Comparison of Demography, Resource Utilization and Outcomes of COVID 19 patients admitted during First and Second waves at a tertiary care institute in Kanyakumari, South India

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Abstract:

Introduction: The novel Coronavirus disease 19 (COVID-19) affected India, predominantly in two time periods – the first wave from March to December 2020, and the second wave that raged from April to July 2021. Although the time duration of second wave was shorter than the first, the onslaught of the disease was much more severe during the second wave. **Objective:** To compare the demographic characteristics and clinical outcomes of COVID-19 patients admitted during the first and second pandemic waves. **Method:** Demographic characteristics, duration of hospitalization, critical unit admission, and mortality data of 137 and 345 COVID-19 positive individuals, from first and second waves respectively, were retrospectively analyzed in a teaching hospital in South India. Descriptive statistics, Independent t test, chi square tests and regression analysis were used for statistical analysis, with significance level prefixed at 5%. **Results:** Median age of hospitalisation was 46.2 years and 48.39 years during first and second waves respectively, with male preponderance in second wave. There was a statistically significant difference in mean duration of stay (9.04 days v/s 7.53 days), mean Spo2 at admission (98.4% v/s 96.6%), ventilation requirement (1.5% v/s 8.7%), oxygen requirement and ICU care between the two waves. **Conclusion:** During the second COVID wave, significantly higher hospitalisation rates, intensive care requirements and inpatient mortality was observed. Elevated C Reactive Protein levels, lymphocytopenia, history of diabetes and other co-morbidities were associated with poor outcomes in both waves.

Key Words : COVID-19, Critical care, Demography, Outcome

Introduction:

Following the initial outbreak in Wuhan, China, the global Coronavirus disease 2019 (COVID-19) pandemic began in March 2020. It has since spread to every country on the planet.[1] It is a respiratory disease of varying severity caused by the SARS-CoV-2 virus.[2] India, the second most populous and diverse country, bore the onslaught of the first COVID-19 wave from March to December 2020. The second wave began abruptly in April 2021 and gradually declined by July 2021.[3] The second wave came as a surprise, putting the under-prepared health-care system under severe strain. The increase in cases was rapid, and media organizations reported a shortage of essential medicines, oxygen, and hospital beds.[4-5]

The literature on similarities and differences in disease characteristics between the two waves in India is limited to a few studies from tertiary care centres based in Indian cities. The various disease characteristics and predictors of adverse clinical outcomes from different hospital settings need to be explored. Such a comparative study between clinical courses of different strains of pandemic causing virus will help in preparation and management of future outbreaks. This study was aimed at identifying the differentials in demography, clinical course and the outcomes of RT-PCR positive hospitalized COVID-19 patients during the first and second waves in a rural teaching hospital located in southern part of India.

Method:

This record based study was conducted in a tertiary care teaching institute in Kanyakumari district, Southern Tamil Nadu, India. For the purposes of this study, COVID Wave-1 was defined as the period from April to December 2020, and COVID Wave-2 as the period from April to June 2021[3] Case files of 137 COVID-19 patients in COVID wave 1 and 485 patients in COVID wave 2, confirmed with Real Time Polymerase Chain Reaction (RT-PCR) positive results, were retrospectively analysed. The study was approved by Institutional ethics committee [IHEC No: 1/ Protocol no: 56/ 2021 dated 06-09-2021].

All adult and pediatric patients who were hospitalised in COVID wards with positive RT-PCR, obtained from a nasopharyngeal swab were included in the study. Those patients who got discharged against medical advice were excluded from the study. Along with the demographic data, duration of hospitalization, ICU admission, and mortality data of both the waves were collected, tabulated, and analysed. Clinical outcomes like admission to Intensive care units (ICU), oxygen supplementation required, Non Invasive Ventilation (NIV) required were recorded. Biochemical parameters like C Reactive protein (CRP) levels, D DIMER levels, lymphocyte counts (LC) were recorded. Lymphocyte counts less than 20% were defined as lymphocytopenia. Clinical history of diabetes (DM), hypertension and other co-morbid medical conditions like cardiovascular diseases (CAD), chronic kidney disease (CKD), hypothyroidism, malignancy, etc were also recorded. Discharge was advised when the patient turned COVID negative on a RT PCR test on nasopharyngeal swabs.

