ORIGINAL ARTICLE JIACM 2022; 23 (3-4): 112-117

Predicting the Disease Severity and Mortality in COVID-19 Patients based on Disease Characteristics: An Observational Study in Indian Setting

Pawan Kumar, Bhanwar Lal Bhakar*, Bhupender Arya*, Sanjiv Maheshwari**, Shaitan Singh Jat***, Kavin Kumar****, Yash Devgan****, Aakash Garg****, Ala Ram****, Pragya Maheshwari*****, Sonakshi Mangal******, Kopal Maheshwari*****, Vishakha Notani*****, Shivalika Sharma*****, Vaishnavi Bansal******

Abstract

Introduction: *The emergence of newer mutated variants of COVID-19 virus has posed a significant challenge. The present study is aimed at investigating the clinical characteristics of COVID-19 and the parameters that may serve as predictors of severity and mortality related to COVID-19 in an Indian setting.*

Methods: *The observation study was carried-out by using the data of COVID-19 patients admitted between July 2020 to June 2021 at JLN Medical College, Ajmer, Rajasthan, India. The demographic and clinical data of clinically significant parameters were collected. The statistical difference between recovery and death and between patients who required long-term oxygen and those who did not was evaluated for various demographic and clinical variables. Chi-square and Fisher exact test were performed for categorical variables and t-test for continuous variables. Regression analyses were also carried-out for different variables with respect to survival and death, and for oxygen dependency.*

Results: *Variables namely age, duration of hospital stay, overweight, breathlessness, O_2 mask therapy, BiPAP support, and ventilator usage were found to be significantly different between recovered and expired subjects (P 0.00). The study has noted hypertension (25.06%) and diabetes (23.73%) as the common comorbidities noted in COVID patients, followed by coronary artery disease (2.98%) and asthma. The study has validated the role of oxygen saturation and requirement of oxygen in predicting mortality among COVID-19 patients. The study identified age as a significant predictor of mortality, obesity as a risk factor in COVID-19 patients, gender as a factor influencing the requirement of oxygen, and fever as an independent factor related to oxygen therapy. Bilevel positive airway pressure was given to majority of expired patients (83%) compared to 10% in recovered patients.*

Conclusion: *Variables namely age, BMI, duration of hospital stay, breathlessness, O_2 mask therapy, BiPAP support, and ventilator usage could be predictive in COVID-19 severity and mortality. The variables to be considered for predicting oxygen dependency are age, urban/rural, gender, duration of hospital stay, weight, height, BMI, fever, cough, breathlessness, diabetes, hypertension, and CAD.*

Key words: *COVID-19, BMI, diabetes.*

Introduction

Corona virus disease (COVID-19) has emerged as a global pandemic causing significant catastrophic effects on world demographics. According to WHO data for 28 October 2021, nearly 244,897,472 confirmed cases including 4,970,435 deaths were reported. The corresponding number of confirmed cases and deaths reported for India were 3,42,31,809 including 4,56,386 deaths[1,2]. Early detection of disease and timely treatment are paramount to control severity and reduce mortality among COVID-19 patients[3]. The illness can be classified as severe in patients with the following clinical signs: SpO_2 < 94% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) < 300 mmHg, respiratory frequency > 30 breaths/min, or lung infiltrates > 50%, and breathlessness. Respiratory failure, septic shock, and/or multiple organ dysfunctions are seen in critically ill patients[4].

Age, duration of fever, interval from illness onset to viral clearance, dyspnoea, lung capacity of patients, pre-existing co-morbidities such as obesity, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, respiratory disease, kidney disease, and malignancy are important factors associated with severity and mortality. Hence, they can be considered as high-risk factors among COVID-19 patients[5,6]. Oxygen saturation and requirement of oxygen support play a vivid role in mortality among COVID-19 patients. A study by Lee *et al*, reported that CRP, neutrophil, lymphocyte count along with age and hypertension status were able to predict risk of supplement oxygen requirement among COVID-19 patients[7]. Several studies have suggested

**Assistant Professor, **Senior Professor and Head, ***Senior Resident, ****Resident, *****Junior Resident, ******MBBS Student, Department of Medicine, JLN Medical College, Ajmer - 305 001, Rajasthan.*

