Original Article

A comparative study between first three waves of COVID-19 pandemic with respect to risk factors, initial clinic-demographic profile, severity and outcome

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Abstract

Introduction: During the 2 years and 9 months from March 2020 to December 2022, the SARS-CoV-2 virus raged across the country. Cases occurred in three particular time clusters recognised by World Health Organisation as coronavirus disease 2019 (COVID-19) waves. In this study, we compare the clinical parameters of adult non-obstetric COVID-19 patients admitted to our rural tertiary care hospital during the three distinct waves of the pandemic. **Materials and Methods:** Retrospective chart analysis of 272, 853 and 97 patients admitted with SARS-CoV-2 infection to the only rural medical tertiary care centre in the Sunderbans of West Bengal in the first, second and third waves, respectively, was done after obtaining ethical and scientific clearance. Clinical [vital parameters, oxygen requirement, mental status, risk factor assessment, duration of hospital stay, modified-emergency warning score (m-EWS), quick Sequential Organ Failure Assessment (qSOFA), confusion, uraemia, respiratory rate, blood pressure, age ≥ 65 years (CURB65)], epidemiological variables (age, gender, and vaccination status), laboratory parameters and in-hospital outcome were recorded and analysed statistically. **Results:** Statistically significant ($P < 0.05$) m-EWS and qSOFA scores were recorded during the second wave of the pandemic. The second wave also recorded the highest mortality (14.89%) compared to the first (12.87%) and third (11.96%) waves, though this was not statistically significant. The highest duration of hospital stay was recorded in the first wave of the pandemic (mean = 9.99 days, $P < 0.01$). The difference in mortality rates between patients with and without co-morbidity ($P < 0.05$) was observed during Wave-1, across any pandemic wave, and overall but not in Wave-2 and Wave-3. **Conclusion:** The second wave of the COVID-19 pandemic was the most severe in comparison with the other two waves, while the outcome was poorer in those with co-morbidities, especially in the first wave.

Keywords: COVID-19, CURB65, m-EWS, pandemic wave, qSOFA

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Background

The world witnessed a devastating coronavirus disease 2019 (COVID-19) pandemic over the last few years beginning

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in December 2019, caused by SARS-CoV-2, a highly mutating enveloped RNA virus. As regards, clinical presentation and outcome of the mutating virus behaved significantly differently during different waves of the pandemic. Differences were also noted in the pandemic presentations in various parts of the world. This difference in the behaviour of the pandemic is likely due to the combination of various known (including the high mutation rate of these RNA viruses) and unknown reasons. In the initial part of the pandemic, it was difficult to understand the nature of the disease in the first wave. Primarily, the elderly population with high-risk associations were affected and caused high mortality. In the second and third waves, relatively younger populations were affected even without significant risk associations with relatively low mortality rates. Vaccination against COVID-19 started in West Bengal in the first quarter of 2021. Apparently, the vaccinated population behaved differently. Re-infection and infection after vaccination both were common in the late second and third waves of the pandemic. A comparative review from Egypt[1] in 2022 on three pandemic waves mentioned the efficacy of vaccination against new strains and its positive role in the prevention of re-infection.

Patrucco *et al.* (2022)[2] mentioned the diversity of factors influencing the natural course of COVID-19 infection. Thakur *et al.*[3] mentioned that even increased resource allocation during the second wave of the SARS-CoV-2 pandemic could not mitigate the harsh might of the infection. In contrast, Hoogenboom[4] in the resource-rich Western world and Joshua *et al.*[5] in resource-poor Nigeria identified better outcomes in the second pandemic wave. Souyris *et al.*[6] mentioned that the second wave of the pandemic in 2021 was a prime example of a simultaneous pandemic wave in the country. Ayala *et al.*[7] recommend monitoring of the COVID-19 data to identify future pandemic waves. Thus diverse factors from virus mutation to changes in knowledge, attitude and practice related to handling and managing COVID-19 cases with progression of the time all affected the nature of the respective pandemic waves.