Statistical Package for the Social Sciences (SPSS) version 22 was used for statistical analysis. Descriptive statistics, Fishers exact tests, Independent t tests, and chi square tests were used for statistical analysis. Categorical variables were compared between waves using a Chi square (χ2) test and Fishers exact test. Significance level was fixed at 5%.

Results:

In this study, 137 patients admitted during the first wave of COVID-19 during the months of April –December 2020 and 345 patients admitted with confirmed COVID during second wave in April –June 2021 were included, to give a total sample of 482 patients. The age group distribution of the patients across both waves is as given below in Figure 1.

In the first wave, there were 137 patients admitted. Mean age of the patients was 46.2 years + Standard deviation (SD) of 18.5 years. A majority of patients were of the 18-59 age group (66.4%), while elderly patients (aged more than 60 years) formed slightly more than a quarter of the patients (27%) and children below 18 years formed 6.5% of the patients. Also, majority of patients admitted were males when compared to females (54% versus 46%).

In Second wave, the mean age of the patients was higher than 2020 wave at 48.39 years ($\pm$ 19.3 SD). However this was not statistically significant (p>0.05; Independent t test). While the 18-59 year age group remained the predominant group out of the three age groups at 59.4%, more elderly people and children were admitted at 33% and 7.5% of the total patients respectively. There was a similar gender pattern as seen in previous year with 54.8% males versus 45.2% females.

In first wave, history of Diabetes Mellitus was seen in 35% cases and hypertension in 22.6% cases. Other co morbid conditions were seen in 19.7% cases. In second wave, out of the 345 cases admitted, 45.8% (158) cases had pre existing Diabetes Mellitus and 19.4% (67 cases) had pre existing hypertension. Moreover, 13.3% cases had some other associated co-morbid condition. The overall prevalence of co-morbidities other than hypertension and diabetes in this study across both waves was 15.14% with predominant conditions being CAD (39.7%), CKD (10.9%), malignancy (10.9%) and hypothyroidism (8.2%).

Clinical course:

The clinical course of patients in hospital during first wave ranged from 1 to 77 days of hospital stay with the mean duration being 9.04 days ($\pm$ 2.9 days SD). The mean SpO2 at the time of hospital admission was 98.4% ($\pm$ 1.5 %). Out of the 137 patients admitted during the first wave, 1 patient died giving a case fatality rate (CFR) of 0.7% and referral rate was 4.38% (6 referrals). The recovery rate was 94.89% with 130 cases being discharged after turning COVID RT-PCR negative. ICU care was required in 1.5% cases with 1.5% cases requiring NIV and 0.7% (1case) requiring intubation. Oxygenation was supplemented in 7.4% cases. Dialysis was not required for any case during first wave. Enoxaparin and steroids remained the mainstay of treatment in 74% and 29.4% cases respectively with Remdesivir being used only in 5.8% cases. The mean values of biochemical parameters are as given below in Table 1. The proportion of cases with Lymphocyte count less than 20% (lymphocytopenia) was 26.3%.

During second wave, the clinical course ran for a shorter mean duration of 7.53 days ($\pm$/- SD 5.2 days). This difference in mean days of hospital stay was statistically significant (independent t test; $p < 0.05$). The mean SpO2 at the time of admission was also lower, i.e, 96.65% ($\pm$ 2.9%). This was also statistically significant as per independent t test with a p value less than 0.05. The recovery rate was 89.85% and CFR was 2.3%. The proportion of cases with lymphocytopenia was 31.3%.