Corresponding Author: Dr Sanjiv Maheshwari, Senior Professor and Head, Department of Medicine, JLN Medical College, Ajmer - 305 001, Rajasthan. Tel: 9460479888, E-mail: doctor.sanjiv@gmail.com.

various laboratory markers and factors that are found to be beneficial for the early recognition of severe illness. Laboratory markers such as neutrophil-to-lymphocyte ratio, lymphocyte and neutrophil count, platelet volume, albumin, c-reactive protein, ferritin, lactate dehydrogenase level, and red blood cell distribution width have been found to be associated with severity and mortality in COVID-19 patients[8,-12]. However, no significant and authentic data are available to correlate the clinical marker with the disease severity and mortality.

The rural healthcare setting in India is challenging with underdeveloped healthcare services, poor infrastructure, and lack of proper diagnostic facilities[13]. With the emergence of newer mutated variants of COVID virus, identifying the symptoms and factors that are associated with severity in COVID-19 patients is beneficial in predicting the disease severity and referring the patients who are at risk to a higher healthcare centre. The present study is intended to investigate the clinical characteristics of COVID and the parameters that may serve as predictors of severity and mortality related to COVID-19 in an Indian setting.

Material and Methods

This observational study was carried by extracting the data of COVID-19 patients admitted between July 2020 to June 2021 (including 1st and 2nd wave) at JLN Medical College, Ajmer Rajasthan, India. The study included data of adult patients of both the gender, diagnosed with COVID-19 infection by RT-PCR technique and excluded the subjects with missing details or insufficient information. The demographic and clinical data collected were age, gender, clinical symptoms, presence of comorbidities like hypertension, diabetes, COPD/asthma, coronary artery disease and obesity, details of oxygen requirement, duration of hospital stay, and survived or succumbed to death. The statistical difference between recovery and death and between patients who required long-term oxygen and those who did not was evaluated for various demographic and clinical variables. Chi-square and Fisher's exact test were performed for categorical variables and t-test for continuous variables. Regression analyses were also carried-out for different variables with respect to survival and death, and for oxygen dependency by running python code in Jupyter Notebook (6.2.0).

Results

The study recruited a total of 1513 patients and 607 patients were excluded due to missing information. The study considered the data of 906 patients with a mean age of 51.59 years and male-to-female ratio of 1:0.58. Requirement of long-term oxygen was noted for 510 (56.29%) patients. The corresponding proportion of subjects noted with comorbidities hypertension, diabetes, COPD/asthma and coronary artery disease were 25.06%, 23.73%, 3.09%, and 2.98% respectively. Categorisation according to BMI showed that 25.06% of the patients were overweight and 5.52% were obese. The details of clinical and demographic characteristics and the distribution of comorbidities are briefed in Table I. The distribution of co-morbidities demonstrated that around 61% of patients did not have any associated co-morbidities. Hypertension (25.06%) and diabetes (23.73%) were the most common co-morbidities noted among the COVID patients followed by obesity (5.52%), coronary artery disease (2.98%) and COPD/asthma (3.09%) (Table I).

Table I: Demographic/clinical characteristics and distribution of co-morbidities.

Clinical factors		
Variables		**Mean ± SD***
Age		51.59 ± 18.12
Gender (M/F)		572/334
Urban		626 (69.09%)
Rural		280 (30.91%)
Weight (kg)		65.32 ± 10.33
Height (meter)		1.65 ± 0.09
BMI	Underweight	31 (3.42%)
	Ideal	598 (66.0%)
	Overweight	227 (25.06%)
	Obese	50 (5.52%)
Duration of hospital stay		8.25 ± 4.87
Distribution of co-morbidities		
(n = 906)		
Co-morbidities		n (%)
Diabetic mellitus		215 (23.73%)
Hypertension		227 (25.06%)
COPD/asthma		28 (3.09%)
Coronary artery disease		27 (2.98%)

**Mean and standrad deviation for all continues variables. Number and percentage for categorical variables.*

Comparison between recovered and expired subjects demonstrated that the incidence of hypertension was more in recovered than in expired patients ($P < 0.05$), and this may be due to more number of subjects belonging to the recovered category than expired. Whereas, the duration of hospital stay was more in expired patients than recovered ($P < 0.05$, Table III). Most of the subjects received at least one form of oxygen treatment, and the requirement of

mechanical ventilation was more among expired patients (P < 0.05). Statistically significant difference was noted for the variables namely advanced age, overweight, longer duration of hospital stay, longer O_2 therapy, bilevel positive airway pressure (BiPAP) support, and ventilator usage upon comparison between the 2 groups. Among the co-morbidities, hypertension was found to be statistically significant between the groups (P 0.00, Table II).