Definitions of COVID-19 Waves: The World Health Organisation (WHO) states that COVID-19 resurgence represents a visible growth in new COVID-19 cases that are registered following at least two consecutive weeks of low or no transmission, assuming optimal surveillance and testing activities.[8] A COVID-19 wave is a situation envisaged where a sudden increase in number of COVID-19 cases is observed beyond what is expected. There is no consensus definition of a COVID-19 wave in scientific literature although some WHO experts define a COVID-19 wave depending on the shape of the epidemic curve, which requires mathematical calculations.[9] Actionable thresholds during the start and end of a COVID-19 wave are the resurgence response and the 'under control' phase, respectively. The COVID-19 resurgence-response threshold is defined as an increase of at least 20% of incident cases in the preceding 2 weeks (7-day moving averages) or a sudden 30% increase in cases exceeding the numbers of the previous 7-day peak average. A controlled transmission relates to either an increase in incident cases in terms of the 7-day moving average being less than 10% for two consecutive weeks, or a steady reduction or epidemiological steady numbers over two consecutive weeks. WHO states that a threshold of a resurgence alert is achieved when a 10–20% increase in the number of confirmed COVID-19 cases has been recorded (the 7-day moving average). Scientific evidence that for a geographical area to be classified as under control, none of the criteria for a resurgence alert or response are present.[9,10] At the peak of the wave, the numbers of newly registered cases start to plateau slowly and then decline instead of an abrupt upward trajectory.

Official data[11,12] and Figure 1 are available from the websites of the Department of Health and Family Welfare, Government of West Bengal throughout the duration of the COVID-19 pandemic beginning in April 2020 (first case in India). These are testimony to the adequate testing and surveillance done during the entire period and led to the observation of three COVID-19 waves between April 2020 and March 2022. It was only after the lockdowns were lifted in a phased manner starting on 8 June 2020 that the first COVID-19 wave started emerging. After scorching for nearly 2 years, in the week starting 14 March 2022, the majority of private COVID-19 hospitals in West Bengal closed and cases plummeted.[10] Although the COVID-19 pandemic was officially declared over by WHO only on 5 May 2023,[13] the acute phase of the pandemic in West Bengal was over by the second week of March 2022. Our government-run rural COVID-19 hospital was established in October 2020 and closed in May 2022.

The aim of this study was to compare the clinical profiles of admitted COVID-19 patients and their outcomes during the first three waves of the pandemic in a rural tertiary care hospital in West Bengal.

Methodology

Ethical and Scientific approval: Both ethical and scientific committee approval were obtained from the Institutional Ethical and Scientific Review Committee (No 2023/262 dt 27.07.2023).

Data Collection: Retrospective clinical and laboratory data of all non-obstetric adult COVID-19 patients [diagnosed with a COVID-19 real-time polymerase chain reaction (RT-PCR) positive result] admitted in the COVID-19 hospital from October 2020 (when our COVID-19 hospital became functional) to February 2022 from Electronic Medical Records and Bed Head Tickets (BHTs) were collected.

Defining COVID-19 Waves in West Bengal State, India: According to the WHO's definition of COVID-19 waves, from 7 April 2020 through 13 March 2022, the available[12,13] epidemiological week (EW)-wise aggregated data facilitated the identification of seven phases of the epidemic, including three waves and four under-control and alert periods [Figure 1]:

- Phase I: 04/07/2020–07/05/2020 (EW14/2020–EW24/2020)