A higher proportion of patients required ICU care in Second wave than first wave, this difference being statistically significant ($p<0.05$). Moreover, patients needing intubation (2.6%), NIV (8.7%), oxygenation

Figure 1: Age distribution of patients in first wave (N1=137) versus Second wave (N2=345)
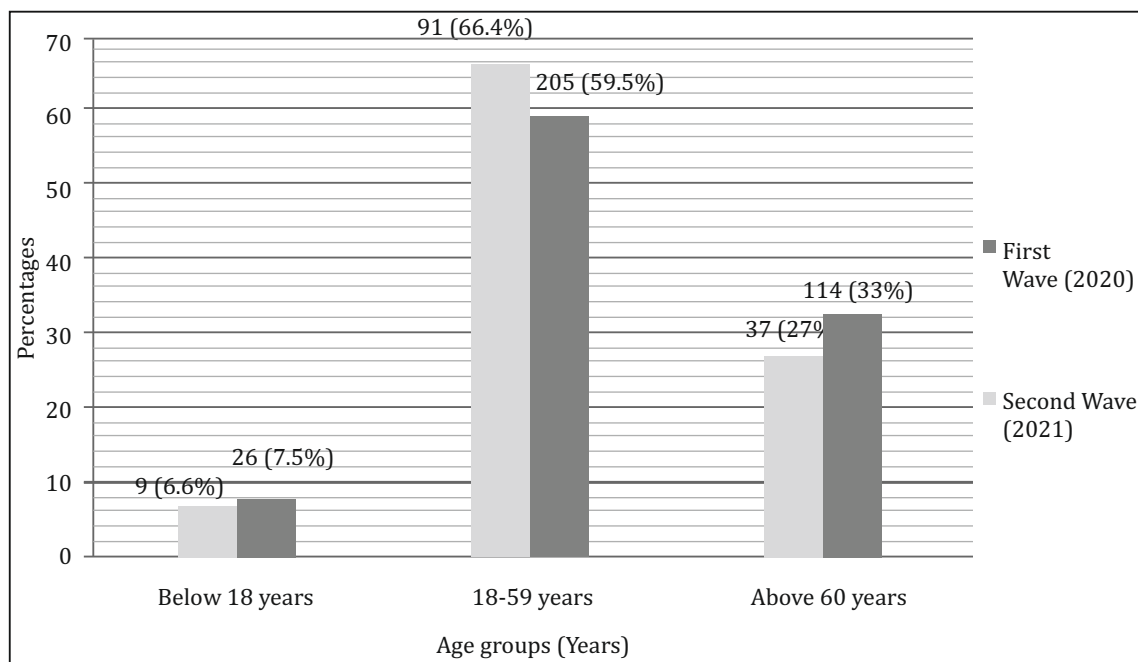
Table 1 : Comparison of Clinical Course And Biochemical Parameters in First wave (N1=137) Versus Second wave (N2=345)

Clinical course	First wave (N1=137)	Second wave (N2=345)	Statistical test value	p value
	n (%)	n (%)		
Steroids treated	40 (29.4%)	162 (47%)	11.66[#]	0.001*
Remdesivir Treatment	8 (5.8%)	57 (16.5%)	9.59[#]	0.002*
Enoxaparin treated	21 (74%)	162 (47%)	37.73[#]	<0.001*
ICU care required	2 (1.5%)	31 (9%)	8.708[#]	0.003*
Oxygenation required	10 (7.4%)	48 (13.9%)	3.959[#]	0.047*
Intubation required	1 (0.7%)	9 (2.6%)	1.7[#]	0.192
NIV required[+]	2 (1.5%)	30 (8.7%)	8.23[#]	0.004*
Number of deaths	1 (0.7%)	8 (2.3%)	1.35[#]	0.245
Biochemical parameters				
Mean CRP level	20.03	22.26	-0.67[$]	0.503
Mean D- DIMER	342.89	398.07	-0.733[$]	0.464
Mean Ferritin	269.84	322.43	-1.067[$]	0.287
Mean Lymphocyte count	29.18	26.76	1.801[$]	0.072
Cases with Lymphopenia	36 (26.3%)	108 (31.3%)	1.18[#]	0.277

#Chi square test; $Independent t test; *statistically significant (p<0.05); +NIV- Non Invasive Ventilation

(13.9%) and dialysis (1.2%) also increased in second wave. The differences in patients requiring Remdesivir, Steroids and Enoxaparin in 2021 versus 2020 were also statistically significant as shown in detail above in Table 1.