Table II: Comparison of the variables for the significance level between recovered and expired subjects.

Predictors (n = 906)		Recovery (n = 801)	Expired (n = 105)	P-value
Age		49.97 ± 17.97	63.94 ± 14.1	< .0001
Urban/rural		569 (232)	57 (48)	0.00
Gender (M/F)		503 (298)	69 (36)	0.56
BMI	Underweight	29 (3.62%)	2 (1.90%)	0.53
	Ideal	545 (68.04%)	53 (50.48%)	0.00
	Overweight	185 (23.10%)	42 (40.0%)	0.00
	Obese	42 (5.24%)	8 (7.62%)	0.44
Duration of hospital stay		8.06 ± 4.8	9.66 ± 5.05	0.00
Fever		606 (75.66%)	95 (90.48%)	0.00
Cough		538 (75.66%)	78 (74.29%)	0.14
Breathlessness		483 (67.17%)	96 (91.43%)	0.00
O_2 mask therapy		401 (50.06%)	96 (91.43%)	0.00
BiPap support		84 (10.49%)	88 (83.81%)	0.00
Ventilator usage		5 (0.62%)	49 (46.67%)	0.00
Diabetic mellitus		185 (23.10%)	30 (3.75%)	0.21
Hypertension		183 (22.85%)	44 (5.49%)	0.00
Coronary artery disease		15 (1.87%)	5 (0.62%)	0.07

**Mean and standard deviation for all continuous variables. Number and percentage forcategorical variables. ǂChi-square and Fisher-exact test was used for categorical variables and t-test for continuous variables.*

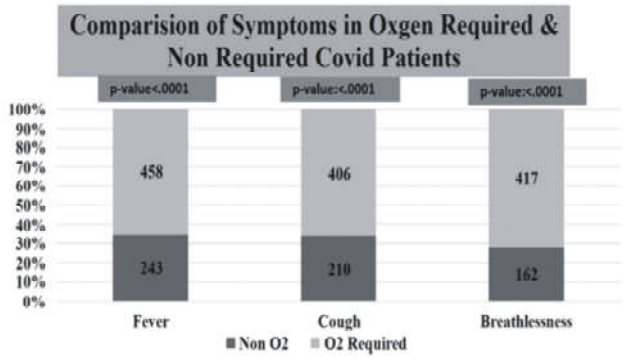

Fig. 1: *The above is the graph for comparison of symptoms oxygen required and not required patient.*

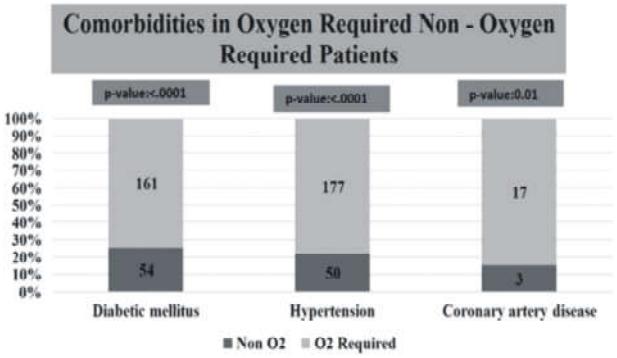

Fig. 2: *The above is the graph for comparison in oxygen required and non-oxygen required patients.*

Comparison of variables for oxygen dependency demonstrated statistically significant difference for variables namely, fever, cough, breathlessness, diabetes, hypertension and coronary artery disease (Fig. 1 and 2).

