Original Research Article

Study of correlation between ratio of partial pressure of arterial oxygen and fractional inspired oxygen (PaO2/FiO2) and duration of hospital stay in COVID-19 patients

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Abstract

Background: COVID-19 can lead to fatal co-morbidities especially acute respiratory distress syndrome (ARDS) with some patients progressing very rapidly to respiratory distress and ending up with ICU admission and some succumbing to death. COVID-19 mainly affected the respiratory system with damage to other organs.

Objective: The aim of the study was to measure the correlation between ratio of partial pressure of arterial oxygen and fractional inspired oxygen (PaO2/FiO2) and duration of hospital stay in covid-19 patients.

Materials and methods: We prospectively studied a series of 32 COVID-19 patients admitted to the General Medicine Department of Malla Reddy Institute of Medical Sciences, Hyderabad. We attained the arterial blood gas study of the patients within the first 24 hours of admission and calculated ratio

of partial pressure of arterial oxygen and fractional inspired oxygen (PaO2/FiO2). Data entry was done using Microsoft Excel 2013 and analysis using SPSS 16v. Qualitative data were entered in Frequencies and percentage and Quantitative data was expressed in Mean and Standard deviation. Pearson correlation coefficient was used to find the correlation between PAO2/FiO2 and Hospital stay in days. P value of <0.05 was considered to be statistically significant.

Results: Patients with lower ranges of PaO2/FiO2 ratio were found to have prolonged hospital stay (PHS, >21 days). The mean PaO2/FiO2 ratio was 248.38 ± 128.67, minimum and maximum being 67.3% and 435.1% respectively. In patients with hospital stay of >21 days the mean ratio was 136.74 ± 60.89, while in the patients with stay of <21 days, the mean ratio was 360.03 ± 62.61 (p value <0.0001). The mean PAO2/FiO2 in those with prolonged hospital stay (>21 days) was significantly low compared to those with duration of hospital stay <21 days. This finding was statistically significant as the p value calculated to be <0.05. No significant association was found between the presence of co-morbidities (diabetes; hypertension), age, gender distribution with prolonged hospital stay.

Conclusion: A significant correlation was observed with a Low PaO2/FiO2 ratio on admission and prolonged hospital stay in Covid-19 patients.

Key words

PaO2, FiO2, Duration, Hospital stay, COVID-19, Partial pressure of arterial oxygen, Functional inspired oxygen.

Introduction

The novel coronavirus disease COVID-19 outbreak, caused by the severe acute respiratory syndrome coronavirus 2, was initially reported in Wuhan, China, in late 2019 [1].On February 11, 2020, WHO termed this disease as coronavirus disease 2019 (COVID-19) [2] and, subsequently on March 11, 2020, WHO declared COVID-19 as a global pandemic since the SARS-CoV-2 viral infection has spread rapidly in a growing number of countries [3].The coronavirus disease 2019 (COVID-19) outbreak has spread worldwide with overwhelming speed, infecting >48.3 million individuals and causing >1.23 million deaths across ~200 countries as of 2nd of November, 2020 [4]. The clinical spectrum of COVID-19 disease is wide, ranging from asymptomatic infection or mild upper respiratory tract symptoms (80%) to severe viral pneumonia with respiratory failure and death (20%) [6-10]. Common clinical symptoms include fever, fatigue, cough, anorexia, shortness of breath, sore throat, headache, and chest tightness, as well as minor symptoms such as nausea, vomiting, diarrhoea, and gastrointestinal complication were also reported and have been observed during various stages of this disease [5]. COVID-19 can lead to fatal co-morbidities especially acute respiratory distress syndrome (ARDS) with some patients progressing very rapidly to respiratory distress and ending up with ICU admission and some succumbing to death. COVID-19 mainly affected the respiratory system with minor damage to other organs. Studies reported that acute myocardial injury (7.2–17%) and acute renal injury (2.9–15%) could occur in severe patients. The reported incidence of ARDS was 15.6–31%, higher than that of other organ injuries [6 11-14]. Thus, fully understanding the characteristics of COVID-19-related ARDS is conducive to early identification and precise treatment.