Factors affecting clinical course and outcomes:

The detailed description of factors affecting the clinical outcomes of mortality, NIV, intubation and O2 supplementation are described below in Table 2. Patients who had co-morbid conditions like CAD, CKD, etc were statistically more likely to die than patients without co-morbid conditions. Deaths also had a statistically significant association with elevated CRP levels. There was a statistically significant higher rate of intubation in patients who had co-morbid conditions and elevated CRP levels.

NIV was statistically associated more with diabetic patients, patients with co-morbidities, elevated CRP categories and lymphocytopenia.

Oxygenation was required more for male patients, patients with co-morbidities, diabetes, lymphocytopenia and elevated CRP levels. All these associations were highly statistically significant with p value less than 0.01. Conversely, a higher proportion of patients below 60 years required oxygenation when compared to elderly patients and this was statistically significant.

Dialysis requirement was higher in patients with co-morbid conditions than those without any associated conditions (p value 0.012, Fisher's exact test). This may be because upto 10.96% (8) of patients with co-morbid conditions had CKD and COVID could have aggravated their renal dysfunction.

Table 2 : Factors affecting clinical outcomes in COVID patients across both waves (N=482)

Factors	N	Deaths		Intubation		NIV		O2 theraphy	
		Yes n=9	Critical value (p)	Yes n=10	Critical Value (p)	Yes n=32	Critical value (p)	Yes n=59	Critical value (p)
Comorbid conditions									
Present	73	8[*]	38.81[#]	8[*]	33.42	12[*]	0.001[$]	20[*]	18.39#
Absent	409	1	<0.001	2	<0.001	20		39	<0.001
Elevated CRP									
Yes	256	8[*]	4.71[#]	9[*]	0.023[$]	25[*]	8.61[#]	47[*]	19.03[#]
No	226	1	0.03	1		7	0.003	12	<0.001
Lymphocytopenia									
Present	144	4	0.462[$]	5	0.751[$]	20[*]	17.41[#]	32[*]	19.04[#]
Absent	338	5		5		12	<0.001	27	<0.001
Diabetes Mellitus									
Present	206	4	0.586[$]	5	0.751[$]	20[*]	5.47[#]	37[*]	10.96[#]
Absent	276	5		5		12	0.019	22	0.001
Gender									
Males	263	6	0.52[$]	7	0.36[$]	19	0.32[#]	42[*]	7.49[#]
Females	219	3		3		13	0.572	17	0.006
Age category									
>60 years	151	4	0.471[$]	5	0.299[$]	15	3.85[#]	28	8.13[#]
<60 years	331	5		5		17	0.05	31[*]	0.004

*Statistically significant (p<0.05)# Chi-square test; $Fishers exact test

Regression analysis was done on the factors which had a statistically significant association with clinical course outcomes using binary logistic regression model. The statistically significant predictors of requirement of NIV and oxygen supplementation therapy after excluding the factors not significant from the regression model are as given below in Table 3.

The total number of Healthcare Workers (HCW) infected was 17 and 14 in the first and second waves respectively. All infected HCWs were asymptomatic or had mild disease and were discharged after short hospitalization. There was no intensive care requirement or mortality among HCWs.

