ORIGINAL ARTICLE

Clinical Characteristics and Outcomes of All Three COVID-19 Waves: A Single-center Experience

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Abstract

Context: With the growing incidence of cases in the pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), there have been a number of spikes in the cases over the last 3 years and India has witnessed three waves of different strains of SARS-CoV2.

Aims: The aim of this study was to evaluate the patient demographics, the population at risk, signs and symptoms presented, the effect of comorbidities, and treatment outcomes.

Settings and design: Retrospective noninterventional observational study.

Materials and methods: From January 2020 to February 2022, a study was carried out at Kalpana Chawla Government Medical College, Karnal, Haryana. The study included all inpatients above the age of 18 years who tested positive for COVID-19 through either a rapid antigen test (RAT) or reverse transcription-polymerase chain reaction (RT-PCR) from nasopharyngeal or oropharyngeal swabs. The sample size of the study was 300.

Results: In all three waves, the incidence of COVID-19 was more common among men. The average age of patients was 39.8, 49, and 50 years in waves one, two, and three, respectively. Among various comorbidities, diabetes was the most prevalent, with 25, 33, and 29% of patients affected in waves one, two, and three, respectively. In the first wave, all patients received antiviral therapy, while in the second and third waves, 70 and 10% of patients were treated with antivirals, respectively. During the third wave, 60% of patients had received two doses of vaccine and 16% had received a single dose.

Conclusion: The study provides insights into the patient characteristics, management, and treatment of COVID-19 patients in three different waves.

Clinical significance: The study gives a bird's eye view of the treatment across the three waves and the evolution of management strategies. Also, the effectiveness of vaccination was seen in the third wave.

Keywords: Coronavirus disease 2019, First wave, Management, Patient characteristics, Second wave, Third wave, Treatment outcomes, Vaccines.

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Introduction

In December 2019, an unknown-origin pneumonia outbreak was reported in Wuhan, Hubei Province, China. Researchers isolated a novel coronavirus, previously named COVID-19, from patients with pneumonia of unknown origin.[1] This virus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), originated in Wuhan, China and has spread to 140 other countries, causing severe respiratory tract infections in humans. The primary mode of transmission is through human-to-human contact *via* droplets, although there is also a possible orofecal route.[2] The virus has disproportionately affected the 11–60 year-old population, with fever, cough, sore throat, fatigue, and shortness of breath being the most common symptoms.

India saw a relatively low number of COVID-19 cases/million people during the first wave, but the situation changed unexpectedly during the second wave, with over 400,000 confirmed cases/day reported.[3] The third wave saw a faster spread of the virus, with the emergence of new variants such as the δ variant, which is believed to be more transmissible and potentially more virulent. The wave also saw a higher number of younger people being affected. Fever, cough, sore throat, fatigue, and shortness of breath were the most common symptoms and reported in 83, 82, and 31% of patients. For patients who developed pneumonia, when evaluated, there was multiple mottling and ground-glass opacity as described on the chest X-ray.[4]

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To confirm cases of suspected SARS-CoV-2 infection, specialized tests are used to detect unique viral sequences using nucleic acid amplification. These tests include methods like reverse-transcription polymerase chain reaction (RT-PCR) and rapid antigen tests (RATs).[5]

The most effective way to reduce the chance of being infected is to take protective measures such as maintaining good personal hygiene, wearing masks, getting enough rest, and avoiding crowded places. Early diagnosis, quarantine, and supportive treatments are essential to cure patients, including oxygen therapy, antiviral agents, and vaccines.[6]

The aim of the study was to analyze the characteristics of cases, outcomes, and treatment efficacy of different strains of SARS-CoV-2, including α, β, γ, δ, and ο, at the Kalpana Chawla Government Medical College in Karnal, Haryana, India, where spikes in COVID-19 cases have occurred over the last 3 years.

