Identifying Risk Factors For ICU Admission During The Second Wave Of COVID 19 In A Tertiary Care Centre In Western India

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Abstract: Background: The substantial morbidity and mortality seen during second wave of coronavirus disease 2019 (COVID-19) pandemic necessitated identifying demographic, clinical and laboratory markers to assist the clinicians in early recognition of severe disease. We aimed to identify new factors or confirm previously identified factors for risk of ICU (Intensive care unit) admission during the second wave of COVID-19 infection. Material And Methods: This retrospective, single-centre study was conducted from April 1 2021-May 30 2021. Data on demographic profile, clinical symptoms, and laboratory findings on admission was collected and compared between ICU and non-ICU patients. Result: Total 440 patients were included. Among these, 184(41.8%) needed ICU admission. The mean age was 52.75±14.46 years. 283(64.3%) patients were males. The most common symptoms were fever (70.7%), cough (65.5%), and shortness of breath (54.1%). As seen in previous studies, mean age, leucocyte count, CRP, S. ferritin, LDH, D-Dimer and comorbidities like diabetes mellitus, COPD, obesity were found more commonly in ICU patients as compared to non-ICU patients. (P= 0.0107, 0.0447 and 0.0314 respectively for diabetes, COPD and obesity). Presence of more than one comorbidity was associated with greater ICU admission (ICU vs. Non-ICU: 92(50%) vs. 99 (38.7%), p=0.0234). Time from symptom onset to hospitalization was also significantly longer in ICU patients (7.5±1.05 days vs 4.0±1.26 days; p=0.004). Conclusion: The study confirms that COVID patients who need ICU admission have significantly higher mean age, leucocyte count, CRP, S. ferritin, LDH, D-Dimer and comorbidity. In addition, COVID patients in ICU had significantly lower s. albumin levels and late presentation to hospital. [Gosai K Natl J Integr Res Med, 2022; 13(2): 71-76, Published on Dated:10/02/2022]

Key Words: Covid 19, Intensive care unit, Risk factors

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Introduction: The outbreak of coronavirus disease 2019 (COVID-19) began in Wuhan, Hubei Province in December 2019 and has rapidly spread throughout the world since then[1]. The World Health Organization (WHO) declared the COVID-19 outbreak a global pandemic in March 2020, and as of 25th March 2022, more than 476 million confirmed cases and more than 6 million deaths have been reported worldwide[2]. Severity of the disease depends on several factors. Studies have shown that patients with comorbidities (diabetes mellitus, hypertension, renal disease, COPD, cardiac disease), history of smoking, male gender and age greater than 60 years were more likely to die or develop undesirable outcomes[3-7].

Knowledge of the association between demographic and clinical factors and different severity and outcome provides insight into the underlying pathophysiological mechanisms (immunity, coagulopathy and comorbidities). This knowledge also guides us to make sound clinical decision, especially in a scenario of shortage in healthcare resources such as ICU beds.

Additionally, exploring demographic factors influencing COVID-19 outcomes can guide policymakers in, for instance, the prioritization of non-pharmaceutical interventions and screening[8]. There are, however, no established prognostic models that reliably predict the need for escalated (intensive care unit, ICU) care or mortality due to COVID-19 infection. Lacking this, effective triage of patients was challenging in a resource-constrained environment especially during the second wave. Here, we aim to see how a COVID patient's characteristics on admission (demographics, clinical features, comorbidities, lab parameters) are linked to the likelihood of being admitted to an Intensive Care Unit (ICU).

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Material & Methods: This was retrospective cohort study, carried out at a 750 bedded tertiary care hospital, at Vadodara, Gujarat, India. All RT-PCR positive patients admitted between April 2021 to May 2021 were included in study. It was conducted after getting approval from the Institutional ethics committee.

Inclusion Criteria: 1. Laboratory (RTPCR) confirmed cases of COVID-19 disease. 2. Age ≥ 18 years.

Exclusion Criteria: 1. Missing data of clinical or laboratory characteristics 2. Who did not give written informed consent.

After obtaining ethical clearance from Institute's ethical committee, the records were obtained from MRD department of the hospital. Data collected include demographics (Age, Gender etc), symptoms (fever, cough, dyspnoea, myalgia, etc.), vital signs at admission (heart rate, blood pressure and respiratory rate), laboratory parameters on admission (CBC, blood glucose level, CRP, D- DIMER, RFT) and radiological findings. Type of disease was defined as mild, moderate and severe disease based on ICMR guidelines[9]. Duration from the onset of symptoms to admission, total length of stay in hospital, and mortality were also recorded.

