Original Article

Comparison between Clinical Profile and Outcome of Patients Admitted with Moderate and Severe COVID-19 Illness in the First and Second Wave of COVID-19 in a Tertiary Care Centre in South India

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Abstract

Background: SARS-coronavirus-2 has caused large number of infections globally. The infections have presented in a wave form in most of the countries. There have been differences in the clinical presentation, course, and the outcomes in the different waves. **Aim:** This study describes the clinical features and course of the patients admitted with COVID-19 illness between the first and second wave of COVID-19 in a tertiary care center in South India. **Materials and Methods:** This was a cross-sectional study where case record analysis of the patients admitted with moderate and severe COVID-19 illness in a tertiary care center in South India was performed. Patients admitted between August 1, 2020, and November 30, 2020, were considered to be affected in the first wave and those admitted between April 30, 2021, and July 30, 2021, were considered to be in the second wave of COVID-19. First wave and second wave periods were determined by a steep surge in infections in India as per the epidemiological data. The symptoms, comorbidities, clinical profile, severity, laboratory parameters, need for assisted ventilation, medications used, and outcome were compared between the two-time frames. **Results:** A total of 123 patients' data were analyzed in each wave. 72 (58%) patients had fever, while 64 (52%) patients had fever in COVID second wave. In the first wave, five (4%) patients had diarrhea, and four (3.2%) patients had vomiting, whereas in second wave, 43 (34%) patients had diarrhea, and 25 (20 percent) patients had vomiting ($P < 0.001$). It was seen in the present study that more number of patients in the age group of 31 to 40 years had more serious illness and adverse outcomes in second wave compared with patients in first wave where age group of 51-60 years was more seriously affected. In COVID first wave, 80 (65.0%) were having moderate COVID-19 illness and 43 (35%) had severe illness. In the second wave, 70 (57%) had moderate illness and 53 (43%) patients had severe illness. In the first wave, 31 patients (25%) required non-invasive ventilation (NIV), whereas 79 patients (64%) required NIV in second wave ($P < 0.001$). First wave resulted in 12 (9.7%) deaths, whereas second wave resulted in 20 (16.2%) deaths. **Conclusion:** The patients with COVID-19 illness in the second wave presented with more non-respiratory symptoms like vomiting, diarrhea, and joint pains. The patients who had severe illness in the second

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wave were comparatively younger than the patients of the first wave. The requirement of ventilatory support and immunosuppressants was more in the second wave.

Keywords: *COVID-19 infection, COVID-19 severity, second wave of COVID-19*

Introduction

In December 2019, China reported a cluster of pneumonia cases[1] in Wuhan, Hubei Province, which was fast spreading and deadly in severity. This was later termed as coronavirus disease-19 (COVID-19), which was caused by the severe acute respiratory syndrome coronavirus-19 (SARS-CoV-2). By January 30, 2020, WHO had declared COVID-19 as Public Health Emergency of International Concern (PHEIC)[2] and as a pandemic on March 11, 2020.[3] The onset of the pandemic had presented an uncharted territory for the medical fraternity worldwide to wade through, with researchers, scientist, and doctors working swiftly to answer various questions such as the mode of transmission of the virus, its infectivity, and fatality while putting together a treatment protocol and developing effective vaccines.

Since the beginning of the pandemic, 221 countries have been affected[4] disturbing the flow of economic and social activities globally with many countries having to undergo nationwide lockdown to contain the spread of virus, imposing bans on international travel as well. India underwent a nationwide lockdown on March 22, 2020, for 4 months with phase wise unlocking in June 2020.[5] The virus has shown a wave pattern[6] with a peak when there is an increase in the number of cases and a valley where the cases have substantially gone down. Many countries in the European Union have already observed the second wave.[7] The data reported from the other countries suggest that there was a difference in the age range, symptoms, and clinical severity between the first wave and the second wave.[8-10] India experienced a surge of cases for the second time in April of 2021 where the number of cases doubled from the first peak. There were double mutant and triple mutant strains in circulation which are more pathogenic than the initial strain.[11] To contain the spread of the second wave, many states took the independent call to undergo lockdown and impose travel restrictions; meanwhile, the vaccination program in India was sped up. The understanding about the differences in the clinical presentation of the patients in first and second wave can help the treating doctors for early identification of illness and timely and appropriate management of the illness. The objective of this study was to compare and analyze the clinical profile and outcomes of the patients admitted with moderate to severe illness in the first and second wave of COVID-19 by using data from two equal periods of time that is August 1, 2020, to November 30, 2020, and April 30, 2021, to July 30, 2021.