Materials and methods

We prospectively studied a consecutive series of 32 COVID-19 patients admitted to the General Medicine Department of Malla Reddy Institute of Medical Sciences, Hyderabad, between the month of May and October 2021. COVID-19 patients were diagnosed according to the World

Health Organization (WHO) interim guidance and had evidence of RT-PCR positive status. We performed the arterial blood gas study of the patients within the first 24 hours of admission and calculated ratio of partial pressure of arterial oxygen and fractional inspired oxygen (PaO2/FiO2) which had the evidence of a significant and independent association with the prolonged hospitalization in COVID-19 patients [5]. The data regarding the presence of habits of smoking, Presence of co-morbidities of Diabetes and hypertension is also collected.

Exclusion Criteria: We excluded the patients with previous history of heart diseases, respiratory illness, habit of smoking and other chronic systemic illness which can affect the arterial oxygen levels. The criteria for patient discharge included absence of fever for at least three days, significant improvement on chest CT, resolution of respiratory symptoms, and a negative throat-swab sample for viral RNA.

Data entry was done using Microsoft Excel 2013 and analysis using SPSS 16v. Qualitative data was entered in Frequencies and percentage and Quantitative data was expressed in Mean and Standard deviation. Independent t test was used to find the significant association between two parametric variables and Chi square test was used to find the significant association between Non-Parametric variables. Pearson correlation coefficient was used to find the correlation between PAO2/FiO2 and Hospital stay in days. P value of <0.05 was considered to be statistically significant. The study was done with the approval of Institutional ethics committee.

Results

The demographics of age and gender distribution were discussed in **Table - 1 and 2** respectively. The mean age was 49.40 ± 14.93, most of them between 26-45 years (43.8%) and the majority of patients were males (65.6%) and females (34.4%).

Table - 1: Age distribution.

Age (Years)	Frequency	Percentage
26 – 35	7	21.9%
36 – 45	7	21.9%
46 – 55	6	18.8%
56 – 65	6	18.8%
66 – 75	6	18.8%
Mean ± SD	49.40 ± 14.93	

Table - 2: Gender distribution.

	Frequency	Percentage
Male	21	65.6%
Female	11	34.4%
Total	32	100%

Table - 3: Co-morbidities.

	Frequency	Percentage
DM	1	3.1%
HTN	2	6.2%
DM + HTN	5	15.7%
None	24	75%
Total	32	100%

Table - 4: Duration of hospital stay.

	Frequency	Percentage
<21 days	16	50%
>21 days	16	50%
MEAN ± SD	22.31 ± 9.68	

Table - 5: PAO2/FiO2.

	Minimum	Maximum	Mean ± SD
PaO2/ FiO2	67.3	435.1	248.38 ± 128.67

Table - 3 gives the details of presence of co-morbidities Diabetes and Hypertension, with majority having neither of the both (75%).

Of the 32 patients studied 16 (50%) were admitted in the hospital for <21 days and other 16 (50%) were admitted for > 21 days. The mean duration of hospital stay was found to be 22.31 ± 9.68 (**Table – 4**).

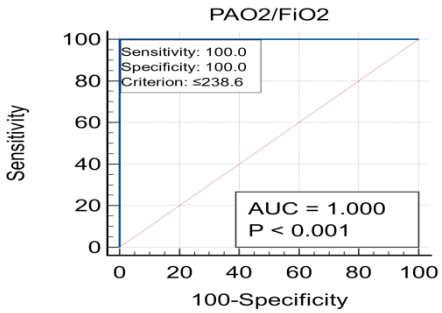
Table - 6: Prolonged hospital stay and Association with variables.

	<21 days	**> 21 days**	**P value**
Age	47 ± 13.39	51.81 ± 16.40	0.44
PAO2/FiO2	360.03 ± 62.61	136.74 ± 60.89	<0.0001*

Table - 7: Duration of Hospital stay and other variables.

		<21 days	**> 21 days**	**P value**
Gender	Male	12	9	0.27
	Female	4	7	
Co morbidities	Yes	6	2	0.10
	No	10	14	

ROC CURVE:



ROC ANALYSIS

Youden index J	1.0000
Associated criterion	≤238.6
Sensitivity	100.00
Specificity	100.00

Table – 8: Standard error and significance.