Two study investigators independently checked the collected data. All cases were divided into ICU and Non-ICU (Admitted in wards) groups. The ICU and Non-ICU groups were compared for demographic features, clinical characteristics, presence of any comorbid conditions, symptom onset to hospitalisation and laboratory and radiological parameters at admission to identify risk factors for ICU admission.

Statistical Analysis: All the collected data was entered in Microsoft excel sheet. The data was analysed using SPSS software (version 22.0).

Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are expressed as frequencies and percentages (%).

Chi square test was applied to compare categorical variables and independent t-test was applied to compare continuous variables, as appropriate. For all the statistical analyses, p-value < 0.05 was considered statistically significant.

Results: A total of 440 hospitalized patients with COVID-19 confirmed by RT-PCR were included in this study. Among these, 184(41.8%) needed ICU admission while 256(58.2%) were managed in COVID designated wards. Mean age of the patients was 52.75±14.46 years There was a significant difference between the ICU and Non-ICU patient with regards to age distribution (55.4±13.04 years in the ICU patients vs 50.8±15.15 years in the non-ICU patients, p=0.0009). 283(64.3%) of the total patients were males and 157 (35.7%) were females.

120 (27.3%) patients had mild disease, 246 (55.9%) had moderate disease and 74 (16.8%) patients had severe disease. The most common comorbidity seen was hypertension (29.8%), followed by diabetes (27.1%), chronic kidney disease (6.1%), cardiovascular disease (3.9%), COPD (3.2%), Obesity (2.3%), thyroid disease (2.3%), stroke (2.1%) and chronic liver disease (1.13%). Comorbidities like diabetes mellitus, COPD and obesity were found more commonly in ICU patients as compared to non-ICU patients, (P= 0.0107, 0.0447 and 0.0314 respectively). We also found that presence of more than one comorbidity was associated with greater ICU admission (ICU vs. Non-ICU: 92 (50%) vs. 99 (38.7%), p=0.0234)(Table 1).

The most common symptoms at presentation were fever (70.7%), cough (65.5%), and shortness of breath (54.1%), sore throat (47.5%), fatigue (42.5%) and headache (37.5%). Less common symptoms were rhinorrhoea (29.1%), myalgia (27.7%), loss of taste (22.5%), loss of smell (20%), diarrhoea (11.3%) and nausea/vomiting (7.9%) Breathlessness was significantly more common in ICU patients (ICU vs Non ICU patients;123 (66.8%) vs. 115 (44.9%), p<0.001), while non-ICU patients had higher rates of loss of taste (15.8% vs. 27.3%; p=0.059) and loss of smell (14.1 % vs. 24.1%; p=0.0128).

Time from symptom onset to hospitalisation was 5.75±2.14 days. Statistically significant difference was noted in ICU vs Non-ICU patients with regards to time from symptom onset to hospitalisation (7.5±1.05 days vs 4.0±1.26 days; p=0.004). (Table 1)

In terms of laboratory investigations, patients admitted in ICU showed significantly higher white blood cell count (12.50±5.1×103 cells/µL vs. 8.58±3.96×103 cells/µL; p< 0.001), CRP

(79.3±50.9 mg/L vs. 48.1±31.7 mg/L; p< 0.001),LDH(1014±538.5U/L vs. 467.7±187.8 U/L; p< 0.001), Ferritin (497.4±512.3 U/L vs. 298.7±237.9 U/L; p= 0.0226), D-Dimer levels (1792±2288 vs. 997.9±1015.3; p-0.0314) and lower albumin level (2.52±0.43 vs.2.98±0.23. p=0.0011) as compared to Non ICU patients. PaO2 level in ABG at admission was also significantly lower in ICU patients when compared to non ICU patients (58.95±20.73vs. 89.86±9.42mmHg; p-0.0011). However, no significant difference was noted in other laboratory parameters like AST, ALT and creatinine levels between the two groups(Table 2).