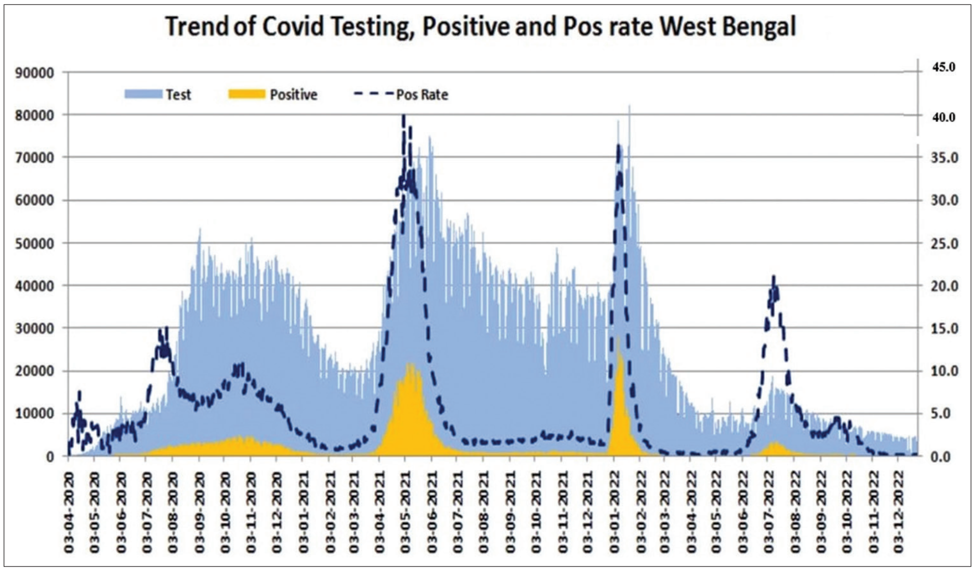

Figure 1: Trend of COVID-19 testing and positivity rate in West Bengal from April 2020 to December 2022

- Phase II: 07/06/2020–01/10/2021 (EW28/2020–EW01/2021) = First wave
- Phase III: 01/11/2021–03/28/2021 (EW02/2021–EW12/2021)
- Phase IV: 03/29/2021–07/04/2021 (EW13/2021–EW26/2021) = Second wave
- Phase V: 07/05/2021–12/26/2021 (EW27/2021–EW51/2021)
- Phase VI: 12/27/2021–02/06/2022 (EW52/2021–EW05/2022) = Third wave
- Phase VII: 02/07/2022–03/13/2022 (EW06/2022–EW10/2022)

Timing of Waves: Patients were considered to have been infected in Wave-1 if admitted from 12 October 2020 (inception date of our COVID-19 hospital) to 10 January 2021, in Wave-2 if admitted between 29 March 2021 and 4 July 2021, and in Wave-3 if admitted between 27 December 2021 and 6 February 2022.

Sampling: All the patients matching the inclusion criteria (a total of 1368) admitted during the specified time were included in the study.

Inclusion Criteria: All adult patients >12 years of age with positive RT-PCR for SARS-CoV-2 were included in the study.

Exclusion Criteria: Patients <12 years of age and pregnant patients were excluded.

Study Design: Retrospective cross-sectional study.

Statistical Analysis: All the collected data will be incorporated in a Microsoft Excel 16 sheet as a grand chart and the variables will be analysed by Jamovi statistical software version 2.3 [2022 version]. The descriptive numerical data are represented as mean and standard error (SE). The categorical variables are represented as percentages. Ratios in the three groups were tested for significant differences using the Chi-squared goodness of fit test. For quantitative data in three groups (COVID-19 Wave-1, Wave-2 and Wave-3), the Kruskal–Wallis (KW) test was done to detect differences between groups. A P value of < 0.05 was considered statistically significant at a 95% confidence interval. Parameters showing the significant difference on the KW test were then tested with a post-hoc Dunn multiple comparison test with Bonferroni correction for detecting differences between individual groups. Two-tailed Chi-square test was performed to compare mortality rates in each pandemic wave, across waves and overall between those with and without co-morbidities.

Results and Analysis

The age, gender distribution, risk factor analysis, length of hospital stay, COVID-19 vaccination status and time period of discharge of the admitted patients are presented in Table 1. The time distribution of the COVID-19 waves is depicted in Figure 2 plotting the number of COVID-19 patients admitted in our hospital throughout the period from October 2020 to February 2022.

The pulse rate, respiratory rate, oxygen perfusion as determined by pulse oximetry, requirement of supplemental oxygen, mean systolic blood pressure, temperature at admission, modified-emergency warning score (m-EWS), quick Sequential Organ Failure Assessment (qSOFA) score, confusion, uraemia, respiratory rate, blood pressure, age ≥65 years (CURB65) score and mortality characteristics of the admitted patients during the three separate waves are mentioned in Table 2.