Area under the ROC curve (AUC)	1.000
Standard Error [a]	0.000
95% Confidence interval [b]	0.891 to 1.000
Significance level P (Area=0.5)	<0.0001

[a] DeLong et al., 1988, [b] Binomial exact

Table – 9: PAO2/FiO2 values and coordinates of the ROC curve.

PAO2/FiO2	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
<67.3	0.00	0.0 - 20.6	100.00	79.4 - 100.0		1.00
≤238.6	100.00	79.4 - 100.0	100.00	79.4 - 100.0		0.00
≤435.1	100.00	79.4 - 100.0	0.00	0.0 - 20.6	1.00	

Table -10: Pearson correlation coefficient between duration of hospital stay and PAO2/FiO2.

PAO2/FiO2	Variable	R value	P value
	Hospital stay in days	-0.89	<0.0001*

Based on ROC analysis, at the cutoff point 238.6, PAO2/FiO2 with 100% sensitivity and 100% specificity and the Area under the curve was 1 (0.89 – 1.0) predict poor outcome

The mean PaO2/FiO2 ratio was 248.38 ± 128.67, minimum and maximum being 67.3% and 435.1% respectively (**Table – 5**).

In patients with hospital stay of more than 21 days the mean ratio was 136.74 ± 60.89, while in the patients with stay of less than 21 days the mean ratio was 360.03 ± 62.61(p value <0.0001).

The mean age of the patients admitted for <21 days was 47 ± 13.39, and for > 21 days was 51.81 ± 16.40 with p value 0.44 (**Table – 6**).

Of the 21 male patients, 12 were admitted for <21 days and 9 patients were admitted for>21 days. Of the 11 female patients, 4 were admitted for < 21 days and 7 for > 21 days (**Table – 7**).

There was no significant association found with the age distribution and prolonged hospital stay, with p value 0.27. The presence of co-morbidities was also not significantly associated with prolonged hospital stay, p >0.05.

The Area under the ROC curve for PAO2/FiO2 ratio was 1.0 (95% confidence interval 0.891 to 1.000) (**Table - 8**).

Based on correlation analysis, a significant negative correlation (r=-0.89; p<0.0001*) was observed between PAO2/FiO2 and duration of hospital stay in days. Lower the ratio more was the prolongation of hospital stay (**Graph – 1, Tables - 9 and 10**).

Discussion

Most patients with Covid-19 have mild symptoms, whereas some may progress to serious complications like Acute Respiratory Distress Syndrome (ARDS) and multi-organ failure leading to ICU admission and mortality. Emergency physicians should identify parameters and patients with severe symptoms, hypoxemia with the need for oxygen supplementation, or high risk for clinical deterioration that require admission for further management and monitoring [20].

In the present study, the mean PAO2/FiO2 in those with prolonged hospital stay (>21 days) was 136.74 ± 60.89 which is significantly low compared to those with duration of hospital stay <21 days. This finding was statistically significant as the p value calculated to be <0.05. The study observed, Of the 21 male patients 42.8% patients got admitted for>21 days, while of 11 female patients 63.6% patients got admitted for > 21 days. The data found no significant association between sex distribution and prolonged hospital stay, p value >0.05.

However, in a study done by Peckham, et al. male sex was identified as a risk factor for mortality and Intensive care admission [18].

A study done by Jian-Min Jin, et al. observed men's cases tended to be more serious than women's , the number of men who died from COVID-19 is 2.4 times that of women [19].

The study observed the mean age of patients admitted for >21 days (51.81 ± 16.40) was more than those with admission of <21 days (47 ± 13.39). However, p value was not statistically significant.

The findings are in consistency with the study done by Dimitris Bertsimas, et al, which observed increasing age as an important predictor of severity and mortality in covid-19 [16].

The study observed no significant association between presence of co morbidities and prolonged stay. However, presence of co morbidities like diabetes and hypertension were observed to be playing a role as risk factors for severity of illness in covid19 [17].