Table 1: Baseline Demographics And Clinical Characteristics Of Patients With Covid-19 Infection

Parameters	Total (n=440)	ICU (N=184)	Non-ICU (N= 256)	P value
Age (Mean±SD)	52.75±14.46	55.4±13.04	50.8±15.15	0.0009±
Gender				
Male	283 (64.3%)	124 (67.4%)	159 (62.1%)	0.2984
Female	157 (35.7%)	60 (32.6%)	97 (37.9%)	
Type Of Disease				
Mild	120 (27.3%)	0	120 (46.9%)	<0.001±
Moderate	246 (55.9%)	110 (59.8%)	136 (53.1%)	0.1970
Severe	74 (16.8%)	74 (40.2%)	0	<0.001±
Comorbidity				
Hypertension	131 (29.8%)	62 (33.7%)	69 (26.9%)	0.0972
Diabetes Mellitus	119 (27.1%)	62 (33.7%)	57 (22.3%)	0.0107±
Chronic Kidney Disease	27 (6.1%)	16 (8.7%)	11 (4.3%)	0.0901
Chronic Cardiac Disease	17 (3.9%)	11 (5.98%)	6 (2.3%)	0.0890
COPD	14 (3.2%)	10 (5.4%)	4 (1.6%)	0.0447±
Obesity	10 (2.3%)	8 (4.3%)	2 (0.8%)	0.0314
Thyroid Disease	10 (2.3%)	4 (2.2%)	6 (2.3%)	0.9061
Cerebrovascular Diseases	9 (2.1%)	4 (2.2%)	5 (1.95%)	0.8718
Chronic Liver Disease	5 (1.13%)	3 (1.6%)	2 (0.8%)	0.7091
More than one comorbidity	191 (43.4%)	92 (50%)	99 (38.7%)	0.0234±
Symptoms				
Fever	311 (70.7%)	130 (70.7%)	181 (70.7%)	0.9908
Cough	288 (65.5%)	125 (67.9%)	163 (63.8%)	0.4088
Breathlessness	238 (54.1%)	123 (66.8%)	115 (44.9%)	<0.001±
Sore throat	209 (47.5%)	80 (43.5%)	129 (50.4%)	0.1817
Fatigue	187 (42.5%)	85 (46.2%)	102 (39.8%)	0.2181
Headache	165 (37.5%)	65 (35.3%)	100 (39%)	0.4847
Rhinorrhoea	128 (29.1%)	44 (52.4%)	84 (32.8%)	0.0547
Myalgia	122 (27.7%)	47 (25.5%)	75 (29.3%)	0.4475
Loss of taste	99 (22.5%)	29 (15.8%)	70 (27.3%)	0.0059±
Loss of smell	88 (20%)	26 (14.1%)	62 (24.2%)	0.0128±
Abdominal Pain	67 (15.2%)	24 (13.04%)	43 (16.8%)	0.3439
Diarrhea	49 (11.3%)	14 (7.6%)	35 (13.7%)	0.0657
Nausea/Vomiting	35 (7.9%)	15 (8.2%)	20 (7.8%)	0.8967
Symptom onset to hospitalisation	5.75±2.14	7.5±1.05	4.0±1.26	0.004±

COPD- Chronic Obstructive Pulmonary Disease [a]p value indicates difference between ICU and Non ICU patients. P ≤0.05 was considered to be statistically significant (Table 1).

CRP- C reactive protein, LDH- Lactate dehydrogenase, ALT- Alanine aminotransferase, AST- Aspartate aminotransferase, PaO2- Partial pressure of oxygen [a]p value indicates difference between ICU and Non ICU patients. P ≤0.05 was considered to be statistically significant (Table2).

Table 2: Laboratory Findings

Parameter	Normal Range	ICU	Non-ICU	P value
Haemoglobin gm/Dl	12-15	12.07±2.06	11.9±2.21	0.5030
Leucocyte count $\times 10^3$ (cells/µL)	4-11	12.50±5.1	8.58±3.96	< 0.001±
Platelet count $\times 10^5$	1.5-4	2.2±1.16	2.08±1.23	0.5691
CRP	< 3 mg/L	79.3±50.9	48.1±31.7	< 0.001±
LDH	132-248 U/L	1014±538.5	467.7±187.8	< 0.001±
Ferritin	20-250 U/L	497.4±512.3	298.7±237.9	0.0226±
D-Dimer	<500ng/ml	1792±2288	997.9±1015.3	0.0314±
Albumin	3.4-5.4g/dl	2.52±0.43	2.98±0.23	0.0011±
ALT	7-50 U/L	33.43±13.77	36.29±10.36	0.6686
AST	5-40 U/L	24.8±5.59	32.8±12.81	0.2365
Creatinine	0.5-1.2mg/dL	1.27±1.03	1.13±0.70	0.5938
PaO2	80-100mmHg	58.95±20.73	89.86±9.42	0.0011±