In both the second and third waves, almost equal proportions of the male and female population were vaccinated with at least the first dose of any vaccine either Covishield™ or Covaxin™. During the third wave majority (71%) of the vaccinated patients completed their second dose. The average duration of admission in the first wave was one to two weeks. Almost 43.8% of patients in the first wave were discharged by this time which reduced from 29.8% to 27.6% from the second to third wave. The difference in admission period had statistical significance ($P < 0.01$). From the available 272 patients' retrospective data during the first wave, 24 (8.82%) were severely hypoxic at admission and 38 (13.97%) patients had moderate hypoxia. Among the total 853 patients of the second wave, 231 (27.08%) and 82 (9.61%) had moderate and severe hypoxia, respectively. During the third wave, 13 (13.40%) and 7 (7.22%) had moderate and severe hypoxia, respectively, out of 97 patients [Table 2].

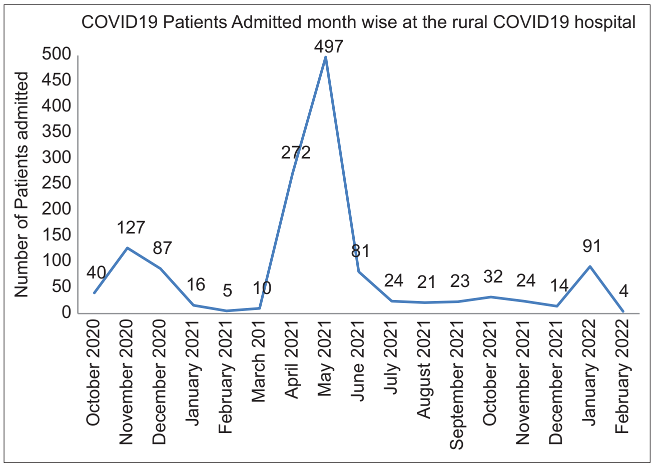

Figure 2: Time distribution showing the plot of the number of COVID-19 patients admitted every month in the period from October 2020 to February 2022

During the pandemic period, observed mortality was 12.87% in the first wave, slightly higher at 127 (14.89%) in the second wave and 11 (11.96%) in the third wave. The mortality differences though were not statistically significant [Table 2]. The outcome was significantly poorer ($P < 0.05$) among those with co-morbidities than in those without during the pandemic Wave-1, across any pandemic and overall [Table 3]. In contrast, there was no statistically significant difference in Wave-2 and Wave-3 [Table 3].

Discussion

We present a study on a large population of patients affected during the three COVID-19 waves with robust retrospective data recovery. Our study demonstrates the third COVID-19

Table 1: Epidemiologic and risk factor parameters among COVID-19 patients admitted in different pandemic waves

