himral P, Bhawani R. Comparative Analysis of First, Second, and Third Waves of COVID-19 Infection in Himachal Pradesh – North India: A Retrospective Study. Indian J Chest Dis Allied Sci 2023;65(2):85–91.

Source of support: Nil

Conflict of interest: None

Introduction

Coronavirus disease-2019 (COVID-19) is a highly contagious illness, caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) virus. The history of COVID-19 dates back to early December 2019, when a cluster of pneumonia cases due to an unknown cause were discovered in an animal food market in Wuhan, China.[1] The cases multiplied at an unprecedented scale and spread across continents. Soon, it was declared a public health emergency of International Concern and then a pandemic by the World Health Organization (WHO) on January 30, 2020 and March 11, 2020, respectively. In December 2020, India became the second country to record 10 million confirmed cases after the United States.[2]

Following a period of lull, India witnessed a second peak in early March–April 2021, with over 31 million positive cases reported by the end of July 2021, before declining.[3] On July 23, 2021, WHO issued an alert citing 16 new variants, including B.1.427, B.1.429, B.1.466.2, C.36.3, etc., and predicted quick transmissibility and severity of illness with newer strains.[2] A review of the literature revealed notable disparities in age pattern, symptomatology, severity, and mortality rates over three waves. According to Iftimie et al. and Soriano et al., patients in the second wave were younger

and had lower death rates than those in the first wave.[4,5] Another study from Spain found that hospitalized patients were more severely affected in the second wave than in the first.[6] Contou et al. conducted a similar study in France and found no significant differences between the two waves.[7] According to Reddy et al., the positivity rate was significantly higher during the second wave (14.3%) compared to the first wave (4.4%), most likely due to increasing testing rates.[8] The third wave, which hit India in January 2022 was characterized by milder disease (death rate of 5.4%)[9] Better understanding of the pathophysiology of disease, implementation of COVID-appropriate behavior, upscaling of infrastructure, and mass vaccination may have influenced disease epidemiology in the third wave.

Much of the literature reported is from Western countries. There is a scarcity of data from India comparing the three waves of COVID-19. So, we planned this study to observe the pattern of sociodemographic characteristics, clinical symptoms, comorbidities, and treatment outcomes in three waves and do a comparative analysis.

Methods

This was a cross-sectional study conducted in the departments of Pulmonary Medicine and Medicine at Shri Lal Bahadur Shastri Medical College and Hospital (SLBS GMCH) in Ner Chowk, Mandi, Himachal Pradesh, India. It is a tertiary care hospital located in the northwest Himalayas, catering to a population of about 26 lakhs. It was declared a dedicated COVID-19 hospital (DCH) by the state government on April 20, 2020. A total of 300 patients were enrolled, 100 in each wave. The existing data of COVID-19 positive patients admitted during the peak months of the first (from 1 November 2020 to 20 November 2020) and second waves (from 20 April 2021 to 20 May 2021) and the first 100 patients admitted during the third wave (from 15 January 2022 to 15 February 2022) were included in the analysis. The Institutional Ethics Committee approved the study (letter No. 67).

Three groups were compared in terms of clinical characteristics, laboratory parameters, days of hospital stay, and mortality. The study cohort consisted of COVID-19-positive patients more than 18 years of age, confirmed on a rapid amplification test (RAT) or reverse transcriptase polymerase chain reaction (RT-PCR) on an oropharyngeal swab or nasopharyngeal swab. These were further classified as mild, moderate, and severe categories, based on the National COVID-19 Management Protocol, version 3, 2020, issued by the Ministry of Health and Family Welfare, India, as applicable.[10] In the case of multiple admissions of the same patient, only the index admission was considered. Asymptomatic cases, pediatric cases (age less than 18 years), pregnant females, and patients with insufficient records, were excluded. Demographic data, including age, gender, place of residence, and vaccination status, was collected. Detailed information about presenting complaints and the history of medical comorbidities such as cardiovascular disease, diabetes, hypertension, chronic renal disease, thyroid disease, and malignancy was recorded. Baseline blood tests such as complete blood count, renal and liver function tests, and radiological testing such as, a chest radiograph and/or a chest tomography were performed. Inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), ferritin, and D-dimer were tested based on the availability of facilities in the institution.