Discussion:

Despite aggressive and extensive measures to control the pandemic by governments around the world, the SARS-CoV-2 virus continues to mutate into highly contagious variants. The second major variant of concern, the delta CoV (Indian strain; B.1.617.2) caused widespread illness during second wave. This was the reason for the phenomenal speed of the COVID 19 spread during the second wave. Even though preferential vaccination for individuals above 60 years was provided by the government of India, due to limitations in vaccine coverage it did not succeed in bringing down the hospitalization in that age group during second wave.[6] Due to closure of educational institutions children and young adults faced less exposure during both the waves.[7,8]

In this study, a statistically significant difference was found in mean duration of stay (9.04 days v/s 7.53), mean SpO_2 admission (98.4% v/s 96.6%), NIV requirement (1.5% v/s 8.7%), oxygen requirement (7.4% v/s 13.9%), ICU care, and use of Remdesivir,

Table 3 : Regression Model of Predictors of Adverse Clinical Outcomes in COVID cases (N=482)

Outcome	Predictors	Nagelkerke R^2	P value	Adjusted OR
NIV	Elevated CRP	0.144	0.048*	2.49
	Lymphocytopenia		0.005*	3.09
	Co-morbid conditions		0.018*	2.67
Oxygen therapy	Elevated CRP	0.174	0.001*	3.13
	Lymphocytopenia		0.007*	2.25
	Co-morbid conditions		0.006*	2.5
Intubation	Elevated CRP	0.287	0.086	6.29
	Co-morbid conditions		<0.001*	21.85
Death	Elevated CRP	0.338	<0.001*	44.09
	Co-morbid conditions		0.123	5.33

*Statistically significant (p<0.05)

Steroids, Enoxaparin in treatment between the first and second COVID waves. A retrospective cross-sectional study from Dhaka Medical College Hospital among 100 confirmed COVID-19 patients in May 2020 showed a younger mean age of patients as 41.7 ± 16.3 years with a male preponderance (63%). Hypertension (21%), diabetes mellitus (16%), heart diseases including ischemic heart disease (IHD) (8%) and renal diseases including chronic kidney disease (CKD) (8%) were frequent co-morbidities.[9] Frequency of comorbid conditions other than diabetes and hypertension in the Dhaka study were similar to the present study, though the mean age in this study was higher (46.2 years) in 2020. The presence of diabetes and hyperglycemia led to worse outcome among COVID patients in this study. Similar correlation was found between diabetes and worse outcome in COVID was also noted in a study by Aman Rajpal et al.[10]

Increase in C Reactive Protein was related to severity of the disease as per this study which was in line with the study conducted by Sharifpour et al in 2020.[11] The incidence of lymphocytopenia was related to have worse outcomes in this study which was similar to the study conducted by Qianwen Zhao et al.[12]   Jain et al reported that, in addition to the older persons, the pediatric and younger individuals were also more infected in India in the second wave, which is not in line with findings in this study.[5] Revathishree K et al described a similar mean age (41years) and gender distribution in first wave in Chennai in 2020. They had a mortality rate of 0.8%, slightly higher than 0.7% mortality rate in 2020 in the present study.[13] However, in the second wave, mortality rate in this study was higher as were the adverse outcomes like ICU admission, use of steroids, NIV etc. This was mirrored in a similar study depicting differentials among 19,852 RT-PCR confirmed COVID-19 patients in first and second COVID waves in North India by Budhiraja et al. They too had higher levels of mortality, up by almost 40%, more O2 therapy, similar ICU admission rates, and more cases requiring invasive ventilation. Also, they had a higher number of hospitalizations in patients with co-morbidities in wave 2.[14] Similar findings were noted in the present study also.

A retrospective study of 550 hospitalised cases of SARS-CoV-2 infection in South Africa[15] compared the characteristics, biological severity markers, treatments, level of care and outcomes of the patients during the two waves. During the second wave the admissions were of significantly older patients,

which are reflected in this study too. Also, there were more patients without any co-morbidities during second wave, which is in contrast to this study. Patients admitted to the ICU and/or were mechanically ventilated were much lower in number during second wave, as opposed to this study. Their observation of overall increased mortality figures in the second wave is in agreement with this study.[15]

Conclusion:

COVID-19 has challenged the Indian healthcare system with its extent, speed of spread and constantly mutating variants. In contrast to first wave in 2020, 2021 wave had more adverse outcomes and mortality, despite shorter duration of hospitalization. Associated comorbid conditions, elevated CRP levels and lymphocytopenia were the predictors of adverse clinical outcomes in COVID identified in the present study.

