

## Correlation of the SpO<sub>2</sub>/FiO<sub>2</sub> (S/F) ratio and the PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) ratio in patients with COVID-19 pneumonia



## Correlación de la relación SpO<sub>2</sub>/FiO<sub>2</sub> (S/F) y la relación PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) en pacientes con neumonía COVID-19

Dear Editor,

The clinical spectrum of SARS-CoV-2 infection varies widely ranging from asymptomatic infection to severe viral pneumonia with respiratory failure.<sup>1</sup> Some patients of COVID, who develop respiratory failure have hypoxemia but without signs of respiratory distress also termed as "silent hypoxemia". This silent hypoxemia may be responsible for the quick deterioration because it gives a false sense of well-being even when the oxygen debt is actually increasing.<sup>2,3</sup> This mandates regular monitoring of oxygen levels in these patients. SpO<sub>2</sub>/FiO<sub>2</sub> (S/F) ratio has been found to have good correlation with PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) ratio in adult and pediatric patients with pneumonia, acute respiratory distress syndrome (ARDS) and acute lung injury in various studies.<sup>4-6</sup> However, in COVID patients, there can be discordance between S/F ratio and P/F ratio due to multiple reasons like shift of oxyhemoglobin dissociation curve to left or right, inaccuracy of SpO<sub>2</sub> at lower levels of saturation and during critical illness.<sup>7</sup> Moreover, the linear correlation between SpO<sub>2</sub> and FiO<sub>2</sub> is lost when SpO<sub>2</sub> is 100% and even the PaO<sub>2</sub> cannot be estimated when SpO<sub>2</sub> is 100%.

The aim of this study was to assess the correlation between S/F and the P/F ratios in patients with COVID pneumonia requiring oxygen therapy and to find whether initial S/F ratio on admission can indicate the requirement of invasive mechanical ventilation (IMV) later in the course of the disease.

This was a prospective observational study conducted in tertiary care COVID center, AIIMS, India after ethical committee approval (IEC-856,4.9.20 dated 14.10.20). Adult patients of  $\geq 18$  years of age suffering from moderate to severe COVID (RT-PCR positive) requiring oxygen support or IMV admitted in the intensive care unit (ICU) were included after consent. The patients were administered oxygen with different interfaces as per their baseline SpO<sub>2</sub> and clinical condition to target SpO<sub>2</sub> 92–94% (88–92% in patients with COPD) (life scope bedside monitor from nihonkohden BSM-37630 series). The first arterial blood gas (ABG) analysis (werfen diagnostic corporation, Gem premiere-3000) was done at the time of admission to ICU, and subsequent analysis were done according to clinical condition of patients at the physicians discretion. No specific time points was selected, however, ABG s were done at different FiO<sub>2</sub> in the same patient were recorded. The FiO<sub>2</sub> and SpO<sub>2</sub> were noted at the time of ABG analysis. The FiO<sub>2</sub> delivered with standard facemask was calculated as 0.4 with 5–6 l of oxygen, 0.5 with 6–7 l and 0.6 with >7l of oxygen flow and with non rebreathing mask (NRBM) as 0.9 with 12–15 l of flow. The exact FiO<sub>2</sub> was set on the high flow nasal cannula (HFNC) machine and non invasive ventilation (NIV) machine according to the patient requirements. The demographic

data, vitals, FiO<sub>2</sub>, S/F ratio and P/F ratio and outcomes were noted.

Assuming significant correlation with  $r=0.65$ , the calculated sample size was 80 for 80% power with 5% level of significance at two sided test. A total of 80 patients were enrolled in this study and 249 observations were noted. Data was analyzed using Statistical software packages IBM SPSS, version 21.0. The correlation between S/F ratio and P/F ratio was established using spearmann correlation coefficient and linear regression test was used to develop the equation for S/F and 95% confidence interval were reported.

The mean age of study population was  $52 \pm 13$  years and 65% were males. Out of 80 patients, 60 had comorbidities, diabetes mellitus being the most common. The initial respiratory support varied with 37.5% on facemask, 28.7% on NRBM, 8.7% on HFNC/NIV and 25% on IMV (Supplementary file 1). The mean initial S/F ratio of the patients was  $159.77 \pm 72.14$  and mean P/F ratio was  $147.86 \pm 103.26$ . A scatter plot of S/F and P/F ratios [249 observations] demonstrated a linear correlation (Fig. 1). The value of  $r$  was 0.86, almost similar as in study by Rice et al.<sup>9</sup> ( $r=0.89$ ) indicating a positive correlation.

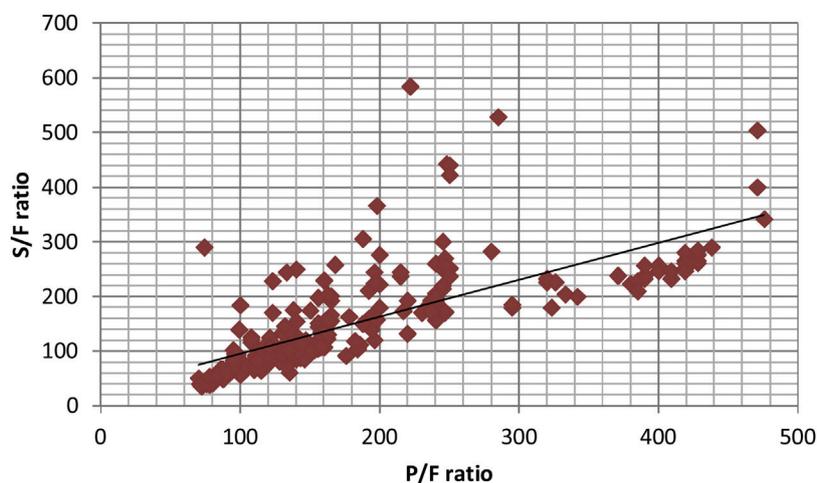
The SF ratio could be predicted well from PF ratio, described by the linear regression equation  $\text{SpO}_2/\text{FiO}_2 = 0.80 (\text{PaO}_2/\text{FiO}_2) + 59.8$  [95% CI for regression coefficient 0.71–0.89]. Based on this equation, SF ratio of 219 and 299 corresponds to PF ratio of 200 and 300 [ $p < 0.001$ ] which is similar to results by Rice et al.<sup>9</sup> (S/F ratio of 235 and 315 surrogates for P/F ratio of 200 and 300). Rice et al.<sup>9</sup> had included patients with ALI/ARDS due to various causes like sepsis, trauma, pneumonia and aspiration and those who were on IMV as per ARDS net trial protocol, whereas we included patients on oxygen as well as patients on IMV.