Statistical Analysis

All the data were recorded on a Microsoft Excel sheet and analyzed using Statistical Package for the Social Sciences (SSPS) software, version 26. Numerical data were assessed as means and standard deviation. Categorical data were assessed as frequency and percentages. Means were compared using an unpaired t-test (normally distributed data) or Mann–Whitney tests (skewed data). The normal distribution of the data was calculated using the Kolmogorov–Smirnov test. The comparison of groups was done using the Chi-square test or Kruskal–Wallis test as applicable. In all comparisons, a *p*-value of below 0.05 was considered significant. The relationship between laboratory parameters and outcomes was assessed by logistic regression analysis. Comparisons between groups were done using Kaplan–Meier analysis.

Results

The demographic profile of patients is summarized in Table 1. The mean ages of study participants in the first, second, and third waves were 56.94 ± 14.80 years (mean ± SD), 54.92 ± 14.98 years, and 61.29 ± 18.69 years, respectively. During the first and second waves, the majority of patients were less than 60 years of age (55 and 68%, respectively), unlike the third wave, where 62% of patients were above the age of 60 years. The difference was not statistically significant ($p = 0.07$). In all three waves, males outnumbered females, but a statistically significant difference was not found ($p = 0.19$). The hospital stay was maximum during the second wave (mean ± SD; 12.22 ± 8.81 days) when compared to the first (5.21 ± 3.43 days) and the third wave (3.71 ± 2.74 days); $p = 0.008$.

The common clinical manifestations and underlying disorders among patients in each wave are summarized in Table 1. The top three symptoms reported by patients during the first wave were shortness of breath (71%), fever (63%), and cough (55%). Fever and cough were more incidental in the first and second waves ($p < 0.001$ and $p = 0.001$, respectively) of the disease compared to the third one. Nausea and vomiting were predominant in the third wave, $p < 0.001$. Dysgeusia was reported in the first wave only. Diabetes, hypertension, and coronary artery disease (CAD) were the top three comorbidities observed in the study participants across three waves. Diabetes was the most common underlying disorder in the admitted patients during the first wave ($p < 0.001$), and CAD was predominantly seen in the third wave ($p = 0.006$). The laboratory profile of patients is summarized in Table 2. The laboratory parameters such as total leukocyte count and neutrophil-to-lymphocyte ratio (NLR) were higher in the second wave, with $p = 0.004$ and $p < 0.001$, respectively. Incidence of liver dysfunction was more common in the second wave; serum aspartate transaminase levels (AST; $p = 0.001$), alanine transaminase levels (ALT; $p < 0.001$), and hypoalbuminemia ($p < 0.001$). There was no statistically significant difference in renal function abnormalities across the three waves (urea, $p = 0.454$; creatinine, $p = 0.124$). Furthermore, ESR was significantly raised in study participants during the second wave as compared to the first and third waves ($p < 0.001$). The severity of illness and subsequent need for supplementary oxygen (57% on a non-rebreathing mask) and non-invasive ventilation (continuous positive airway pressure 9%; high-flow nasal cannula 8%) were higher during the second wave. Treatment options varied across three waves and were consistent with National Guidelines during that time.[10,11] Patients during the first wave received remdesivir (75%), dexamethasone (81%), anticoagulation (84%), ivermectin (55%), doxycycline (52%), and

Table 1: Baseline characteristics, treatment, and outcomes of study population in first, second, and third waves of COVID-19

Characteristics	*First wave N = 100*	*Second wave N = 100*	*Third wave N = 100*	*p-value*
Age (mean ± SD)	56.94 ± 14.80	54.92 ± 14.98	61.29 ± 18.69	0.16
Age-group (years)				
<40	15	24	16	0.07
41–59	40	34	22	
≥60	45	42	62	
Gender				
Male	68	57	58	0.19
Female	32	43	42	
Severity				
Mild	25	5	28	0.011*
Moderate	28	17	20	
Severe	47	78	52	
Comorbidities				
Diabetes	37	15	24	0.002
Hypertension	27	31	36	0.389
CKD	8	2	8	0.119
CAD	3	5	14	0.006
Hypothyroid	5	6	7	0.838
Symptoms				
Fever	63	55	27	0.00
Cough	55	47	30	0.001
SOB	71	83	63	0.150
Diarrhea	5	1	3	0.253
Anosmia	4	1	0	0.710
Dysgeusia	3	0	0	0.048
Sore throat	6	2	2	0.191
Myalgia	8	7	2	0.145
Nausea/vomiting	5	2	20	0.00
Pharmacotherapy				
Remdesivir	75	12	9	0.027*
Dexamethasone	81	95	46	
Anticoagulation (LMWH)	84	95	48	
Favipiravir	11	0	0	
Ivermectin	55	0	0	
Doxycycline	52	0	1	
Antibiotic	61	95	50	
Hospital stay (days)				
≤5	66	21	82	0.008*
6–7	17	13	8	
≥8	14	65	10	
Mean ± SD	5.21 ± 3.43	12.22 ± 8.81	3.71 ± 2.74	
Respiratory support				
Oxygenation	50	74	60	0.061
Non-invasive ventilation	17	16	2	
Invasive ventilation	6	4	0	
Outcomes				
Discharge	73	61	82	0.002*
Death	27	38	15	
Referral	0	0	2	