Discussion: Although India has been severely affected by SARS CoV infection, real world data of Indian COVID patients is inadequately available. Data regarding the risk factors in patients that lead to severe disease and thus needing ICU care, have been inadequately studied in India. We studied the demographics, clinical features, comorbidities and laboratory parameters of patients on admission to identify the risk factors that lead to greater ICU admissions.

In our study we found that older patients had greater chances of getting severe disease, thus requiring ICU admission. Previous studies have shown that patients more than 60 years of age have more severe disease, requiring ventilatory support leading to greater mortality[10-13]. 64.3% of our patients were males and we did not find gender association in severity or mortality. This was in contrast to a meta analysis conducted by Augusta et al. The results of meta-analysis indicated that male sex was a risk factor for mortality (both in the general population and hospitalized patients); for a lower recovery rate and for disease severity in COVID-19 infected patients[14]. This might be related to delayed admission of females as compared to males.

All our patients who were admitted in ICU had at least one comorbidity. We also found that presence of more than one comorbidity was an independent risk factor for ICU admission. These finings were similar to finding by WHO-China Joint Mission reports that suggested that elderly and those with comorbidities are more susceptible to severe infection[15]. In our study hypertension was the most common comorbidity found followed by Diabetes mellitus. Similar results were found by Alfonso et al[15]. For diabetes, a meta-analysis of six studies with 1527 patients found the prevalence to be twice as high in the ICU/severe group compared to non-severe COVID-19 patients[16]. On disaggregating this outcome into two (non-ICU and ICU groups), we found the prevalence of diabetes to be 1.5 times higher while hypertension 1.3 times higher in the ICU group.

Consistent with studies conducted by Zhou et al.[11], Patel et al.[17] and a metanalysis conducted by Sun et al.[18], fever and cough were the most common symptoms found in our study. Dyspnoea was the only symptom significantly associated with disease severity and ICU admission, alongside various comorbidities (COPD, diabetes and obesity). Patients with dyspnoea were 1.5 times more likely to have an ICU admission compared to those without dyspnea. The significant association of dyspnea in this analysis with ICU admission suggests that silent hypoxia was less common during the second wave.

Studies have shown increased pro inflammatory cytokines in serum of COVID-19 patients. Also, anti-inflammatory agents for COVID-19 therapy highlight the critical role of inflammation in the progression of COVID-19[20,21]. In our study patients admitted in ICU showed significantly higher white blood cell count, CRP, LDH, Ferritin and D-Dimer levels. Similar observations were made by Zeng et al.[22] and Ji et al.[23] who showed association of inflammatory markers with severe disease and thus need for ICU admission. We also found low albumin levels to be associated with critical illness and ICU admission. Similar observations were made in a metanalysis conducted by Aziz et al.[22]. Hypoalbuminemia status has been associated with critically ill

patients and mortality across numerous clinical settings[23]. The pathophysiology behind hypoalbuminemia in disease state (such as pancreatitis, infection, trauma, burns etc) is thought to be secondary to increased capillary permeability, decreased protein synthesis, decreased half-life of serum albumin, decreased serum albumin total mass, increased volume of distribution, and increase expression of vascular endothelial growth factor[24]. The hallmark of severe COVID-19 includes the cytokine storm and interplay of some of the above mechanisms[25].

Strengths and Limitations: Although this is a retrospective study, carried out on COVID admissions during second wave, this study confirms results of previous studies on a good sample size to give insight on factors at admission to be considered to classify patients needing ICU or ward admissions.

Since COVID has continued to bother the world even after more than two years of its emergence with its changing strains, these results may be useful in forming strategies when encountered with COVID strain similar to that seen in the second wave.

Conclusion: The study confirms that COVID patients who need ICU admission have significantly higher mean age, leucocyte count, C-reactive protein (CRP), S. ferritin, lactate dehydrogenase (LDH), D-Dimer and comorbidity.

COVID patients in ICU also have significantly lower s. albumin levels and late presentation to hospital.These results may be useful in forming strategies when encountered with COVID strain similar to that seen in the second wave.

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