Around 54% of the variance was explained by the model and had higher effect size according to criteria. The model was statistically significant (P 0.00) and the variables that showed the significance difference between survival and death (P < 0.05) were rural/urban, presence or absence of fever, cough, BiPap support, ventilator usage, and duration of hospital stay (Table III).

Table III: Results of regression analysis with respect to survival and death.

	COEF	Std ERR	t	P > |t|	(0.025)	(0.975)
Intercept	0.9277	0.04	23.095	0	0.849	1.006
Gender	-0.0041	0.016	-0.266	0.791	-0.035	0.026
Rural/urban	0.045	0.016	2.823	0.005	0.014	0.076
BMI ideal	0.02	0.026	0.763	0.446	-0.031	0.071
Overweight	0.0059	0.029	0.205	0.837	-0.051	0.062
Fever	0.0069	0.02	0.34	0.734	-0.033	0.047
Breathlessness	-0.0278	0.018	-1.57	0.117	-0.062	0.007
O_2 mask therapy	-0.0233	0.018	-1.294	0.196	-0.059	0.012
Cough	0.0494	0.017	2.849	0.004	0.015	0.083
BiPap support	-0.3159	0.022	-14.113	0	-0.36	-0.272
Ventilator usage	-0.6079	0.034	-17.732	0	-0.675	-0.541
Hypertension	-0.0305	0.018	-1.664	0.096	-0.066	0.005
CAD	-0.0858	0.049	-1.761	0.079	-0.181	0.01
Age	-0.0003	0	-0.669	0.503	-0.001	0.001
Duration of hospital stay	0.0032	0.002	2.049	0.041	0	0.006

Regression analysis based on oxygen dependency showed variance of 32% and higher effect size. The variables that showed statistical difference with reference to oxygen

requirement status were presence or absence of fever, cough, breathlessness and age (Table 4).

Table IV: Results of regression analysis with respect to oxygen dependency.

	COEF	std ERR	t	P > (t)	(0.025)	(0.975)
Intercept	-0.0188	0.02	-0.941	0.347	-0.058	0.02
Gender	-0.0095	0.008	-1.17	0.242	-0.025	0.006
BMI ideal	-0.0308	0.014	-2.236	0.026	-0.058	-0.004
BMI overweight	-0.0147	0.015	-0.978	0.328	-0.044	0.015
Fever	-0.0041	0.011	-0.388	0.698	-0.025	0.017
Breathlessness	0.0106	0.009	1.146	0.252	-0.008	0.029
O_2 mask therapy	0.9336	0.009	101.03	0	0.915	0.952
Cough	0.0157	0.009	1.723	0.085	-0.002	0.034
Hypertension	0.0085	0.01	0.885	0.376	-0.01	0.027
CAD	0.0292	0.026	1.141	0.254	-0.021	0.079
Age	0.0013	0	5.03	0	0.001	0.002
Duration of hospital stay	0.0016	0.001	1.953	0.051	-0.0000077	0.003

Discussion

In the current study, variables – namely age, duration of hospital stay, overweight, breathlessness, O_2 mask therapy, BiPAP support, and ventilator usage – were found to be significantly different between recovered and expired subjects. In concurrence with the current findings, an Uttar Pradesh-based retrospective observational study has reported that advancing age, gender, and duration of stay may influence the COVID-19 outcome. The association between the hospital duration and clinical outcome was found to be statistically significant ($P < 0.001$)[14].

The study noted hypertension (25.06%) and diabetes (23.73%) as the common co-morbidities noted in COVID-19 patients, followed by coronary artery disease (2.98%) and asthma. Patients with comorbidities are at higher risk for critical illness due to COVID-19. Co-morbidities such as coronary artery disease, diabetes and hypertension are associated with worst outcome in COVID-19[7,15-17]. A meta-analysis by Pititto *et al* has concluded that diabetes, hypertension and cardiovascular disease are important risk factors influencing severity and mortality in COVID and their intensive treatment is paramount while managing the infection[18]. Similarly, another meta-analysis of 40 studies concluded that coronary artery disease (CAD) in COVID-19 patients is linked to poor prognosis[19]. CAD was found to be related to ICU admission ($P = 0.002$), disease progression ($P = 0.003$), severe/critical COVID-19 ($P < 0.001$), and mortality ($P < 0.001$)[19]. The current study has noted a significant association between the presence of co-morbidities and oxygen requirement. CAD was present in 3.33% patients with oxygen requirements as opposed to 0.76% patients not requiring oxygen. Similarly, diabetes was noted in 31.57% patients requiring oxygen compared to 13.64% patients without oxygen requirement.