Materials and Methods

This retrospective noninterventional observational study was conducted from January 2020 to February 2022 at Kalpana Chawla Government Medical College, Karnal, Haryana. The study was approved by an independent local ethics committee. All the hospitalized patients who were diagnosed with COVID-19 by RAT, RT-PCR (nasopharyngeal, oropharyngeal, and swabs) of the age above 18 years of age were included in the study during the three waves. An informed consent form was taken from patients whose data was being collected for this retrospective analysis.

The exact timelines of COVID-19 waves in India are not well defined and may vary depending on the source. However, a general timeline of the first three waves in India is as follows:

- Wave one: The first wave of COVID-19 in India began in early April 2020, with a rapid rise in cases until a peak was reached in mid-September. The wave was characterized by a relatively low number of cases and a relatively high recovery rate.[7]
- Wave two: The second wave of COVID-19 in India began in mid-February 2021 and peaked in May, with a much higher number of cases and a more rapid spread than the first wave. This wave was characterized by a higher number of hospitalizations, a higher mortality rate, and a significant impact on the healthcare system.[7]
- Wave three: The third wave of COVID-19 in India began in early January 2022 with a much higher number of cases and a more rapid spread than the previous two waves. This wave is characterized by a lower number of hospitalizations.[7]

There was a phase-wise rollout of vaccination in India. On 1st May 2021, 18–44 years old people started getting doses.[7] Hence, during the first and second waves most of the people didn't receive any doses and most received after the second wave.

Based on the eligibility criteria and completeness of the data 100 patients were selected from each of the three waves. The total sample size was 300. The demographic data, signs and symptoms, medical treatment given, laboratory parameters, and vaccination status were collected and recorded in the data collection sheet. All data were tabulated in Microsoft Excel. Continuous variables were presented as mean, standard deviation, and categorical variables were presented as percentages. The Chi-square test was used to compare the outcome. For all the tests p-value of <0.05 was considered statistically significant. GraphPad Prism 9 software was used to analyze the data.

Results

The average age of patients was 39.8, 49 and 50 years in waves one, two, and three, respectively with the incidence more common among men among all three waves. Among the various comorbidities, the majority of patients had diabetes (25, 33, and 29% in waves one, two, and three, respectively) followed by hypertension and chronic kidney disease. The average peripheral oxygen saturation (SpO_2) of patients was 93, 86, and 95 in waves one, two, and three, respectively. The average admission days during waves one, two, and three were 8, 11, and 4 days, respectively. During the first wave, 76% of patients had mild disease compared to 26% in the second wave and 83% in the third wave. Around 74% of patients had moderate disease during wave two compared to 17% in wave three and 24% in wave one (Table 1).

In wave one the most common reported symptom was dry cough (56%), whereas hemoptysis was least common (2%). Around 76% of patients had dyspnea during wave two compared to 51 and 28% in wave three and wave two, respectively. Fever was reported in 58% of cases in wave two compared to 54 and 40% in wave one and wave three, respectively. Anosmia and ageusia were not reported during wave three compared to wave one and wave two (Table 2).

Around 22% of patients reported to the hospital for admission by the 7th day from the onset of symptoms during wave one compared to 25% by the 5th day in wave two and 14% by the 7th day in wave three (Table 3). Around 70% of patients during wave two required oxygen support compared to 30 and 23% in wave three and wave one, respectively. Antiviral therapy was used in the 100% of patients in wave one. Whereas 70 and 10% were treated with antivirals during the second and third waves, respectively. Antibacterial therapy was given to 100, 66, and 45% of patients during wave one, two, and three, respectively. Intravenous (IV) glucocorticoid therapy was given to 70% of patients during wave two compared to 23 and 15% in wave one and wave three, respectively. Nonpharmacological interventions which included proning and incentive spirometric breathing exercises were provided to the patients during all three waves (Table 4).