Materials and Methods

This was a cross sectional study with case record analysis of the patients admitted with moderate to severe COVID-19 illness in a tertiary care centre in South India. Consecutive patients admitted between August 1, 2020, and November 30, 2020, were considered to be affected in the first wave and those admitted between April 30, 2021, to July 30, 2021, were considered to be in the second wave of COVID-19 with the two groups in equal time period of three months. The time frame of first and second wave was as per the surge of COVID-19 cases detected in India as per epidemiological data. Inclusion criterion was patients admitted with moderate to severe COVID-19. Diagnosis was confirmed by with reverse transcriptase-polymerase chain reaction (RT-PCR) for COVID-19 using nasopharyngeal and Oro-pharyngeal swab samples. As per Indian Council of Medical Research guidelines, patients with moderate COVID-19 illness includes patients with a respiratory rate more than 24 per minute or oxygen saturation less than 93% on ambient air, and severe illness are those patients whose saturation is less than 90% on ambient air or respiratory rate more than 30 per minute.[12]

While retrieval of relevant data from the patient's medical records was performed, due care was taken not to disclose personal details and identification of the patients. The symptoms, comorbidities, clinical profile, severity, laboratory parameters, need for assisted ventilation, medications used and outcomes were compared between the two-time frames. The study was done after obtaining the clearance from the Institutional Ethical Committee (MSRMC/EC/SP-09/05-2021).

Calculation of sample size

The sample size was calculated as per a similar study conducted by Contou *et al*. This study involved eighty-two patients who were critically ill during the first wave and fifty during the second wave. In the first wave, 88% patients required Invasive mechanical ventilation (IMV), whereas 64% of patients required IMV in the second wave. The study observed that the median D-dimer during 1st and 2nd wave of COVID-19 was 2510 [1655-9222] ng/ml and 1665 [1060-3372] ng/ml, respectively. In the present study, expecting a similar result with 80%

power, 95% confidence level and with effect size of 0.41, required a minimum of 123 patients in each group.

Statistical analysis

The descriptive statistics of D-dimer, CRP, neutrophil-lymphocyte ratio, and lactate dehydrogenase was analyzed and summarized in terms of mean with standard deviation or median with inter-quartile range (IQR). Independent t test was used to compare D-dimer, CRP, PT, and CBC between two waves of COVID-19. Categorical variables are reported as numbers (percentages) and compared using χ^2 test. A P value <0.05 was considered significant. Statistical analysis was performed using SPSS 18 (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.).

Results

A total of 123 patients' data were analyzed in each wave. In the first wave, 38 (30%) patients with moderate and severe disease were in the age group of 51-60 years. This was followed by the age group of 41-50 years with 26 (21%) patients having moderate and severe disease. In the second wave, 31 (25%) patients were in the 31- to 40-year age group with patients. This difference was found to be statistically significant (P = 0.021) [Table 1]. In the first wave, 80 (65%) patients were males and 43 (35%) were females in the first COVID-19 wave. In the second wave, 86 (70%) patients were males and 37 (30%) patients were female (P = 0.433). In COVID-19 first wave, 80 (65.0%) were having moderate COVID-19 illness and 43 (35%) had severe illness. In the second wave, 70 (57%) had moderate illness and 53 (43%) patients had severe illness. In the wave 1, 79 (64 percent) of patients had comorbidities such as HTN, Type 2 DM, whereas 72 (58%) of patients in COVID wave 2 had comorbidities. In COVID first wave, 72 patients (58%) had fever, while 64 (52%) had fever in COVID second wave [Table 2]. In the first wave, 70 (56%) patients had cough and in the second wave cough was seen in 67 (54%) of patients. In the first wave, five (4%) patients had diarrhea, four (3.2%) patients had vomiting, and 6 (5%) patients having abdominal pain, whereas in second wave, 43 (34%) patients had diarrhea, 25 (20%) patients had vomiting, 26 (21%) individuals had abdominal pain. Rashes were observed in 3 (2.4%) of patients in the first wave whereas, 18 (14.6%) of patients in second wave had rashes. In addition, eight (6.5%) patients in first wave experienced joint discomfort, whereas 13 (10%) of wave 2 patients had joint pain. The difference between the two waves with respect to symptoms is statistically significant (P < 0.001). The symptoms experienced by the patients have been explained in the Table 3. The mean CRP among patients in COVID-19 first wave was 7.84 ± 6.93, mean D dimer was 1.97 ± 1.64, whereas mean CRP was 9 ± 7.986 and D Dimer was 2.12 ± 1.38 in second wave. The inflammatory markers have been explained in the Table 4. In the first wave, 31 (25%) patients required NIV, while 79 (64%) patients required NIV in second wave (P < 0.001). In the first wave, 62 (50%) patients required remdesivir, and 94 (76%) patients required remdesivir in the second wave. In the first wave, 90 percent of patients required steroids, whereas 96 percent of patients in COVID-19 wave 2 required steroids. In the first wave, five (4%) patients required tofacitinib, whereas 29 (23%) patients required tofacitinib (P = 0.003). First wave resulted in 12 (9.7%) deaths, whereas second wave resulted in 20 (16.2%) deaths. All the patients who died were suffering from moderate and severe disease at the time of admission. The medications used and outcome of the patients are described in the Table 5.