Several studies have validated the role of oxygen saturation and requirement of oxygen in predicting mortality among COVID-19 patients. The present study has also corroborated the same, as most of the patients received at least one form of oxygen treatment, and the need for mechanical ventilation was more among seriously ill expired subjects. A retrospective cohort study among 369 adult patients with COVID-19 admitted to a tertiary care hospital in Lima, Peru has also noted that oxygen saturation values < 90% on admission and age > 60 years were significantly correlated with mortality. The study has highlighted the need for early identification of hypoxaemia and timely hospital care to reduce COVID-related mortality[20].

Studies have reported age as significant predictor of mortality and it is also considered as a major factor while estimating the need for oxygen supplement among COVID-19 hospitalised patients[21,20,7]. In the present study, mean age of fatalities was 64 compared to 50 years for the recovered patients, and 59 vs 42 with regard to the requirement of oxygen. A significant difference in incidence and mortality rate of COVID-19 has been observed between urban and rural population[22,23]. In line with this finding, the current study has noted significant difference between expired and recovered patients with regard to urban/rural status.

Several studies have reported obesity as a risk factor in COVID-19 patients and the association of high BMI with mortality and oxygen requirement during hospitalization in COVID-19 patients[24-27]. The present result has noted that among the expired subjects, 40% were overweight and 7.62% were obese. A meta-analysis involving by Cai *et al*, has concluded that obese patients have higher risk of infection, hospitalisation, disease severity, ICU admission, mechanical ventilation, and COVID-19-associated mortality[28].

Present study has identified gender as a factor influencing the requirement of oxygen. Biole *et al*, reported that requirement of oxygen supplementation was more among men than women. In contrast, Raimondi *et al*, has noted that women required more oxygen nasal cannula than men[29,30]. The incidence of hypertension was found to be more in recovered than in expired patients ($P < 0.05$). However, this finding is not generalisable, as it could be attributed to more number of recovered patients (801) than expired (105). Mostly tterminally ill patients experience shock and reduced blood pressure, so this finding may not

be clinically useful.

Fever has been identified as an independent factor related to oxygen therapy and high-grade fever is more common among critically ill COVID-19/deceased patients[31,32]. In the current study, fever was common in majority of deceased and patients with oxygen requirement than in recovered and patient without oxygen requirement. Breathlessness was found to be significantly associated with the risk of mortality and considered as independent factor in relation to oxygen therapy[33,31]. In the present study, breathlessness was prevalent among expired and oxygen-required patients compared to deceased patients and patient with oxygen requirements. Cough is considered as most prevalent symptoms in COVID-19 patients[34-36]. Cough is significantly different between patients with or without oxygen requirement. The mean duration of hospital stay is significantly difference between expired and recovered patients and patients with or without oxygen requirement.

Bilevel positive airway pressure is considered in COVID-19 patients with type 2 respiratory failure such as chronic obstructive pulmonary disease[37]. In the present study, bilevel positive airway pressure was provided to majority of expired patients (83%) compared to 10% in recovered patients. Oxygen therapy is significantly associated with mortality in COVID-19 patients[31]. In the present study, the requirement of oxygen mask therapy was more in expired patients (91%) compared to recovered subjects (50.06%). Richardson *et al* in a study from New York reported that oxygen therapy was required by 27.8% of the patients who were admitted to the hospital. Among the hospitalised subjects, 12% of the patients required mechanical ventilation and 88% of them succumbed to death[38]. In our study, requirement of mechanical ventilation was more among expired patients as compared to recovered patients.

Although several studies have tried to develop statistical prediction models for COVID-19, very few studies have evaluated the data from real-world settings to understand the parameters that may serve as predictors of COVID severity. The present study holds significant relevance, as literature review shows that very few studies from India have evaluated the factors predictive of COVID-19. The major limitations of the current study were observational design and not evaluating the role of biochemical parameters in predicting COVID-19 severity and outcome. Although the study has reported urban/ rural and gender status as factors the requirement of oxygen, it has not studied the effect of each parameter separately such as male and female, and urban and rural.