Parameter	Pandemic Wave-1 (*n*=272)	Pandemic Wave-2 (*n*=853)	Pandemic Wave-3 (*n*=97)	*P*
Male	171 (62.87%)	471 (55.25%)	51 (52.58%)	0.06
Female	101 (37.13%)	383 (44.78%)	46 (47.42%)	0.06
Age (mean±2SE) (years)	54.40±2.01	50.27±1.07*	53.09±4.22	<0.05
No risk factor present	127 (46.69%)	667 (78.19%)	37 (36.96%)	<0.05
Risk factors present				
Diabetes mellitus	50 (18.38%)	58 (6.80%)	16 (16.50%)	<0.05
Hypertension	60 (22.06%)	64 (7.50%)	23 (23.71%)	<0.05
Ischaemic heart disease	32 (11.76%)	31 (3.63%)	8 (8.70%)	<0.05
COPD	08 (2.94%)	05 (0.59%)	10 (10.87%)	<0.05
Asthma	0 (0.0%)	0 (0.0%)	2 (2.17%)	–
Post tubercular lung cavity	0 (0.0%)	0 (0.0%)	1 (1.09%)	–
Chronic liver disease	01 (0.37%)	0 (0.0%)	0 (0.0%)	–
Cerebrovascular accident	03 (1.10%)	0 (0.0%)	0 (0.0%)	–
Hypothyroidism	04 (1.47%)	03 (0.35%)	5 (5.43%)	<0.05
Neurological abnormalities	01 (0.37%)	01 (0.12%)	1 (1.09%)	0.2
CKD	01 (0.37%)	01 (0.12%)	2 (2.17%)	<0.05
Malignancy	01 (0.37%)	01 (0.12%)	01 (1.09%)	<0.05
Thalassemia	0 (0.0%)	0 (0.0%)	01 (1.09%)	–
Drug addiction	0 (0.0%)	0 (0.0%)	01 (1.09%)	–
Pregnancy	03 (1.10%)	02 (0.24%)	0 (0.0%)	–
Cholelithiasis	2 (0.74%)	0 (0.0%)	0 (0.0%)	–
Fracture	1 (0.37%)	0 (0.0%)	0 (0.0%)	–
Anaemia	66 (24.26%)	85 (9.96%)	50 (51.55%)	<0.05
Severe arthritis	0 (0.0%)	1 (0.12%)	01 (1.09%)	–
Vaccinated with COVID-19 vaccine – any number of doses	0 (0.0%)	17 (1.99%)	68 (70.10%)	<0.001
Vaccinated with COVID-19 vaccine – two doses	0 (0.0%)	10 (1.17%)	53 (54.64%)	<0.001
Length of hospital stay (mean±2SE) (years)	9.99±1.47	9.07±0.54	5.97±0.95	<0.001
Discharge/death in the first week (by day 7)	116 (42.80%)	457 (53.58%)	72 (74.22%)	<0.01
Discharge after day 28 of hospitalisation	04 (1.48%)	34 (3.99%)	0 (0.0%)	<0.01

Ratios in the three groups were tested for significant differences using the Chi-squared goodness of fit test. For quantitative data like age, the Kruskal–Wallis (KW) test was used. *KW test after post-hoc correction shows *P* value significant at <0.05 compared to pandemic Wave-1

Table 2: Clinical parameters among COVID-19 patients admitted in different pandemic waves

Parameter	Pandemic Wave-1 (*n*=272)	Pandemic Wave-2 (*n*=853)	Pandemic Wave-3 (*n*=97)	*P*
Pulse rate	84.96±1.80	91.80±1.15*	85.91±1.67	<0.001
Respiratory rate	22.75±0.55	23.59±0.34*	21.84±0.45**	<0.001
Mean SpO2 at admission	93.30±1.37***	92.51±0.74*	94.31±2.46**	<0.001
SpO2 at admission >94%	210 (77.21%)	540 (63.31%)	77 (79.38%)	<0.05
Moderate hypoxia (SpO2 between 85 and 94%)	38 (13.97%)	231 (27.08%)	13 (13.40%)	<0.05
Severe hypoxia (SpO2 <85%)	24 (8.82%)	82 (9.61%)	07 (7.22%)	0.72
Requirement of supplemental oxygen	99 (36.40%)	378 (44.31%)	31 (31.96%)	<0.05
Mean systolic blood pressure (mmHg)	119.07±2.12	118.89±1.05	118.51±2.26	0.316
Temperature at admission (degree F)	98.00±0.10	97.87±0.05*	97.69±0.10**	0.005
qSOFA score	0.74±0.08	0.85±0.04*	0.76±0.08	<0.001
CURB65	0.79±0.12	0.64±0.06	0.68±0.12	0.207
m-EWS	7.65±0.60	8.22±0.30*	8.61±0.66	0.015
Mortality	35 (12.87%)	127 (14.89%)	11 (11.96%)	0.50

*=*P* value significant at <0.05 compared to pandemic Wave-1, **=*P* value significant at <0.05 compared to pandemic Wave-2, ***=*P* value significant at <0.05 compared to pandemic Wave-3 [post-hoc Dunn test (Bonferroni correction alpha=0.017) following Kruskal–Wallis test]; SE=Standard error

Table 3: Comparison of outcomes in COVID-19 patients with and without risk factors

