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Internal Medicine Section

Clinical, Laboratory and Radiological Profile of COVID-19 Patients during the Second Wave with Special Reference to Vaccination Status

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ABSTRACT

Introduction: Coronavirus Disease-19 (COVID-19) has been creating havoc worldwide since the first report in December, 2019. Vaccination against the disease was thought to bring respite, reducing the severity of disease, morbidity and mortality. However, considering the fact that no vaccine is fully efficient, people may get COVID-19 even after full vaccination.

Aim: To determine the clinical, laboratory, radiological features of COVID-19 including the outcome and compare these between vaccinated and unvaccinated patients.

Materials and Methods: The prospective observational study was conducted in a dedicated COVID-19 hospital in Odisha, India, from May 2021 to June 2021. Detailed history including symptoms and vaccination status, laboratory parameters, and radiological investigations were collected from 200 patients. The cases were classified as mild, moderate and severe as per the Ministry of Health and Family Welfare (MoHFW) guidelines. All the patients were followed till the end of hospital stay. The results were expressed as the mean±standard deviation and percentages. Chi-square test was used to compare the categorical variables, and unpaired t-test was used to compare two discrete variables. A p-value of less than 0.05 was considered significant.

Results: Majority of the patients were unvaccinated (65%) and belonged to the age group of 39-59 years (58.5%). Among the non vaccinated patients, 32.3% had moderate disease, while 35.4% had severe disease. In the vaccinated group, 51.4% had moderate disease, whereas only 28.6% patients developed severe disease. Increased Neutrophil to Lymphocyte Ratio (NLR), D-dimer levels, and radiological evidence of pneumonia in chest radiology were witnessed in both groups. Inflammatory markers between the vaccinated and unvaccinated groups did not show any statistical significance (p>0.05). A total of 12 (6%) patients died, out of which five were vaccinated (p=0.6).

Conclusion: Vaccination is found to be protective in terms of disease severity and mortality. Vaccination of all individuals is recommended to curb the wrath of the virus.

Keywords: Coronavirus disease-2019, Morbidity, Mortality vaccines, Severe acute respiratory syndrome-coronavirus-2

INTRODUCTION

The second surge of COVID-19 has hit various parts of the world, with many countries reporting more patients in intensive care or high dependency units. Many deaths have been attributed to lack of timely hospitalisation, oxygen support, medicines, and physician care [1,2]. Some places like Northern Italy, however, have reported a lesser in-hospital mortality and use of mechanical ventilation during the second wave [3]. The second surge of cases in India started around March 2021, after a brief period of recession in the number of reported cases [4]. The number of cases in India rose sharply between March and May, 2020 and became the third leading country by April 10, 2021 [5]. The increase in COVID-19 transmission in India was due to several potential factors like increase in cases of Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) variants with increased transmissibility, along with reduced adherence to public health and social measures [6].

In its weekly epidemiological update released on 11th May, 2020, the World Health Organisation (WHO) declared the B.1.617 lineage of the virus as a 'variant of concern'. The lineage was first reported in India in October 2020 [7]. In addition, the B.1.1.7 variant from the UK was also circulating throughout India, along with the P.1 lineage from Brazil, and the B.1.351 lineage from South Africa [7]. Moreover, the Indian SARS-CoV-2 Consortium on Genomics (INSACOG) was formed on 25th December, 2020 to carry out genomic sequencing and analysis of circulating COVID-19 viruses. It reported mutations in variants that could evade immunity and had increased infectivity [7]. These new variants have also contributed to the surge of the second wave of COVID-19 infection in India. In Odisha, where the index study was conducted, as on 23rd May 2021 there were 6,92,382 confirmed cases with 5,89,610 recoveries [8].

To mitigate the health hazards due to COVID-19, the Government of India started the vaccination programme on 16th January, 2022 with population above 60 years getting the first priority [9]. In India, as on May 23, 2021, a total of 10.9 percent of population has been vaccinated for the first time and three percent population have obtained full vaccination [10]. The risk of COVID-19 recurrence or re-infection is currently unknown, although few have been described in case reports [11,12]. Studies from western countries have reported lesser hospitalisation, requirement of invasive ventilation and death in vaccinated people [13,14]. A study from India also revealed lower mortality among vaccinated group [15].

The study was aimed to determine the clinical, laboratory and radiological features of COVID-19 confirmed cases admitted in a dedicated COVID-19 hospital during the second wave of the pandemic and to compare these data between vaccinated and non vaccinated patients.

MATERIALS AND METHODS

The single centre, prospective observational study was conducted at a tertiary care hospital at Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India. The study spanned between May, 2021 and June, 2021. The study was approved by the Institutional

Ethics Committee (vide letter number KIIT/KIMS/IEC/678/2021 dt. 31.05.21) (CTRI registration: CTRI/2021/06/034269).

Inclusion criteria: All COVID-19 Reverse Transcription-Polymerase Chain Reaction (RT-PCR)-tested patients ≥18 years of age who were admitted to the dedicated COVID-19 hospital, KIMS during the study period were included.

Exclusion criteria: Pregnant females were not included in the study.

Study Procedure

A detailed clinical history including clinical features, co-morbidities and vaccination status against COVID-19 was recorded. All patients were evaluated for complete blood picture, biomarkers like C-reactive Protein (CRP), D-dimer, chest radiograph and/or High Resolution Computed Tomography (HRCT) thorax. The patients were triaged as mild, moderate and severe as per MoHFW criteria and treated as per WHO guided standard protocol for COVID-19 illness in wards or intensive care units [8]. The cases were defined as follows:

Mild disease: Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.

Moderate disease: Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including SpO_2 ≥90% on room air.

Severe disease: Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) plus one of the following: respiratory rate >30 breaths/min; severe respiratory distress; or SpO_2 <90% on room air.

All patients were followed-up till the end of their hospital stay. The discharge criteria for patients included:

- Three days of being afebrile
- No supplemental O_2 requirement
- Haemodynamic stability
- Normal or reducing biomarkers

STATISTICAL ANALYSIS

The results are expressed as the mean±standard deviation and percentages. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 19.0. The chi square test was used to compare the categorical variables. The unpaired t-test was used to compare two discrete variables. The one way analysis of variance will be used to compare more than two discrete variables. A p-value of less than 0.05 was considered significant.

RESULTS

Among the 200 cases included in the study, 130 (65%) were unvaccinated, while 70 (35%) were vaccinated with either single or both doses of COVID-19 vaccine. Males predominated both the groups (70% and 74.3%, respectively). Majority of the patients belonged to the age group of 39-59 years [Table/Fig-1]. Severe disease was predominantly seen in the unvaccinated group (35.4%), while the vaccinated group commonly had a moderate disease (51.4%). The mean duration between vaccination and onset of symptoms was 5.8±2.23 days in mild disease, 4.35±1.65 days in moderate disease, and 6.23±3.3 days in severe disease (p=0.71).

Cough and breathlessness were the most common pulmonary complaints, which were more so in patients with severe disease. Fever was the most common extrapulmonary symptom. Diabetes mellitus and hypertension were the most common co-morbidities reported.

Mean NLR and biomarkers like CRP, and D-dimer were least in patients with mild disease and increased with disease severity. The comparison of these values between vaccinated and unvaccinated group was not statistically significant [Table/Fig-2-5].

Group	Severity	Age group (years)				Gender	
		N (%)	18-38	39-59	≥60	Male	Female
Non vaccinated (n=130)	Mild	42 (32.3%)	17	24	1	28	14
	Moderate	42 (32.3%)	11	25	6	28	14
	Severe	46 (35.4%)	19	20	7	35	11
Vaccinated (n=70)	Mild	14 (20%)	2	7	5	10	4
	Moderate	36 (51.4%)	1	28	7	26	10
	Severe	20 (28.6%)	1	13	6	16	4
Total		200	51	117	32	143	47

[Table/Fig-1]: Age and gender distribution.

Mild illness n (%)		Non vaccinated 42 (75%)	Vaccinated 14 (25%)	p-value
Age group (years)	18-38 (n=19)	17 (40.48%)	2 (14.3%)	0.07
	39-59 (n=31)	24 (57.14%)	7 (50%)	0.64
	≥60 (n=6)	1 (2.38%)	5 (35.7%)	0.00048
	Mean±SD	45.09±8.07	49.86±13.1	0.3
Gender distribution	Male (n=38)	28 (66.7%)	10 (71.43%)	0.74
	Female (n=18)	14 (33.3%)	4 (28.57%)	0.74
Pulmonary manifestations	Cough	-	9 (64.3%)	<0.00001
	Chest pain	-	-	0.28
	Breathlessness	16 (38.1%)	4 (28.6%)	0.26
Extra pulmonary manifestations	Fever	32 (24.6%)	9 (64.3%)	0.19
	Loose motions	2 (1.5%)	2 (6.7%)	0.1
Co-morbidities	Diabetes mellitus (DM) (n=9)	2 (4.76%)	7 (50%)	0.000
	Hypertension (HTN) (n=10)	1 (2.38%)	9 (64.28%)	<0.000
Laboratory evaluation (Mean±SD)	Neutrophil to lymphocyte ratio (NLR)	4.89±2.126	4.33±2.34	0.52
Biomarkers (Mean±SD)	CRP (mg/L) (Range: <5)	40.25±52.27	51.6±56.96	0.63
	d-dimer (ng/mL) (Range: <0.5)	0.7±1.3	0.9±0.832	0.59
Chest X-ray	Normal	32 (76.2%)	10 (71.4%)	0.36
	Increased broncho-vascular markings	7 (16.7%)	4 (28.6%)	0.17
	Consolidation	3 (7.1%)	-	0.15
Outcome	Survived	42 (100%)	14 (100%)	
	Death	-	-	

[Table/Fig-2]: Profile of patients with mild Illness in vaccinated and unvaccinated groups (N=56).
*(Z Test was used to compare two groups)

Category-Moderate illness Total patients (n=78)		Non vaccinated 42 (53.8%)	Vaccinated 36 (46.2%)	p-value
Age group (yrs), n (%)	18-38 (n=12)	11 (26.2%)	1 (2.8%)	0.07
	39-59 (n=53)	25 (59.5%)	28 (77.8%)	0.76
	≥60 (n=13)	6 (1.3%)	7 (19.4%)	0.86
	Mean±SD	46.02±14.02	55.03±8.44	0.0012
Sex distribution, n (%)	Male (n=54)	28 (66.7%)	26 (72.2%)	0.29
	Female (n=24)	14 (3.3%)	10 (27.8%)	0.29
Pulmonary manifestations, n (%)	Cough	-	23 (63.9%)	<0.00001
	Chest pain	-	-	0.17
	Breathlessness	23 (54.8%)	18 (50%)	0.33
Extra pulmonary manifestations, n (%)	Fever	19 (45.2%)	16 (44.4%)	0.7
	Loose motions	2 (4.8%)	2 (55.6%)	1

Co-morbidities, n (%)	Diabetes mellitus (DM) (n=21)	7 (16.7%)	14 (38.9%)	0.3
	Hypertension (HTN) (n=13)	6 (14.3%)	7 (19.4%)	0.85
	Sickle cell disease (SCD) (n=2)	-	2 (5.6%)	0.36
	Coronary artery disease (CAD) (n=2)	1 (2.4%)	1 (2.8%)	1
	Cerebro-vascular accident (CVA) (n=1)	-	1 (2.8%)	0.5
Laboratory evaluation (Mean±SD)	Neutrophil to lymphocyte ratio (NLR)	5.27±4.7	4.33±2.62	0.2965
Biomarker (Mean±SD)	CRP (mg/L) Range: <5	86.66±79.65	102.78± 94.157	0.4
	D-dimer (ng/mL) Range: <0.5	1.67±5.26	1.4±2.14	0.78
Imaging- CT severity score, n (%)	≤10	6 (14.2%)	6 (16.7%)	0.77
	10-15	9 (21.4%)	12 (33.3%)	0.23
	>15	22 (52.4%)	10 (27.8%)	0.027
Outcome, n (%)	Survived	38 (90.5%)	33 (91.7%)	0.85
	Death within 14 days of admission	3	2	
	Death beyond 14 days of admission	1	1	

[Table/Fig-3]: Profile of patients with moderate illness in vaccinated and unvaccinated groups (N=78).
*(Z Test was used to compare two groups)

Category-Severe illness (ICU admitted cases) Total patients (n=66)		Non vaccinated 46 (69.7%)	Vaccinated 20 (30.3%)	p-value
Age group (years), n (%)	18-38 (n=20)	19 (41.3%)	1 (5%)	0.05
	39-59 (n=33)	20 (43.5%)	13 (65%)	0.49
	≥60 (n=13)	7 (15.2%)	6 (30%)	0.88
	Mean±SD	46.96±11.45	58.19±11.62	0.0004
Gender distribution, n (%)	Male (n=53)	35 (76.1%)	16 (80%)	0.36
	Female (n=15)	11 (23.9%)	4 (20%)	0.36
Pulmonary manifestations, n (%)	Cough (n=48)	30 (65.2%)	18 (90%)	0.018
	Chest pain	-	-	0.25
	Breathlessness (n=57)	40 (86.96%)	17 (85%)	0.4
Extra pulmonary manifestations, n (%)	Fever (n=48)	33 (71.7%)	15 (75%)	0.187
	Altered sensorium (n=1)	1 (2.2%)		0.65
	Anosmia (n=1)	-	1 (5%)	0.5
Co-morbidities, n (%)	Diabetes mellitus (DM) (n=19)	9 (19.6%)	10 (50%)	0.89
	Hypertension (HTN) (n= 20)	9 (19.6%)	11 (55%)	0.8
	Coronary artery disease (CAD) (n=3)	1 (2.2%)	2 (10%)	0.74
	Hypothyroidism (n=1)	1 (2.2%)	-	0.65
Laboratory evaluation, (Mean±SD)	Neutrophil to lymphocyte ratio (NLR)	9.35±6.436	8.03±9.43	0.51
Biomarker (Mean±SD)	CRP (mg/L) Range: <5	106.397±88.84	111.32±89.97	0.8365
	d-dimer (ng/mL) Range: <0.5	1.64±2.08	1.29±1.24	0.54
Imaging- HRCT score, n (%)	≤10 (n=3)	1 (2.2%)	2 (10%)	0.16
	10-15 (n=3)	2 (4.4%)	1 (5%)	0.9
	>15 (n=40)	28 (60.9%)	12 (60%)	0.9
Mortality, n (%)	Survived (n=61)	43 (93.4%)	18 (90%)	0.6
	Death within 14 days of admission	2	2	
	Death beyond 14 days of admission	1		

[Table/Fig-4]: Profile of patients with severe illness in vaccinated and unvaccinated groups (N=66).
*(Z Test was used to compare two groups)

Parameters	Vaccinated group	Unvaccinated group	p-value
CRP (mg/L)	95.2±88.5	90.22±83.69	0.7
D-Dimer (ng/mL)	1.26±1.72	1.52±3.7	0.96
NLR	5.44±5.75	7.03±5.69	0.078

[Table/Fig-5]: Comparison of CRP, D-Dimer and NLR between vaccinated and unvaccinated groups.

The HRCT thorax was done for patients at the time of admission. A Computed Tomography (CT) severity score of more than 15 was predominantly seen in patients with severe disease (60.6%) [Table/Fig-4].

A total of 12 (6%) deaths were reported, out of which 7 (58.3%) were unvaccinated, while 5 (41.7%) were vaccinated. Most deaths in the vaccinated group occurred within 14 days of symptom onset [Table/Fig-6].