Conclusion

Variables namely age, BMI, duration of hospital stay, breathlessness, O_2 mask therapy, BiPAP support, and ventilator usage are beneficial in predicting COVID-19 severity and mortality. The variables to be considered for predicting oxygen dependency are age, urban/rural, gender, duration of hospital stay, weight, height, BMI, fever, cough, breathlessness, diabetes, hypertension and CAD. Developing prediction models based on these variables may assist in triaging the patients effectively during hospital admission. However, further studies are needed for the development and verification of such prediction models.

References

1. WHO Coronavirus (COVID-19) Dashboard (Internet). (cited 2021 Nov 29).
2. India: WHO Coronavirus Disease (COVID-19) Dashboard With Vaccination Data (Internet). (cited 2021 Nov 29).
3. Zheng Y, Xu H, Yang M *et al*. Epidemiological characteristics and clinical features of 32 critical and 67 noncritical cases of COVID-19 in Chengdu. *J Clin Virol* 2020; 127: 1043-66.
4. Clinical Spectrum (Internet). COVID-19 Treatment Guidelines. (cited 2021 Nov 29).
5. Zhou Y, Yang Q, Chi J *et al*. Co-morbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. *Int J Infect Dis* 2020; 99: 47-56.
6. Peres KC, Riera R, Martimbianco ALC. Body Mass Index and Prognosis of COVID-19 Infection. A Systematic Review. *Front Endocrinol (Lausanne)* 2020; 11: 562.
7. Lee EE, Hwang W, Song K-H *et al*. Predication of oxygen requirement in COVID-19 patients using dynamic change of inflammatory markers: CRP, hypertension, age, neutrophil and lymphocyte (CHANeL). *Sci Rep* 2021; 11 (1): 13026.
8. Güçlü E, Kocayiðit H, Okan HD *et al*. Effect of COVID-19 on platelet count and its indices. *Rev Assoc Med Bras* 2020; 66: 1122-7.
9. Li X, Liu C, Mao Z *et al*. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. *Crit Care* 2020; 24 (1): 647.
10. Hu H, Du H, Li J *et al*. Early prediction and identification for severe patients during the pandemic of COVID-19: A severe COVID-19 risk model constructed by multivariate logistic regression analysis. *J Glob Health* 10 (2): 020510.
11. Arshad AR, Khan I, Shahzad K *et al*. Association of Inflammatory Markers with Mortality in COVID-19 Infection. *J Coll Physicians Surg Pak* 2020; 30 (10): 158-63.
12. Lee JJ, Montazerin SM, Jamil A *et al*. Association between red blood cell distribution width and mortality and severity among patients with COVID-19: A systematic review and meta-analysis. *J Med Virol* 2021; 93 (4): 2513-22.
13. Kumar A, Rajasekharan Nayar K, Koya SF. COVID-19: Challenges and its consequences for rural health care in India. *Public Health in Practice* 2020; 1: 100009.
14. JCDR – Clinico-epidemiological Profile and Outcomes of COVID-19 Patients Admitted in Jawaharlal Nehru Medical College and Hospital: A Retrospective Study (Internet). (cited 2021 Nov 29).
15. Guan W, Liang W, Zhao Y *et al*. Co-morbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. *Eur Res J* (Internet). 2020; (cited 2021 Nov 29).