Patient Category		Mortality
Epidemiological Period	Presence or Absence of Co-morbidity	
Wave-1 COVID-19 patients (*n*=272)	With co-morbidity (*n*=145)	29 (20.00%)*
	Without co-morbidity (*n*=127)	6 (4.72%)
Wave-2 COVID-19 patients (*n*=853)	With co-morbidity (*n*=186)	33 (17.74%)
	Without co-morbidity (*n*=667)	94 (14.09%)
Wave-3 COVID-19 patients (*n*=97)	With co-morbidity (*n*=60)	9 (15.00%)
	Without co-morbidity (*n*=37)	2 (5.41%)
Any pandemic wave COVID19 patients (*n*=1222)	With co-morbidity (*n*=391)	71 (18.16%)*
	Without co-morbidity (*n*=831)	102 (12.27%)
Overall admitted COVID-19 patients (irrespective of pandemic wave) (*n*=1368)	With co-morbidity (*n*=475)	90 (18.95%)*
	Without co-morbidity (*n*=893)	109 (12.21%)
Overall (irrespective of waves/co-morbidity) (*n*=1368)		199 (14.55%)

*=*P*<0.05. Chi-square test was used to statistically study the differences in mortality rates between patients with and without co-morbidity during each of the pandemic waves, any pandemic wave and overall in all admitted COVID-19 patients

pandemic wave to have had the least mortality and hospitalisation durations. The reassuring decrease in deaths during the later pandemic waves has been evident in studies from other countries also. Evidence on multiple pandemic waves gathered by 2021 suggested government policies to be effective in reducing deaths across countries also highlighted the importance of the non-pharmaceutical response over time.[14]

We noted a huge majority of admissions were during the second wave with a statistically significant male preponderance in all the waves. The mean age of COVID-19 patients admitted to our hospital was greater than 50 years, similar to another Indian study.[15] Similar to observations by AlBahrani *et al.*[16] in 2022, the young population without any risk factors were predominant during the second wave according to the result of this study.

The majority of the patients in the second wave had no associated risk factors in contrast to the other two waves. Chronic obstructive pulmonary disease (COPD), hypertension, diabetes mellitus and anaemia were the principal risk factors in all the waves. The proportion of patients who had DM was notably highest in the first wave followed closely by the third wave. This difference in the lower proportion of diabetics was statistically significant. A high proportion of patients admitted during the third wave had COPD, hypertension and anaemia as co-morbidities. Mortality rates between patients with and without co-morbidity were significantly different during Wave-1, across any pandemic wave, and overall. In contrast, Wave-2 and Wave-3 did not show a statistically significant difference in outcome between the two groups. These results suggest that the impact of co-morbidity on mortality may vary across different waves of the pandemic. A Canadian population-based retrospective cohort study using linked healthcare data sets[17] highlighted a shift of COVID-19-infected patients towards a younger age group with fewer co-morbidities and lower mortality risk as the pandemic evolved. However, that study also noted higher mortality rates being sustained in case of infections with variants of concern. Probably the rapid mutation rate of the virus is one of the reasons behind this change in the affected age group along with the absence of risk factors in the affected population.

Another reason for the change in the affected age group could be the earlier pickup of vaccinated senior citizens and those with co-morbidities. As previously mentioned, vaccination started in this area by the first quarter of 2021, so naturally all the patients admitted in the first wave were unvaccinated. Predominant during the third wave of hospitalisations were those who received at least a single dose of either Covisheld™ or Covaxin™. A scientific report[18] highlights that the non-vaccinated population caused a major surge of delta wave in the United States. Kinoshita *et al.*[19] during their study on the first and second pandemic waves in Japan in 2022 mention that the only practical strategy to control the disease was to limit the contacts before sufficient vaccination coverage was available. In India, both the pandemic waves and vaccination coverage lagged behind developed countries. So, the actual effects of vaccination were obvious only during the third wave of the pandemic or the omicron wave. The benefits of vaccination were not homogeneous initially as the vaccination programme took time to reach a substantial coverage. Mass scale injections were administered sequentially starting from healthcare professionals and safai karmacharis, aged persons, aged persons with co-morbidities, then middle-aged persons with co-morbidities, middle-aged persons, and finally the young up to 18 years of age. Rather belatedly children between 12 and 18 years were vaccinated in India when the third pandemic wave was nearly over. Another study from Mexico demonstrated that high vaccination coverage prevented further COVID-19 pandemic wave progression.[20] This study also demonstrated a lack of any benefit in the under-14 age group due to poor access to vaccination.[20]