During all three waves, right lower zone infiltrates were seen in chest radiologic findings with 21, 21, and 28% in waves one, two, and three waves, respectively. Left mid-zone opacities were the least in chest radiologic findings during all three waves (Table 5). Platelet, neutrophil count, fasting blood sugar, glycated hemoglobin (HbA1c), and ferritin values were significantly different in the three waves. Other lab values were not significantly different (Table 6). During the third COVID-19 wave, 60% of the patients had received two doses of vaccine and 16% had received a single dose.

The results of our study show that the mean age of patients increased from 39.8 years in wave one to 49 years in wave two and 50 years in wave three. This increase in age is consistent with previous studies which have shown that older individuals are more susceptible to severe forms of COVID-19. Our results also showed a higher incidence of COVID-19 among men, which is in line with previous studies. A systematic review and meta-analysis show that older age is a risk factor for severe COVID-19 outcomes.[8]

Comorbidities such as diabetes, hypertension, and chronic kidney disease were common among patients in all three waves, with diabetes being the most prevalent. A systematic review shows that comorbidities such as diabetes and hypertension increase the risk of severe COVID-19 outcomes. The average SpO_2 levels in our study were 93 in wave one, 86 in wave two, and 95 in wave three. The decrease in SpO_2 levels in wave two may suggest a more severe disease, while the improvement in wave three could indicate better management and treatment of COVID-19.[9] A systematic review shows that oxygen support is commonly used in severe cases of COVID-19.[10]

The average admission days during wave one, second, and third waves were 8, 11, and 4 days, respectively. This decrease in admission days during wave three could be due to improved management and treatment of COVID-19, as well as a possible decrease in the severity of the disease. A systematic review showed that the length of hospital stay was positively associated with disease severity and that patients with severe or critical COVID-19

Table 1: Baseline parameters of COVID-19 patients during the three waves

Baseline parameters	*Wave one*	*Wave two*	*Wave three*	*p-value*
Male	65%	54%	64%	0.54
Age	39.8 ± 14.553	49.01 ± 16.35	50.7 ± 18.04	<0.0001
SpO_2	93.72 ± 6.623	86.82 ± 9.986	95.53 ± 5.47	<0.0001
Smokers	33%	32%	36%	0.88
Obese	2%	7%	3%	0.17
Diabetic	25%	33%	29%	0.57
Hypertensive	19%	16%	18%	0.86
Asthma	4%	1%	4%	0.36
COPD	5%	3%	4%	0.77
Pulmonary tuberculosis	1%	1%	1%	1.00
Old pulmonary tuberculosis	5%	3%	2%	0.47
Chronic kidney disease	16%	14%	11%	0.61
CLD	1%	1%	2%	0.82
HBV	1%	1%	0%	0.57
HCV	2%	1%	0%	0.36
Hypothyroidism	6%	4%	7%	0.65
RA	1%	2%	0%	0.36
SLE	1%	0%	0%	0.31
CVA	6%	2%	0%	0.02
Breast cancer	1%	1%	0%	0.57
Bladder cancer	1%	0%	0%	0.31
Average admission days	8.07 ± 2.72	11.49 ± 4.13	4.64 ± 2.43	<0.0001
Disease severity				
Mild	76%	26%	83%	<0.0001
Moderate	24%	74%	17%	<0.0001

COPD, chronic obstructive pulmonary disease; CLD, chronic liver disease; HBV, hepatitis B virus infection; HCV, hepatitis C virus infection; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; CVA, cerebrovascular accident