*$p < 0.05$. CAD, cardiovascular disease; CKD, chronic kidney disease; COVID-19, coronavirus disease-2019; LMWH, low-molecular-weight heparin; SD, standard deviation; SOB, shortness of breath

Table 2: Laboratory profile of patients in first, second, and third waves of COVID-19

	First wave N = 100		*Second wave N = 100*		*Third wave N = 100*		
Symptoms	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*p-value*
Hemoglobin (gm/dL)	13.31	2.195	13.72	10.244	12.422	2.68	0.329
TLC (cells/µL)	8798	4016.88	11502.017	5353.5136	9910.256	7442.320	0.004
Lymphocyte	21.852	10.9753	15.500	9.4125	17.765	12.407	0.000
Neutrophil	73.95	11.918	80.44	10.485	77.08	14.841	0.001
NLR	4.69	3.24	7.42	4.44	6.71	4.66	0.000
Platelets	185064	97176.698	194404.04	83376.197	195348.98	83390.381	0.662
ESR (mm/hour)	45.69	38.19	51.6	30.439	29.93	29.272	0.000
RBS (mg/dL)	198.36	160.174	184.4	97.977	167.42	108.082	0.301
Bilirubin	0.634	0.2499	0.581	0.5132	0.704	1.0679	0.460
AST (U/L)	73.34	50.455	89.18	96.847	50.14	59.541	0.001
ALT (U/L)	76.54	84.222	86.85	84.697	38.02	40.851	0.000
ALP (U/L)	110.28	79.603	110.66	56.615	103.20	58.979	0.670
Albumin (gm/dL)	3.705	0.5478	3.365	0.4819	3.825	0.6038	0.000
Urea (mg/dL)	50.89	45.487	46.65	37.091	54.66	50.731	0.454
Creatinine (mg/dL)	1.756	3.193	1.097	1.202	1.6184	2.3249	0.124

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease-2019; ESR, erythrocyte sedimentation rate; SD, standard deviation; NLR, neutrophil lymphocyte ratio; RBS, random blood glucose; TLC, total leukocyte count

Table 3: Vaccination status and outcomes in third wave

	Number		*First dose*		*Second dose*		*Third dose*		
Outcomes	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*p-value*
Discharge	11	91.67	4	66.67	66	80.49	1	100	0.082
Death	1	8.33	2	33.33	12	14.63	0	0	
Referred to higher center	0	0	0	0	2	2.44	0	0	
Total	12	100	6	100	82	100	1	100	

antibiotics (61%). During the second wave, dexamethasone (95%), anticoagulation (95%), and antibiotics (95%) remained the top three treatment options. A similar trend was seen during the third wave (dexamethasone, 46%; anticoagulation, 48%; antibiotics, 50%). Drugs like favipiravir and tocilizumab were given to a few patients as per national recommendations. Management decisions during waves largely depended on affordability and availability. Out of 100 patients, six required invasive ventilation during the first wave and four during the second wave. No patient was put on a ventilator during the third wave, while 33% required no supplemental oxygen. The discharge rate was the highest during the third wave (82%), followed by the first (73%), and second (61%). Out of 100 patients, 38 died during hospital stays during the second wave, as compared to the first (27%) and the third wave (15%).

By the time the third wave occurred, 88% of study participants were vaccinated against COVID-19 (81% with two doses, 6% with a single dose, and 1 with a booster dose). A total of 10 patients remained unvaccinated. Vaccination status during the second wave was either largely unknown (66%) or unvaccinated (26%). The majority of patients (78%) during the second wave were categorized as having severe illnesses while only 5% had mild illnesses. During the first and third waves, almost 50% of patients fell into the category of mild-moderate disease. No statistically significant effect of vaccination was found on the outcomes of the third wave (Table 3). Stepwise regression analyses and the odds ratio [95% confidence interval (CI)] for outcomes in the first COVID-19 wave and the second COVID-19 wave compared with the third COVID-19 wave are depicted in Table 4.