Recently, Fukuda et al.<sup>8</sup> reported that S/F was useful for predicting the clinical outcomes in mechanically ventilated patients with acute hypoxemic respiratory failure with bilateral opacities. Similarly, Choi et al.<sup>9</sup> reported S/F ratio on admission as a strong predictor of occurrence of ARDS in COVID patients requiring oxygen therapy.

We examined whether initial S/F ratio can indicate the requirement of IMV. In our study, 19 out of 60 patients required IMV later in the course of the disease (ventilated group) and 41 did not (non ventilated). We compared these two groups (Table 1). There were no differences in the demographic characteristics, initial S/F ratio and P/F ratio, in the two groups, however, the ventilated group patients were significantly more tachycardiac and tachypneic on admission pointing to the fact that patients were able to maintain oxygenation in the initial phase of the disease at the expense of tachypnea and use of accessory muscles.

The median initial S/F ratio [147.5 (71–333)] in our cohort was much lower than in the study by Choi et al.,<sup>9</sup> (287.5 and 452.4) indicating patients were more hypoxemic and in advanced disease in our study probably owing to the delayed presentation to hospital in our cohort. Moreover, factors other than oxygenation e.g. secondary infections, altered sensorium could be reasons for deterioration and mechanical ventilation.

Furthermore, it is imperative to note that some patients with COVID may not have dyspnea despite being hypoxemic, and therefore clinical monitoring of vitals gains paramount



**Figure 1** S/F ratio vs P/F ratio scatter plot. S/F ratio – SpO<sub>2</sub>/FiO<sub>2</sub>; P/F ratio – PaO<sub>2</sub>/FiO<sub>2</sub>. The line represents the best fit linear relationship  $SpO_2/FiO_2 = 0.80(PaO_2/FiO_2) + 59.8$  ( $p < 0.001$ ).

**Table 1** Comparison between patients who required invasive ventilation (ventilated group) and who did not require invasive ventilation (non ventilated group).

Variables	Invasive ventilation group (n = 19) Number (%) / Mean ± SD / Median [Range]	Without invasive ventilation group (n = 41) Number (%) / Mean ± SD / Median [Range]	P-value
Age	49.52 ± 17.79	52.56 ± 12.99	0.457
Male/female	12/7	26/15	0.985
HR (beats/min)	101.93 ± 24.19	88.26 ± 16.37	0.0132*
SBP (mm/Hg)	124.7 ± 22.5	128.8 ± 21.8	0.54
DBP (mm/Hg)	74.8 ± 11.6	72.1 ± 10.6	0.37
RR (breaths/min)	33.47 ± 6.08	27.23 ± 3.55	0.0001*
Accessory muscles use	12 (63)	5 (12.1)	0.0001*
Initial respiratory support			0.012*
Facemask	5 (26.3)	25 (60.9)	
NRBM	9 (47.3)	14 (34.1)	
HFNC/NIV	5 (26.3)	2 (4.88)	
S/F ratio	116 (80–250)	160 (71–333)	0.14
P/F ratio	100 (41–442)	145 (36–528)	0.739

HR – heart rate; RR – respiratory rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; S/F ratio – SpO<sub>2</sub>/FiO<sub>2</sub>; P/F ratio – PaO<sub>2</sub>/FiO<sub>2</sub>; NRBM – non rebreathing mask; HFNC – high flow nasal cannula; NIV – non invasive ventilation.

\* Significant.

importance in these patients. They require aggressive management in order to halt further deterioration.

In conclusion, S/F ratio can be used as surrogate of P/F ratio in patients with COVID pneumonia and can be highly useful in resource limited settings during this pandemic. However, initial S/F ratio on admission cannot indicate the need of invasive ventilation later in the course of the disease.

### Authors' contribution

Ashutosh Kumar – acquisition of data, or analysis and interpretation of data.

Richa Aggarwal – conception and design of the study, analysis and interpretation of data, drafting the article.

Puneet Khanna – conception and design of the study.

Rakesh kumar – drafting the article or revising it critically for important intellectual content.

Kapil Dev Soni – drafting the article or revising it critically for important intellectual.

AnjanTriKha – revising it critically for important intellectual content and final approval of the version to be submitted.

### Funding source

None.

### Conflict of interest

The authors have no competing interests to declare.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.medin.2021.10.005](https://doi.org/10.1016/j.medin.2021.10.005).

## References

- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–62, [http://dx.doi.org/10.1016/S0140-6736\(20\)30566-3](http://dx.doi.org/10.1016/S0140-6736(20)30566-3).
- Tobin MJ, