

ORIGINAL RESEARCH

Mortality, morbidity and its associations in the second peak of second wave of covid-19: A tertiary care hospital study from Kerala, a southern state in India

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ABSTRACT

Background and aim: The second peak of the second wave of covid-19 in India was least studied. Objective of the study was to assess the mortality, morbidity and its associations in the second peak of second wave of covid-19. **Materials and methods:** This was a cross sectional study conducted at a tertiary care centre in Kerala. Covid patients' demographic details, symptomatology, signs, comorbidities, previous history of covid and duration of hospital stay were recorded. Patients were grouped into those with hypoxia requiring oxygen (O₂) supplementation and those requiring high flow oxygen or ventilatory supports. Patients with oxygen saturation (SpO₂) less than 92 are considered hypoxic. Patients were also grouped into those who received steroids, remdesvir and anticoagulants. **Results:** There were total of 190 patients. The mean age was 61.21 years \pm 17.9 standard deviation (SD). Hypertension was the major comorbidity in 91(47.89%) patients. Twelve patients (6.3%) expired. Sixty-one(32.1%) patients suffered hypoxia requiring oxygen supplementation and 21 patients(11%) required high flow oxygen or ventilatory supports. Age, hypertension and cardiovascular diseases showed significant association to hypoxia. Mortality was less in hypoxic patients on Remdesvir though the association was not significant. **Conclusions:** The second peak of second wave of covid suffered less mortality and morbidity when compared with the first wave and initial peak of second wave. Elderly patients were most hospitalised with significant association to hypoxia. Hypertension was the most common comorbidity and showed significant association to hypoxia. Though mortality was less in Remdesvir group, significant association could not be demonstrated.

Keywords: Covid-19, Morbidity, Mortality

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INTRODUCTION

Covid-19 second wave hit India towards March 2021 but it came to south Indian state of Kerala late towards May 2021. The second wave in India had 2 peaks with a 3-month lull period. In Kerala, the interval between 2 peaks were smaller with the second peak in September 2021. Due to still unknown reasons, Kerala had the major case load in India during thesecond peak of second wave. But the mortality was about 0.5 deaths per 100 confirmed cases and fared among the best in the country, though the initial part of second wave hit the state hard with high daily death rates. Studies that compared the mortality and morbidity between first and second waves showed significantly

higher values in elderly and in those with comorbidities, in both the waves.^[1-4] More treatment options were available during thesecond peak of second wave in Kerala, in addition to Remdesvir and Tocilizumab, mainly targeting the risk population. Vaccination had also started and preference was given to the frontline workers and the at-risk populations like elderly and those with comorbidities. The second wave was mostly due to various lineages of the Delta variant while the later Omicron variant was anyway a milder one with less mortality and not requiring many of the drugs required for Delta variant. Hence this study was conducted to assess the mortality and morbidity and their risk factors in the late phase of

second wave and to compare with the studies in the first wave and initial phase of second wave.

MATERIAL AND METHODS

This was a cross-sectional study conducted in the covid wards and ICU, at a tertiary care centre in Kerala state of India. Institutional ethics committee has approved the study. Objective of the study was to assess the mortality, morbidity and its associations in the second peak of second wave of covid-19. All covid patients admitted between September 2021 and December 2021 were included in the study. Patients' demographic details, symptomatology, comorbidities, previous history of covid and duration of hospital stay were recorded. Patients' vital parameters and clinical signs were assessed. They were grouped into those with hypoxia requiring oxygen (O₂) supplementation and those requiring Bilevel positive airway pressure (BiPAP), High-flow nasal cannula (HFNC), Non-rebreather mask (NRBM) or invasive ventilation. Patients with oxygen saturation (SpO₂) less than 92 are considered hypoxic. All hypoxic patients received oxygen supplementation. Patients were also grouped into those who received steroids, Remdesvir and anticoagulants. Data were

analysed using Statistical Package for the Social Sciences (SPSS) software and associations were looked into.

RESULTS

Total number of patients were 190, in which 98 were males and 92 females. The mean age was 61.21 years \pm 17.9 standard deviation (SD). Patients were grouped into 3 groups- 1) those with hypoxia (less than 92% spo₂) requiring O₂ supplementation, 2) those who required BiPAP, HFNC, NRBM or invasive ventilation and 3) those who had more than 2 weeks hospital stay. Four (2.1%) patients had previous history of covid-19. Forty-four (23.15%) patients received Remdesvir. Mortality had no significant association to age, sex, smoking, alcoholism and any of the comorbidities (Table 1). Hypoxia was significantly associated with age and cardiovascular diseases (Table 2). BiPAP/HFNC/NRBM/ invasive ventilation requirement was significantly higher in elderly and significant association was found to hypertension and cardiovascular diseases (Table 3). Prolonged hospitalisation was not significantly associated with age, sex or any comorbidities, (Table 4).

Table 1: Relation of comorbidities with death and survival.

Characteristics	Group	Survivors 178 patients (93.68%)	Death 12 patients (6.3%)	P value
Age	<40 years	26	0	
	40-60 years	54	1	
	>60 years	98	11	0.053
Sex	Male	93	5	
	Female	85	7	0.559
Diabetes	No	109	8	
	Yes	69	4	0.770
Hypertension	No	95	4	
	yes	83	8	0.236
CKD	No	172	10	
	Yes	6	2	0.083
CLD	No	175	11	
	yes	3	1	0.231
Cardiovascular diseases	No	138	7	
	yes	40	5	0.159
Respiratory diseases	No	151	10	
	Yes	27	2	1.00
Connective tissue disease	No	175	12	
	Yes	3	0	1.00
Alcoholism	No	166	11	
	yes	12	1	0.584
Smoker	No	164	11	
	yes	14	1	1.00

(CKD- Chronic Kidney disease, CLD- Chronic liver disease)

Table 2: Association between hypoxia requiring oxygen supplementation and patient characteristics.

Characteristics	Group	Hypoxia requiring O ₂ , 61 patients (32.1%)	No O ₂ requirement, 129 patients (67.89%)	P value
Age	<40 years	2	24	
	40-60 years	18	37	

	>60 years	41	68	0.008
Sex	Male	28	70	
	Female	33	59	0.351
Diabetes	No	36	81	
	Yes	25	48	0.635
Hypertension	No	30	69	
	yes	31	60	0.642
CKD	No	58	124	
	Yes	3	5	0.713
CLD	No	58	128	
	yes	3	1	0.098
Cardiovascular diseases	No	41	104	
	yes	20	25	0.047
Respiratory diseases	No	55	106	
	yes	6	23	0.196
Connective tissue disease	No	60	127	
	yes	1	2	1.000
Alcoholism	No	57	120	
	yes	4	9	1.000
Smoker	No	53	122	
	yes	8	7	0.085

(O₂- Oxygen, CKD- Chronic Kidney disease, CLD- Chronic liver disease)

Table 3: Association between BiPAP/HFNC/NRBM/invasive ventilation requirement and patient characteristics.

Characteristics	Group (Total 190 patients)	BiPAP/ HFNC/ NRBM/ invasive ventilation, 21 patients (11.05%)	Not requiring BiPAP/ HFNC/ NRBM/ invasive ventilation, 169 patients (88.94%)	P value
Age	<40 years	0	26	
	40-60 years	4	51	
	>60 years	17	92	0.036
Sex	Male	12	80	
	Female	9	89	0.489
Diabetes	No	13	104	
	Yes	8	65	1.000
Hypertension	No	6	93	
	yes	15	76	0.035
CKD	No	19	163	
	Yes	2	6	0.217
CLD	No	19	167	
	yes	2	2	0.061
Cardiovascular diseases	No	10	135	
	yes	11	34	0.002
Respiratory diseases	No	19	142	
	yes	2	27	0.747
Connective tissue disease	No	21	166	
	yes	0	3	1.000
Alcoholism	No	20	157	
	yes	1	12	1.000
Smoker	No	17	158	
	yes	4	11	0.067

(BiPAP- Bilevel positive airway pressure, HFNC- High-flow nasal cannula, NRBM- Non-rebreather mask, CKD- Chronic Kidney disease, CLD- Chronic liver disease)

Table 4: Association between duration of hospital stay and patient characteristics(total -189 patients)

Characteristic	Group (Total 189 patients*)	Less than 2 weeks hospital stays, 164 patients (86.77%)	More than 2 weeks hospital stays, 25 patients (13.22%)	P value
Age	<40 yrs	26	0	
	40-60 yrs	45	9	
	>60 yrs	93	16	0.056
Sex	Male	77	14	
	Female	87	11	0.456
Diabetes	No	98	18	
	Yes	66	7	0.424
Hypertension	No	86	13	
	Yes	789	12	0.912
CKD	No	158	23	
	Yes	6	2	0.316
CLD	No	161	24	
	Yes	3	1	0.448
Cardiovascular diseases	No	127	17	
	Yes	37	8	0.479
Respiratory diseases	No	139	21	
	Yes	25	4	1.000
Connective tissue disease	No	161	25	
	Yes	3	0	1.000
Alcoholism	No	152	24	
	Yes	12	1	1.000
Smoker	No	152	22	
	Yes	12	3	0.471

(*One case of stroke was not included as he was transferred to a nearby hospital after 1week and discharged from there after 2 weeks.So total 189 patients.)

Out of the 190 patients 104 patients received anticoagulants, 44 received Remdesvir and 90 received steroids. Among patients who received Remdesvir, 5 patients (11%) expired, 16 patients received O₂ supplementation in 1st week, 31 patients in the 2nd week and 7 patients in the 3rd week. In the same group, 3 patients received either BiPAP/HFNC/NRBM/invasive ventilation in the 1st

week and 6 patients each in the 2nd and 3rd week. Out of 61 hypoxic patients, relation of Remdesvir, steroids and anticoagulants with death, duration of stay and BiPAP/ HFNC/ NRBM/ invasive ventilation is given in Table 5. Though mortality was less in Remdesvir group compared to non-Remdesvir, hypoxic group, there was no significant association (P=0.09).

Table 5: Outcome of hypoxic patients receiving Remdesvir, steroids and anticoagulants.

Hypoxic patient characteristics (n=61)	BiPAP/ HFNC/ NRBM/ invasive ventilation	>2 weeks hospital stays	Death
Patients on Remdesvir (n= 38)	11 (28.94%)	16 (42.10%)	5 (13.15%)
Patients not on Remdesvir (n= 23)	10 (43.47%)	6 (26.08%)	7 (30.43%)
Patients on steroids (n= 54)	19 (35.18%)	20 (37%)	9 (16.6%)
Patients not on steroids (n= 7)	2 (28.57%)	2 (28.57%)	3 (42.8%)
Patients on anticoagulants (n= 57)	20 (35.08%)	22 (38.59%)	11 (19.29%)
Patients not on anticoagulants (n= 4)	1 (25%)	0	1 (25%)

(BiPAP- Bilevel positive airway pressure, HFNC- High-flow nasal cannula, NRBM- Non-rebreather mask)

DISCUSSION

Though there was a late peak for the second covid wave, most of the covid studies and trials were done during the first wave and the first peak of second wave. Studies during the second peak of second wave are less as this period was comparatively less severe, the virus itself was shifting to a less severe variant and covid vaccination was on its way to maximum immunisation coverage among the high-risk

groups. Our study was aimed to assess the mortality, morbidity and its association with various patient characteristics, the effect of Remdesvir, steroids and anticoagulants in the late phase of the second wave. Many single centre studies in India showed that majority of the deceased in both waves were older than 45 years and mean age of admitted patients in most of these studies were more than 50 yrs⁵⁻⁷. In an Indian registry based observational study by National Clinical

Registry for Covid-19(NCRC)which included cases between September 2020 to May 2021from many different states in India(outside Kerala),mean age of the patients in the second wave was significantly lower compared to the first wave [48.7 year vs. 50.7year, $P<0.001$] with higher proportion of patients in the younger age group intervals of <20 years and 20-39 years⁸.But in authors' study conducted in the second peak of second wave,mean age group was again shifted to higher age.Elderly people who were spared during the first wave and the first phase of second wave, were involved in the second peak which comes from the fact that only 4 patients had previous history of covid and covid immunisation was on its half way.As per study by NCRC,approximately 70% of the admitted patients were ≥ 40 years of age in both waves of the pandemic.Butin authors' study, 86% of the admitted patientsin the second peak ofsecond wavewere of the ≥ 40 years age group.

Age was significantly associated with hypoxia⁹and use of BiPAP/HFNC/NRBM/invasive ventilation. This applies to later peak of second wave also, which implies that elderly are still at a risk for disease severity.Comorbidities were significantly a risk factor for disease severity in covid-19^{10, 11}. But in author's study,significance was only found for coronary artery disease and hypertension.In a metaanalysis done in the year 2020 to assess the impact of previous coronary artery disease on covid-19,it was found that there was significant association between coronary artery disease and disease severity in covid but not on mortality¹².Hypertension is reported as the major comorbidity among admitted covid patients in many studies^{13, 14}including authors' study. Pranata et al demonstrated that hypertension increased the severity of infection, ARDS, and mortality in covid-19 patients¹⁵.Hypertension was also the leading comorbidity among covid-19 deaths¹⁴.

Mortality and BiPAP/ventilator use in authors study was very low,6.3% and 11% respectively.Only 32% patients had hypoxia.In NCRC trial, mortality was 13.3% and 10.2% for the second and first waves respectively. Fifty percent patients had hypoxia in the second wave and 43% in the first wave¹⁶.In another retrospective study done based on medical records in New Delhi,the mortality was 19.2% in the first wave and 24% in the second wave¹⁷.These values show that compared to first wave and initial peak of second wave, the late peak of the second wave was a less severe one.One of the possible reasons for the less severity is the increased prevalence of covid antibodies in the general population after the massive initial peak of second wave. According to the fourth nationwide COVID-19 serosurvey in India conducted between June and July 2021, about two-thirds of India's population had SARS-CoV-2 antibodies which was only 24% during the period from December 2020 to January 2021¹⁸.

Remdesvir use was not significantly associated with increased survival,though mortality rate was lower

among hypoxic patients on Remdesvir(13%) compared to hypoxic patients not on Remdesvir(30%).Similarly, among Remdesvir patients, BiPAP/NRBM/HFNC/invasive ventilator use was lesser(28.9%) than those not on Remdesvir (43.4%).But the hospital stay was prolonged more in Remdesvir patients(42.1%) when compared to those not on Remdesvir(26%). In an individual patient data meta-analysis based on RCTs published between January 2020 and March 2021,Remdesvir was shown to reduce mortality in patients hospitalised with COVID-19 who required no or conventional oxygen support¹⁹. In another retrospective cohort study comparing Remdesvir and best supportive care , treatment with Remdesvir was associated with lower mortality rates²⁰.

CONCLUSION

Importance of second peak in the second wave of covid-19 is that it came after the massive and fatal initial peak of second wave. Compared to the first wave and initial peak of second wave, second peak of second wave had less mortality and morbidity.Elderly were still the most hospitalised with significant association to hypoxia.Hypertension was the most common comorbidity and showed significant association to hypoxia.Though mortality was less in Remdesvir group,significant association could not be demonstrated.

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