Conclusion

The impact of this pandemic on health care systems, particularly in terms of hospital staff and bed availability, is a matter of concern. We sought to address this issue by studying the PaO2/FiO2 ratio of the patient on the day of

admission and its correlation with prolonged hospital stay as a tool to assess the severity of the disease.

We found a significant correlation between a Low PaO2/FiO2 ratio on admission and prolonged hospital stay in Covid-19 patients. Hence, it is advisable to use the PaO2/FiO2ratio as a tool to assess the disease severity and make use of it to bestow righteous treatment and management to the patients with covid-19

References

1. Lau SKP, Luk HKH, Wong ACP, Li KSM, Zhu L, He Z, Fung J, Chan TTY, Fung KSC, Woo PCY. Possible Bat Origin of Severe Acute Respiratory Syndrome Coronavirus 2. Emerg Infect Dis., 2020; 26: 1542-1547.
2. WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it. World Health, Organization (WHO); 2020. https://www.who.int/emergencies/diseases/novel-coronavirus2019/technical-guidance/naming-the-coronavirus-disease- (covid-2019)-and-the-virusthat-causes-it.
3. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed., 2020; 91(1):157–60. https://doi.org/ 10.23750/abm.v91i1.9397.
4. World Health Organization (WHO): Coronavirus disease (COVID-19) pandemic. https://www.who.int/emergencies/ diseases/novel-coronavirus-2019. Accessed November 2, 2020.
5. Zinellu A, De Vito A, Scano V, Paliogiannis P, Fiore V, Madeddu G, Maida I, Zinellu E, Mangoni AA, Arru LB, Carru C, Babudieri S, Pirina P, Fois AG. The PaO2/FiO2 ratio on admission is independently associated with prolonged hospitalization in COVID-19 patients. J Infect Dev Ctries., 2021 Mar 31;15(3):353-359.
6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 2020; 395: 497–506.
7. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA, 2020; 323: 1061–1069.
8. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet, 2020; 395: 507–513.
9. Liu X, Zhou H, Zhou Y, Wu X, Zhao Y, Lu Y, Tan W, Yuan M, Ding X, Zou J, Li R, Liu H, Ewing RM, Hu Y, Nie H, Wang Y. Risk factors associated with disease severity and length of hospital stay in COVID-19 patients. J Infect., 2020; 81: E95- E97.
10. Vaira LA, Deiana G, Fois AG, Pirina P, Madeddu G, De Vito A, Babudieri S, Petrocelli M, Serra A, Bussu F, Ligas E, Salzano G, De Riu G. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single-center experience on 72 cases. Head Neck, 2020; 42: 1252–1258.
11. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet, 2020; 395(10223): 507–13.

12. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA, 2020. https://doi.org/10.1001/jama.2020.1585.
13. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med., 2020. https://doi.org/10.1056/NEJMoa2002032.
14. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet, 2020. https://doi.org/10.1016/S0140-6736(20)30566-3.
15. Zheng R, Hu M, Li R, et al. Respiratory treatment procedures in patients with severe novel coronavirus infected pneumonia: an expert opinion. Chin J Crit Care Intensive Care Med., 2020. https://doi.org/10.3877/cma.j.issn.2096-1537. 2020.0004
16. Bertsimas D, Lukin G, Mingardi L, Nohadani O, Orfanoudaki A, Stellato B, et al. COVID-19 mortality risk assessment: An international multi-center study. PLoS ONE, 2020; 15(12): e0243262.
17. Center for Disease Control and Prevention. Groups at Higher Risk for Severe Illness. 2020. https:// www.cdc.gov/aging/covid19-guidance.html.
18. Peckham H., de Gruijter N.M., Raine C., et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. Nat Commun., 2020; 11: 6317. https://doi.org/10.1038/s41467-020-19741-6.
19. Jin J-M, Bai P, He W, Wu F, Liu X-F, Han D-M, Liu S and Yang J-K. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front. Public Health, 2020; 8:152. doi: 10.3389/fpubh.2020.00152.
20. Chavez S, Long B, Koyfman A, Liang SY. Coronavirus disease (COVID-19): A primer for emergency physicians. Am J Emerg Med., 2020. doi: 10.1016/j.ajem.2020.03.036.