Patient's admitted	Duration between vaccination and death	No. of deaths
Patients admitted after 1 dose of vaccine (n=51)	≤14 days	2
	>14 to 28 days	1
Patients admitted after 2 doses of vaccine (n=19)	≤14 days	2
	>14 to 28 days	-

[Table/Fig-6]: Mortality in vaccinated patients.

DISCUSSION

The second surge in COVID-19 cases spread fast in India. There were, however, several differences noted in comparison to the first wave of the pandemic in India. The former affected the younger population and symptoms like shortness of breath were more commonly reported. Newer symptoms like gastro-intestinal and neurological came into picture [16]. Moreover, a part of the population was already vaccinated during the second wave [16]. Although no significant increase in death rate was noted during the second wave, the death rates were alarmingly high owing to the high number of infections [17]. The present study aimed to determine the clinical, laboratory and imaging features of COVID-19 confirmed cases admitted in a dedicated COVID-19 hospital during the second wave of the pandemic and to compare these data between vaccinated and non vaccinated patients.

This study included males and females in the ratio 2.5:1. Majority of the patients belonged to the age group of 39-59 years, with a mean age of 49.96±12.32 years. A study published by Reddy MM et al., from eastern UP reported the mean age of patients during the second wave to be 46.1±16.8 years. A significantly large number of patients belonged to the age groups of 30-44 years, and 45-59 years as compared to the first wave [18]. The study also showed higher number of males being affected during both waves of the pandemic [18]. Kumar G et al., also reported the mean age of patients to be lower during the second wave (48.7 years; p<0.001) with majority of patients belonging to <20 years and 20-34 years. A lesser number of males were affected during the second wave (p=0.02) [19]. The lower mean age of patients during the second

wave were also reported in other countries [20,21]. The higher number of males affected during the first wave was also reported by Rao CM et al., [22].

Cough and shortness of breath were the predominant symptoms, which could be due to the pulmonary involvement. Increased symptomatology in patients during the second wave has been reported previously as well [23]. Kumar G et al., also reported shortness of breath to be a major complaint during the second wave (48.6%; p<0.003) [19]. Extrapulmonary symptoms like gastrointestinal were reported during the second wave of the pandemic [23].

Majority of the patients in the index study had mild (p=0.06) and moderate (p=0.0083) symptoms in both the vaccinated and unvaccinated groups. Severe disease was more common in the non vaccinated group (p=0.32). Singh C et al., reported that severity of disease (30.3% in vaccinated, 51.3% in partially vaccinated and 54.1% in non vaccinated; p=0.035) was significantly lower among vaccinated individuals [24].

Increased levels of inflammatory markers like CRP and D-dimer have been associated with severity of infection [25,26]. A raised NLR has also been associated with severity of disease [27]. This study also showed a similar trend in the above inflammatory markers. There was however no significant correlation between the vaccinated and non vaccinated patients.

Disease enhancement due to vaccine has been studied previously. The proposed mechanism involves a suboptimal humoral response with increased binding to neutralising antibodies thus leading to increased deposition of immune complexes and increased inflammatory response. This could well explain the higher level of CRP in the vaccinated group in our study [28-30].

The recorded mortality was 3.5% in this study. A higher case fatality rate during the second wave has been reported in a report from Chennai [31]. The study by Nath R et al., also supports our study [32]. However, Bogam P et al., reported a lower case fatality rate during the second wave in comparison to the first wave of the pandemic (1.8 per 1000 during first wave and 0.77 per 1000 in second wave) [33]. More deaths were recorded in the unvaccinated group (p=0.6).

Limitation(s)

The study was limited by its small sample size and short duration of only two months during the pandemic.

CONCLUSION(S)

The second wave of the COVID-19 pandemic affected the adult and young population, a scenario much different from the first wave. The usefulness of inflammatory markers like CRP, D-dimer and NLR in predicting disease severity has been well documented. Vaccinated group of people were found to have less chance of developing severe disease. The findings will improve the acceptance of vaccination among the general population. However, COVID appropriate measures and proper control of underlying co-morbidities are indispensable and need to be followed by every individual.

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