Discussion

Disparities were found when three waves were compared in terms of age, gender, symptomatology, and outcomes. Also, SARS-CoV-2 is a highly transmissible virus that spreads via droplets. The course of the COVID-19 pandemic was variable since its onset in December 2019. In India, the cases rose exponentially after the first case was reported on January 30, 2020. To curtail the spread of the disease, the government took measures such as social distancing and nationwide lockdowns. This resulted in a decline in the real-time reproduction number (Rt) from 3.2 in the first week of March 2020 to 1.09 in the third week of April 2020. The emergence of new SARS-CoV-2 variants (B.1.617.1 and B.1.617.2) during April–May 2021 was implicated during the second wave when Rt reached 1.37.[12]

The first COVID-19 case was reported in Himachal Pradesh, India on March 20, 2020. The lockdown was imposed from March 25, 2020 through May 31, 2020. Restrictions were gradually relaxed beginning in June of that year. According to estimates, the first wave peaked in September 2020 and continued until December 2020. This could be attributable to the fact that most cultural and religious gatherings take place during this period. The second wave reached its peak in May 2021. The overall number of COVID-19 cases were 182,957 as of May 25, 2021, with 23,053 active cases and 2,873

Table 4: Stepwise regression analyses and odds ratio (95% CIs) for outcomes in first and second COVID-19 waves compared with third COVID-19 wave

Third wave	*OR (95% CI)*	*Adjusted*						
		Age + Gender	*+Comorbidities*	*+Clinical factors, investigations*	*+Inflammatory markers*	*+Hospital stay*	*+Oxygenation*	*+Treatment*
Mortality								
First wave	2.03 (1.01–4.51)*	2.10 (1.01–4.60)*	2.15 (1.01–4.64)*	2.16 (1.02–4.72)*	2.18 (1.04–4.78)*	2.21 (1.06–4.80)*	1.92 (0.98–3.45)	1.78 (0.91–3.06)
Second wave	2.32 (1.26–4.93)*	2.76 (1.42–6.38)*	3.05 (1.69–6.88)*	3.09 (1.65–7.33)*	3.42 (1.88–8.31)*	3.72 (1.99–9.06)*	3.03 (1.24–6.81)*	2.94 (1.19–6.12)*
Ventilator								
First wave	1.59 (0.83–3.06)	1.66 (0.90–3.15)	1.70 (1.04–3.28)	1.71 (1.06–3.23)	1.48 (0.97–2.39)	1.55 (1.05–2.54)	1.29 (0.92–1.93)	1.18 (0.88–1.71)
Second wave	2.97 (1.30–8.92)*	2.73 (1.22–8.07)*	2.84 (1.27–8.43)*	2.87 (1.25–8.49)*	2.32 (1.13–4.30)*	2.40 (1.17–4.79)*	2.07 (1.06–3.34)*	1.91 (0.98–2.47)

*$p < 0.05$. CI, confidence interval; COVID-19, coronavirus disease-2019

fatalities. The third wave began on January 5, 2022, with the highest number of active cases in January and February, followed by a drop in March 2022. By the 27th of January 2022, the total number of cases was 263,914, including 11,141 active cases and 3,961 deaths.[13,14] The topography, sociocultural background, population size, extent of overcrowding, and access to healthcare are some of the determining factors that affected the disease's spread, which peaked differently in urban and rural areas.

The mean age of study participants during the first and second waves was between 54 and 57 years. In all three waves, there were more males than females, with the first wave having the highest gender disparity (2.13:1). Similar gender biases were observed in all three waves according to numerous studies from India and elsewhere.[5,12,15,16] The first wave's outbreak of cases was linked to cluster events or large gatherings, which could help to explain this. In addition, compared to female members, male members often leave their homes for work or socializing. Other contributing factors may include, a higher prevalence of infections in males and differences in immune responses between males and females.[17] In this study, the younger age-group (18–40 years) was mostly affected during the second wave, whereas the elderly age-group (age ≥ 60 years) was mostly afflicted during the third wave as shown in Table 1. Similarly, Iftimie et al. revealed that patients affected during the second wave were younger than those affected during the first wave (67 ± 18 vs 58 ± 26 years, $p < 0.001$).[4] Due to mobility issues, the working class, which typically falls into the 18–60 age-group, is more likely to be exposed to the SARS-CoV-2 virus. By the time the third wave came, most of the individuals had already been infected during the first and second waves, rendering them less susceptible to illness. Furthermore, COVID-19-appropriate behavior and a nationwide vaccination drive could be responsible for such findings.[12,16]