Table 1: Age distribution of patients admitted with moderate and severe COVID-19 in wave 1 and wave 2

Age	COVID-19 wave 1	COVID-19 wave 2	*P*
11-20	1 (0.8%)	1 (0.8%)	X^2 - 7.68
21-30	3 (2.4%)	4 (3.2%)	*P* – 0.02
31-40	13 (10.5%)	31 (25.2%)	
41-50	26 (20.0%)	20 (16.2%)	
51-60	38 (31.6%)	26 (21.1%)	
61-70	23 (18.6%)	13 (10.5%)	
71-80	14 (11.3%)	15 (12.1%)	
More than 80	5 (4.0%)	8 (6.5%)	

Table 2: Demographics, comorbidities, and severity of patients admitted in COVID-19 waves 1 and 2

Parameters	COVID-19 wave 1 (*n*=123)	COVID-19 wave 2 (*n*=123)	*P*
Males	80 (65.0%)	86 (69.9%)	X^2-0.83
Females	43 (35.0%)	36 (30.1%)	*P* - 0.36
Moderate COVID-19 illness	80 (65.0%)	43 (35%)	*P* - 0.036
Severe COVID-19 illness	70 (57%)	53 (43%)	
Type-2 Diabetes mellitus	68 (55.2%)	60 (48.7%)	Chi square - 0.32
Systemic hypertension	70 (56.9%)	66 (53.6%)	*P* - 0.52
Chronic kidney disease	12 (9.7%)	10 (8.1%)	

Discussion

This was a cross-sectional study which compared the clinical course and outcome among the patients admitted with moderate and severe COVID-19 illness in the two time frames of COVID waves in a tertiary hospital in South India. This study was conducted when the COVID-19 vaccination was in the initial stages. It was observed that there were many differences between the two waves with respect to the age of the patients, their symptoms, and outcomes. An interesting observation was made regarding non-respiratory complaints like diarrhea, vomiting, abdominal pain, and rashes which were more commonly seen among the patients in the second wave. These findings of our study were concordant with study performed by Iftimie S and colleagues which demonstrated that patients from the second wave frequently presented with a higher frequency of vomiting weakness, abdominal pain, and acute kidney failure.[7]

It was seen in the present study that higher proportion of patients in the age group of 31 to 40 years had more serious illness and adverse outcomes in second wave compared with patients in first wave where those in the 51- to 60-year age group were more seriously affected. Patients requiring ventilatory support were comparatively younger in the second wave. These findings were similar with the study performed by David Flunck *et al*., which reported that the patients who got admitted in the second wave were younger than the patients in the first wave in Europe.[9] It was observed the frequency of use of medications like remdesivir, corticosteorids, and tofacitinib was more frequent in the second wave. This shows that the patients admitted in the second wave had more severe illness and required more medications frequently. These findings were similar to the study conducted by Saito S *et al*. which noted that more number of patients from the second wave received remdesivir.[10] The findings of our study were concordant with the study conducted by Contou D and colleagues where the patients admitted in COVID-19 second wave received more glucocorticoids.[8]