Declaration:

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Conflict of Interest: Nil

References:

1. Moriarty LF, Plucinski MM, Marston BJ, Kurbatova EV, Knust B, Murray EL et al. Public health responses to COVID-19 outbreaks on cruise ships—worldwide, Feb–Mar 2020. Morbidity and Mortality Weekly Report. 2020 Mar 27; 69 (12):347.

2. Ortiz-Prado E, Simbaña-Rivera K, Gómez-Barreno L, Rubio-Neira M, Guaman LP, Kyriakidis NC et al. H Clinical, molecular epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19), a comprehensive literature review. Diagn Microbiol Infect Dis. 2020 Sep 1; 98(1):115094.

3. Siddiqui AF, Wiederkehr M, Rozanova L, Flahault A. Situation of India in the COVID-19 pandemic: India's initial pandemic experience. Int J Environ Res Public Health. 2020; 17(23):8994.

4. Kumar A. Photojournalism and COVID-19 deaths in India. Media Asia. 2021; 48 (4): 360-362.

5. Jain VK, Iyengar KP, Vaishya R. Differences between First wave and Second wave of COVID19 in India. Diabetes Metab Syndr. 2021 May-June; 15 (3): 1047–1048.

6. Pandey A, Sah P, Moghadas SM, Mandal S, Banerjee S, Hotez PJ et al. Challenges facing COVID-19 vaccination in India: Lessons from initial vaccine roll out. J Glob Health.2021;11: 03083

7. Ranjan R, Sharma A, Verma MK. Characterization of the Second Wave of COVID-19 in India. Current Science 2021 July 10; 121 (1): 85- 93.

8. Mowla SGM, Azad KAK, Kabir A, Biswas S, Islam MR, Banik GC et al. Clinical Profile of 100 Confirmed COVID-19 Patients Admitted in Dhaka Medical College Hospital, Dhaka, Bangladesh. J Bangladesh Coll Physicians Surg. 2020; 38: 29–36.

9. Hossain MI, Parvin S, Islam MS, et al. Demographic profile and outcome of patients admitted to a COVID dedicated hospital in Bangladesh during the second wave. Med (Baltim). 2021; 100 (37): e27281.

10. Rajpal A, Rahimi L, Ismail- Beigi F. Factors leading to high morbidity and mortality of COVID-19 in patients with type 2 diabetes. J Diabetes. 2020 Dec; 12 (12): 895-908.

11. Sharifpour M, Rangaraju S, Liu M, Alabyad D, Nahab FB, Creel-Bulos CM et al. C-Reactive protein as a prognostic indicator in hospitalized patients with COVID-19 PLoS One. 2020 Nov 20; 15 (11): e0242400.

12. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Yet al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. Int J Infect Dis. 2020 Jul; 96: 131-5.

13. Revathishree K, ShyamSudhakar S, Indu R, Srinivasan K. Covid-19 Demographics from a Tertiary Care Center: Does It Depreciate Quality-of-Life? Indian J Otolaryngol Head Neck Surg. 2022 Oct: 74 (suppl 2); 2721-2728.

14. Budhiraja S, Indrayan A, Aggarwal M, Jha V, Jain D, Tarai B et al. Differentials in the characteristics of COVID-19 cases in Wave-1 and Wave-2 admitted to a network of hospitals in North India. [Internet] Accessed on 2022 September 19. Available from: https://www.medrxiv.org/ content/10.1101/ 2021.06.24.21259438v1

15. Maslo CI, Messina A, Laubscher A, Toubkin M, Sitharam L, Feldman C, Richards G. COVID19: A comparative study of severity of patients hospitalized during the first and the second wave in South Africa. [Internet] Accessed on 2022 September 19. Available from: https://www.medrxiv.org/ content/10.1101/2021.05.11.21257033v1