Diabetes, hypertension, and cardiovascular diseases were the three most prevalent underlying diseases among the admitted patients across three waves. The frequency of chronic disorders did not significantly differ between the three waves. A study from Spain corroborated the findings.[4] However, a study from India showed that comorbid conditions were significantly higher in patients during the third wave than first or second waves ($p < 0.001$).[16]

In this study, fever and cough were primarily reported in the first wave ($p = 0.001$ and $p = 0.001$, respectively) while gastrointestinal symptoms were more common in the second and third waves. Several studies from India and abroad reported similar findings.[4,5,16] Therefore, the clinician should be aware of the wide clinical spectrum of COVID-19 to avoid missed diagnoses.

In this study, inflammatory markers such as CRP and ESR were significantly raised in hospitalized patients during the second wave, indicating severe illness. Other laboratory parameters such as NLR, deranged LFTs, and hypoalbuminemia were also significantly higher or deranged in the second wave. Due to infrastructural and financial constraints, several biomarkers such as ferritin, D-dimer, interleukin-6 (IL-6), etc. could not be evaluated at our institution during the first and second waves, so comparative analysis could not be done.

As our understanding of COVID-19 pathogenesis evolved, so did treatment options throughout waves. Antivirals were the primary therapeutic options during the first wave, whereas anticoagulants and steroids were preferred subsequently, depending on the severity of the illness (Table 1). Scientific evidence revealed that several drugs such as remdesivir (SOLIDARITY trial, September

15, 2020), hydroxychloroquine, and ivermectin, etc. had little or no impact on survival and were thus gradually withdrawn.[18] Steroids (dexamethasone) were reserved for severe or critically ill patients requiring invasive mechanical ventilation or supplemental oxygen therapy (RECOVERY trial, February 25, 2021).[19] Prophylaxis with low-molecular-weight heparin (LMWH) was recommended because critically ill patients were found to be more susceptible to thromboembolic complications.[18]

In this study, patients with severe disease were more common in the second wave (78%) as compared to the first or third waves (50% each). The mortality rate followed the same pattern as shown in Table 1. Other studies from Spain, Thailand, and India found comparable results in terms of illness severity and mortality.[4,16,20] The findings could be because dominant mutant strains were more transmissible and virulent during the second wave, escaping immune responses. Complacency in adopting COVID-19-appropriate behavior could also be another contributing factor. Some studies, however, showed inconsistent results. Contou et al. and Ghosh et al. found comparable death rates in the first and second waves.[7,21] Magray et al. reported that whereas the second wave had the most cases (I vs II vs III; 26.8, 47, and 26.2%, respectively), the first wave had the most deaths (I vs II vs III; 52.5, 43.5, and 3.9, respectively).[22] Another study found that the second wave had fewer deaths than the first wave (I vs II 13.2% vs 24%, respectively).[4] In comparison to previous waves, the third wave in the current study was characterized by milder illness and fewer deaths (refer to Table 1). Earlier studies by Mitra et al. and Singh et al. found similar results, with death rates of 5.4 and 8%, respectively.[9,16] Our center was DCH, hence we had a higher fatality rate of 15% in this study. Along with better diagnostic and therapeutic options, such findings may be explained by the omicron variant's low pathogenicity and immunity provided by previous COVID-19 infection or vaccination.[2,9,16,18] Variable results could be attributed to differences in study settings and population characteristics.

Limitations

The study had several limitations. It was a retrospective study from a single center. The sample size was relatively small. Several laboratory markers such as IL-6, ferritin, D-dimer, etc. were not measured at the institution, so information about the sensitivity and specificity of biomarkers and their correlation with severity and outcomes could not be deduced. Microbiological analysis of respiratory samples was not done for similar reasons. Data on causes of death such as thromboembolism was not collected.

Conclusion

The second wave was deadly both in terms of severity and mortality as compared to the first and third waves. Males were affected more than females in all three waves. The younger age-group (18–40 years) was largely affected during the second wave, while the elderly age-group was primarily affected during the third wave. Respiratory complaints were predominant during the first wave, while gastrointestinal complaints were more common during the second and third waves. The study gives valuable insight into the dynamics of the COVID-19 pandemic in India, particularly in the sub-Himalayan region. More studies with a larger sample size are required to reach definitive conclusions.