16. Barison A, Aimo A, Castiglione V *et al*. Cardiovascular disease and COVID-19: les liaisons dangereuses. *Eur J Prev Cardiol* 2020; 27 (10): 1017-25.
17. Sanyaolu A, Okorie C, Marinkovic A *et al*. Co-morbidity and its Impact on Patients with COVID-19. *SN Compr Clin Med* 2020; 25: 1-8.
18. De Almeida-Pititto B, Dualib PM, Zajdenverg L *et al*. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. Diabetol Metabolic Syndr 2020; 12 (1): 75.
19. Liang C, Zhang W, Li S. Coronary heart disease and COVID-19: A meta-analysis. *Med Clin (Barc)* 2021; 156 (11): 547-54.
20. Mejía F, Medina C, Cornejo E *et al*. Oxygen saturation as a predictor of mortality in hospitalised adult patients with COVID-19 in a public hospital in Lima, Peru. *PLOS ONE* 2020; 15 (12): e0244171.
21. Bahl A, Van Baalen MN, Ortiz L *et al*. Early predictors of in-hospital mortality in patients with COVID-19 in a large American cohort. *Intern Emerg Med* 2020; 15 (8): 1485-99.
22. Huang Q, Jackson S, Derakhshan S *et al*. Urban-rural differences in COVID-19 exposures and outcomes in the South: A preliminary analysis of South Carolina. *PLOS ONE* 2021; 16 (2): e0246548.
23. Cuadros DF, Branscum AJ, Mukandavire Z. Dynamics of the COVID-19 epidemic in urban and rural areas in the United States. *Ann Epidemiol* 2021; 59: 16-20.
24. Hendren NS, de Lemos JA, Ayers C *et al*. Association of Body Mass Index and Age With Morbidity and Mortality in Patients Hospitalised With COVID-19. *Circulation* 2021; 143 (2): 135-44.
25. Kang IS, Kong KA. Body mass index and severity/fatality from coronavirus disease 2019: A nationwide epidemiological study in Korea. *PLOS ONE* 2021; 16 (6): e0253640.
26. Plourde G, Fournier-Ross E, Tessier-Grenier H *et al*. Association between obesity and hospital mortality in critical COVID-19: a retrospective cohort study. *Int J Obes* 2021; 45 (12): 2617-22.
27. Moriconi D, Masi S, Rebelos E *et al*. Obesity prolongs the hospital stay in patients affected by COVID-19, and may impact on SARS-COV-2 shedding. *Obes Res Clin Pract* 2020; 14 (3): 205-9.
28. Cai Z, Yang Y, Zhang J. Obesity is associated with severe disease and mortality in patients with coronavirus disease 2019 (COVID-19): a meta-analysis. *BMC Public Health* 2021; 21 (1): 1505.
29. May 19 JHM 2021 J-352 POF, 2021 | 10.12788/Jhm.3594. Gender Differences in the Presentation and Outcomes of Hospitalised Patients With COVID-19. *J Hospital Med (Internet)*. 2021; (cited 2021 Nov 29); 16 (6).
30. Raimondi F, Novelli L, Ghirardi A *et al*. Covid-19 and gender: lower rate but same mortality of severe disease in women – an observational study. *BMC Pulmonary Med* 2021; 21 (1): 96.
31. Ni Y-N, Wang T, Liang B. The independent factors associated with oxygen therapy in COVID-19 patients under 65-year-old. *PLOS ONE*. 2021; 16 (1): e0245690.
32. Choron RL, Butts CA, Bargoud C *et al*. Fever in the ICU: A Predictor of Mortality in Mechanically Ventilated COVID-19 Patients. *J Intensive Care Med* 2021; 36 (4): 484-93.
33. Shi L, Wang Y, Wang Y. Dyspnoea rather than fever is a risk factor for predicting mortality in patients with COVID-19. *J Infect* 2020 Oct; 81 (4): 647-79.
34. Larsen JR, Martin MR, Martin JD. Modeling the Onset of Symptoms of COVID-19. *Frontiers in Public Health* 2020; 8: 473.
35. Mizrahi B, Shilo S, Rossman H *et al*. Longitudinal symptom dynamics of COVID-19 infection. *Nat Commun* 2020; 11 (1): 6208.
36. Wu Y-C, Chen C-S, Chan Y-J. The outbreak of COVID-19: An overview. *J Chinese Med Asso* 2020; 83 (3): 217-20.
37. Wang Z, Wang Y, Yang Z *et al*. The use of non-invasive ventilation in COVID-19: A systematic review. *Inter J Infectious Dis* 2021; 106: 254-61.
38. Richardson S, Hirsch JS, Narasimhan M *et al*. Presenting Characteristics, Co-morbidities, and Outcomes Among 5,700 Patients Hospitalised With COVID-19 in the New York City Area. *JAMA* 2020; 323 (20): 2052-9.