Table 2: Symptoms seen in patients during the three waves

Symptoms	*Wave one*	*Wave two*	*Wave three*	*p-value*
Fever	54%	58%	40%	0.17
Dry cough	56%	74%	61%	0.26
Dyspnea	28%	76%	51%	<0.0001
Myalgia	53%	52%	9%	<0.0001
Headache	27%	40%	11%	<0.0001
Nausea or vomiting	10%	9%	1%	0.02
Chest pain	15%	10%	4%	0.04
Diarrhea	4%	2%	2%	0.57
Anosmia	43%	10%	0%	<0.0001
Ageusia	30%	14%	0%	<0.0001
Sore throat	17%	37%	1%	<0.0001
Rhinorrhea	8%	4%	11%	0.20
Hemoptysis	2%	3%	1%	0.60

had longer hospital stays compared to those with mild or moderate disease.[11] A study by Liu et al. showed that early initiation of antiviral therapy was associated with a shorter length of hospital stay for COVID-19 patients. This suggests that improved management and treatment of COVID-19 may result in a reduction in hospital stays.[12]

Our results also showed that during wave one, 76% of patients had mild disease compared to 26% in wave two and 83% in the third wave. This suggests that the severity of COVID-19 may have changed over time, potentially due to the emergence of new variants and the implementation of better treatment and management strategies. Regarding the emergence of new variants, a study by Qi et al. found that the δ variant of SARS-CoV-2 was associated with a higher risk of hospitalization and severe disease compared to other variants.[13] On the contrary, improved management and treatment strategies for COVID-19 can also impact disease severity. For instance, a study by Wang et al. showed that the use of glucocorticoids was associated with a reduction in disease severity for severe COVID-19 patients.[14]

The use of antiviral therapy also varied between the three waves, with 100% use in wave one, 70% use in wave two, and 10% use in wave three. The increased use of antiviral therapy in wave two may suggest a more severe form of COVID-19, while the decrease in wave three could indicate improved management and treatment

Table 3: Onset of symptoms to admission in patients during the three waves

Onset of symptoms to admission	*Wave one*	*Wave two*	*Wave three*	*p-value*
Day 1	2%	0%	0%	0.09
Day 2	7%	6%	0%	0.03
Day 3	20%	15%	0%	0.0001
Day 4	12%	15%	2%	0.008
Day 5	17%	25%	5%	0.001
Day 6	10%	17%	10%	0.26
Day 7	22%	6%	14%	0.01
Day 8	8%	5%	10%	0.43
Day 9	2%	5%	6%	0.38
Day 10	0%	5%	1%	0.03

Table 4: Treatment given in patients during the three waves

Treatment given	*Wave one*	*Wave two*	*Wave three*	*p-value*
Oxygen support	23%	70%	30%	0.0001
Days on NP	3.7 ± 1.08	4.12 ± 1.93	2.3 ± 1.03	
Days on oxygen masks	2.5 ± 1.12	2.98 ± 1.133	1.4 ± 1.33	
Days on NRBM	3.5 ± 0.7	5.3 ± 1.54	2.3 ± 0.2	
Antiviral therapy	100%	70%	10%	0.0001
Antibiotic therapy	100%	66%	45%	0.0001
Glucocorticoid therapy	23%	70%	15%	0.0001
Nonpharmacological therapy	100%	100%	100%	1.00

NP, nasal prongs; NRBM, non-rebreather facemask

Table 5: Chest radiologic findings during the three waves

Chest radiologic findings	*Wave one*	*Wave two*	*Wave three*
Right upper zone infiltrates	14%	12%	8%
Right lower zone infiltrates	21%	21%	28%
Right mid-zone infiltrates	6%	3%	3%
Right scattered infiltrates	4%	8%	6%
Left upper zone infiltrates	17%	8%	6%
Left lower zone infiltrates	9%	15%	17%
Left mid zone infiltrates	6%	0%	5%
Left scattered infiltrates	4%	6%	8%
Left mid-zone opacity	0%	3%	0%
Bilateral scattered infiltrates	11%	20%	8%
No abnormalities detected	8%	4%	11%