Orcid

Manisha Bhardwaj https://orcid.org/0000-0002-7357-4828

References

1. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–1720. PMID: 32109013.
2. World Health Organization. Timeline of WHO's response to COVID-19. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline. Accessed on: August 1, 2021.
3. www.covid19india.org. Coronavirus outbreak in India. Available at: https://www.covid19india.org/. Accessed on: August 1, 2021.
4. Iftimie S, Ló Pez–Azcona AF, Vallverdú I, et al. First and second waves of coronavirus disease-19: A comparative study in hospitalized patients in Reus, Spain. PLoS One 2021;1–13. DOI: 10.1371/journal.pone.0248029.
5. Soriano V, Ganado–Pinilla P, Sanchez–Santos M, et al. Main differences between the first and second waves of COVID-19 in Madrid, Spain. Int J Infect Dis 2021;105:374–376. PMID: 33684560.
6. Cossio Y, Aller MB, Abadias MJ, et al. Comparing the first and second waves of COVID-19 in a tertiary university hospital in Barcelona. F1000Res 2021;10:1197. DOI: 10.12688/f1000research.73988.1.
7. Contou D, Fraisse M, Pajot O, et al. Comparison between frst and second wave among critically ill COVID-19 patients admitted to a French ICU: No prognostic improvement during the second wave? Crit Care 2021;25(1):3. DOI: 10.1186/s13054-020-03449-6.
8. Reddy MM, Zaman K, Mishra SK, et al. Differences in age distribution in first and second waves of COVID-19 in eastern Uttar Pradesh, India. Diabetes Metab Syndr Clin Res Rev 2021;15(6):1–2. PMID: 34731821.
9. Mitra S, Muley A, Bavishi A, et al. Characteristics and outcomes of COVID-19 during the third wave of COVID pandemic: A single-center descriptive study. J Assoc Physicians India 2023;71(2):37–40. PMID: 37354469.
10. Clinical Management Protocol for COVID-19 (In Adults) Version 3 Updated 13.06.2020; Government of India, Ministry of Health and Family Welfare. Directorate General of Health Services (EMR Division). 2020.
11. Clinical Management Protocol for COVID-19 (In Adults) Version 6 Updated 24.05.2021 Government of India Ministry of Health and Family Welfare. Directorate General of Health Services (EMR Division). 2021.
12. Sarkar A, Chakrabarti AK, Dutta S. COVID-19 infection in India: A comparative analysis of the second wave with the first wave. Pathogens 2021;10(9):1222. PMID: 34578254.
13. www.covid19india.org. COVID-19 in Himachal Pradesh. Available at: https://www.covid19india.org/state/HP. Accessed on: April 18, 2023.
14. Sharma P, Rattan S, Katoch V, et al. COVID-19 pandemic: Probing the dynamics in the North Himalayan state. Indian J Community Fam Med 2022;8(1):44. DOI: 10.4103/IJCFM.IJCFM_59_21.
15. Seong H, Hyun HJ, Yun JG, et al. Comparison of the second and third waves of the COVID-19 pandemic in South Korea: Importance of early public health intervention. Int J Infect Dis 2021;104:742–745. PMID: 33556610.
16. Singh S, Sharma A, Gupta A, et al. Demographic comparison of the first, second and third waves of COVID-19 in a tertiary care hospital at Jaipur, India. Lung India 2022;39(6):525–531. PMID: 36629231.
17. Jacobsen H, Klein SL. Sex differences in immunity to viral infections. Front Immunol 2021;12:720952. PMID: 36629231.
18. World Health Organization. Living guidance for clinical management of COVID-19: Living guidance. World Health Organization; 2021. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2. Accessed on: October 1, 2021.

19. RECOVERY Collaborative group; Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with COVID-19. N Engl J Med. 2021 Feb 25;384(8):693–704. PMID: 32678530.
20. Kunno J, Supawattanabodee B, Sumanasrethakul C, et al. Comparison of different waves during the COVID-19 pandemic: Retrospective descriptive study in Thailand. Adv Prev Med 2021;2021:1–8. PMID: 34659835.
21. Ghosh T, Biswas MK. A comparative study between the first and second waves of world threatening COVID-19 disease. Eur J Transl Clin Med 2020;7(11):8234–8256. ISSN: 2515-8260.
22. Magray TA, Nazir U, Rather RH, et al. Demographic and mortality trends across three COVID-19 waves in Kashmir Division, India. Asian J Med Sci 2022;13(10):23–28. DOI: 10.3126/AJMS.V13I10.47234.