At our hospital, the mean duration of hospital stay was lowest in the third wave and highest in the first pandemic wave. The difference in admission period was statistically significant. Overall, during the first COVID-19 pandemic wave, most patients were admitted for one to two weeks. In stark contrast, the majority of the patients were discharged before one week of admission during the third wave.

It was during the second pandemic wave that the highest and statistically significant proportion of the moderately hypoxic (27.08%%, $P < 0.5$) patients were admitted. Furthermore, the majority of the patients admitted during the second pandemic wave required oxygen supplementation. Altered sensorium was not a common presenting feature in any of the three waves. The means of pulse rate and respiratory rates were higher in the second wave compared with the other waves. Among the vital parameters, pulse rate, respiratory rate and axillary temperature had significantly different mean values. In a notable study from the Middle East, similar findings were noted and a conclusion was drawn that more clinically ill patients were detected in the second wave.[21] However, as seen by them[21] and in our study, despite the severity, the experience gained in the first wave and the availability of greater expertise in handling the patients, patients in the second wave required shorter hospitalisation than those in the first.

With respect to clinical scoring systems, the highest qSOFA score means were observed in our second wave, whereas higher mean CURB-65 scores were found during the third pandemic wave. We found a significant difference in the variance of qSOFA values among the three waves but not when the severity was calculated by CURB-65 criteria. In contrast, a single-centre study by Martinot *et al.*[22] observed that death and ICU admissions both were reduced during the second pandemic.

We observed maximum deaths in the second wave followed by the first wave and third wave, respectively. The differences in deaths were not statistically significant among the three waves. This is similar to the findings reported by Ruiz-Huerta *et al.*[23] in their study on 546 patients. Lin *et al.*[24] in their Hong Kong-based study noted that vaccination had saved a large number of patients before the Omicron wave. We could not comment on this part as virus genotype analysis is not available for the majority of COVID-19 patients in our study area. The variants of concern affecting people in West Bengal were different from time to time and also differed between different parts of the West Bengal state. In our opinion, the difference in death rates among the three waves can have multifactorial causation. During the initial part of the first wave, there was a lack of proper guidelines related to triaging of patients, admission criteria and management protocol. Panic among the caregivers also played an important role. Many of the healthcare workers were introduced for the first time with an N95 mask and personal protection kit. Gradually with time, experience and proper implementation of government policies with the availability of vaccines and proper management guidelines and protocols starting from WHO, ICMR and local state government helped us to a great extent. Strict admission criteria were followed in the mid of the second pandemic wave. An increase in vaccination coverage before the third wave, especially among those at high risk of dying is also a possible cause. A large study in Spain also noted that clinically less severe infections occurred during the latter pandemic waves.[25] In the case of this Spanish study, this latter wave was astonishingly the second wave. However, one must note that the Indian pandemic waves and the variants of concern actually did not coincide with other parts of the world, especially Western countries. So, our experience is expected to be slightly different from the results of various Western-based studies.

Limitations of the Study: The single-centre-based approach and the retrospective nature were the main limitations of the study.

Conclusion

We observed the second COVID-19 pandemic wave to be more severe in nature and that the poorer outcome in mortality among those with co-morbidity was most in the first COVID-19 pandemic wave. Initially, we were not prepared to deal with the disease due to its novelty and inadequate knowledge about its pathogenesis, presentation and severity. The highly mutating nature of the virus contributed to the show of its devastating nature despite various government policies like quarantine, effective isolation and lockdown. Vaccination played an important role principally in the third wave along with the later part of the second wave to decrease the threat of the disease more effectively. There is a need for further multicentre or large community-based studies to validate our findings and continuously assess this dangerous viral pathogen.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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