strategies. The use of antibacterial therapy was also evaluated and showed a decrease from 100% use in wave one to 66% use in the second wave and 45% use in the third wave. This decrease in use may suggest improved management of secondary bacterial infections in COVID-19 patients. The use of IV glucocorticoid therapy was found to be highest in wave two, with 70% of patients receiving this therapy compared to 23% in wave one and 15% in wave three. The higher use in wave two may indicate more severe forms of COVID-19, while the decrease in use in wave three may suggest improved management and treatment strategies. A study by Wang et al. found that antiviral therapy, when given early in the course of the disease, was associated with a reduced risk of hospitalization and improved outcomes for COVID-19 patients.[14] In terms of the use of antibacterial therapy, a study by Zhang et al. found that secondary bacterial infections are common in COVID-19 patients and can impact disease outcomes. The study also found that prompt recognition and treatment of secondary bacterial infections can improve patient outcomes.[15] Regarding the use of IV glucocorticoid therapy, a study by Li et al. found that the use of glucocorticoids was associated with a reduction in disease severity and improved outcomes for severe COVID-19 patients.[16]

Finally, our results showed that 60% of patients in the third wave had received two doses of the COVID-19 vaccine, while 16% had received a single dose. A systematic review by Yang et al. shows that COVID-19 vaccines can significantly reduce the risk of severe disease and hospitalization and may also reduce transmission of the virus. Increasing vaccine coverage was associated with reduced grave outcomes and hospitalizations with COVID-19 patients.[17]

Table 6: Laboratory findings at the admission during the three waves

	Laboratory findings			
Parameter	*Wave one*	*Wave two*	*Wave three*	*p-value*
Hemoglobin—gm/dL or mmol/L	12.05 ± 1.35	11.525 ± 1.99	13.55 ± 0.35	0.07
Platelet count—mcL or $*10^9$/L	262.2 ± 90.63	583.4 ± 55.45	252.2 ± 84.33	0.04
WBC count—K/uL	8235.7 ± 1232.06	8232.86 ± 1622.47	8205.3 ± 1374.48	0.81
Neutrophil count—10^9/L	80.45 ± 8.22	76.38 ± 10.291	81.45 ± 4.43	0.002
Lymphocyte count—10^9/L	13.53 ± 7.32	18.11 ± 10.209	12.33 ± 5.32	0.03
FBS—mmol/L or mg/dL	107.14 ± 26.08	128.64 ± 54.849	104.24 ± 29.18	0.005
HbA1c—mmol/L	5.9 ± 1.22	6.676 ± 1.9506	5.4 ± 1.46	0.02
Creatinine—µmol/L	1.12 ± 0.85	1.203 ± 1.251	1.16 ± 0.53	0.58
Albumin—gm/L	3.97 ± 0.4	3.821 ± 0.48	4.05 ± 0.6	0.01
D-dimer—ng/mL	521.4 ± 217.65	590.08 ± 496.81	536.4 ± 223.65	0.20
CRP—mg/L	24.5 ± 17.3	26.4 ± 38.2	23.2 ± 16.2	0.65
LDH—U/L	377.1 ± 106.1	417.64 ± 197.6	353.1 ± 101.1	0.07
Ferritin—pmol/L	437.6 ± 163.1	387.44 ± 169.84	424.6 ± 162.1	0.03

WBC, white blood cells; FBS, fasting blood sugar; CRP, C-reactive protein; LDH, lactate dehydrogenase

Conclusion

The study provides insights into the patient characteristics, management, and treatment of COVID-19 patients in three different waves. Diabetes was most prevalent among patients. The severity of COVID-19 may have changed over time, potentially due to the emergence of new variants and the implementation of better treatment and management strategies. Vaccination was associated with reduced grave outcomes as seen in the patients during the third wave.

Limitations

This was a single-center retrospective study. It gives a perspective of how the COVID-19 patients were managed and their outcomes in a government institute. As no radiologist was available at the institute, contrast-enhanced computed tomography and COVID-19 reporting and data system scoring couldn't be used as study parameters. Diagnosis of COVID-19 was done by RAT/RT-PCR.

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