In the current study it was noted that, in the first wave, 38 (30%) patients with moderate and severe disease were in the age group of 51-60 years. This was followed by the age group of 41-50 years with 26 (21%) patients having moderate and severe disease. In the second wave, most patients 31 (25%) were in the 31-40-year age group with patients. The findings were similar to the study from Japan, also indicated that younger population suffered more severe infection in the second wave as compared with first wave.[10] First wave resulted in 12 (9.7%) deaths, whereas second wave resulted in 20 (16.2%) deaths. The findings of the study were in contrast to the study conducted by Contou *et al*. where the ICU mortality of the patients admitted during the two waves did not differ.[8] Several mutant strains of the virus have been identified in India which were found to be more pathogenic than the initial strains.[11] Moya A and colleagues discussed that there are several factors which govern evolution of RNA viruses and their spread through population including migration of hosts within a population, viral mutation, etc.[13] The double mutation in SARS-CoV-2 B.1.617 strain involving Glu484Gln and Leu452Arg in the spike protein is highly infectious and might have been the cause for COVID-19 surge in India.[11,14,15] As per the study performed in Maharashtra, S protein mutations could be associated with the rise in COVID-19 cases in Maharashtra observed since the month of February 2021.[16] Poor compliance with social distancing guidelines by young people might have facilitated spread of infection in young adults.

The concept of waves in the past pandemics, such as the 1918 influenza epidemic,[7] greatly helped the policymakers to have better understanding of disease pattern, formulate, and interpret better health policies. WHO has clarified that there has to be a substantial rise in new infections followed by steady decrease in the number of cases to be called as a wave.[9] Wave and spike are different as spike is generally an upsurge

Table 3: Frequency of symptoms experienced by patients

Symptoms	COVID-19 wave 1	COVID-19 wave 2
Fever	72 (58.5%)	64 (52.0%)
Cough	70 (56.9%)	67 (54.4%)
Breathlessness	53 (43.0%)	65 (52.8%)
Loss of smell	9 (7.3%)	2 (1.6%)
Diarrhea	5 (4%)	43 (34.9%)
Vomiting	4 (3.2%)	25 (20.3%)
Pain abdomen	6 (4.8%)	26 (21.1%)
Rashes	3 (2.4%)	18 (14.6%)
Joint pains	8 (6.5%)	13 (10.%)

Table 4: Laboratory parameters among the patients

Parameters	COVID-19 wave 1 (*n*=123)	COVID-19 wave 2 (*n*=123)	*P*
Mean CRP	7.84±6.93	9.0±7.98	0.004
Mean D-Dimer	1.97±1.64	2.12±1.38	0.002
Mean neutrophil-to-lymphocyte ratio (NLR)	6.52±3.23	9.48±3.34	<0.001
Mean LDH	320±80.54	420±120	0.01

Table 5: Medications, interventions, and outcome among patients with moderate and severe COVID-19 infection in wave 1 and wave 2

Medication	COVID-19 wave 1	COVID-19 wave 2	*P*
Remdesivir	62 (50%)	94 (76%)	0.001
Steroids	90 (73.1%)	96 (78.0%)	0.02
Tofacitinib	5 (4%)	29 (23%)	0.003
NIV	31 (25.2%)	79 (64.2%)	<0.001
Death	12 (9.2%)	20 (16.2%)	0.01

or a momentary phenomenon[3] Policymakers and epidemiologists describe the COVID-19 epidemics by waves. A working definition can be helpful to describe and communicate about epidemics.[6]

This study showed that the clinical features and course of the COVID illness were different over the different time frames, possibly due to the mutant strains. In India, during the second wave, there were a large number of patients getting admitted which had overwhelmed the health care set up. The public needs to be more vigilant regarding protective measures like social distancing, use of masks, and sanitization to control the COVID infection spread.

The limitations of the study are the small sample, and the study was performed in a single center. However, large multicentric studies and conducting genomic analysis of the virus can help in better understanding of the pandemic.

Conclusion

The patients with COVID-19 illness in the second wave presented with more non-respiratory symptoms like vomiting, diarrhea, and joint pains. The patients who had severe illness were comparatively younger than the patients in the first wave. The requirement of ventilatory support and immunosuppressants was more in the second wave. However, large multicenter studies and conducting genomic analysis of the virus can help in better understanding and control of the COVID-19 illness.

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Conflicts of interest

There are no conflicts of interest.

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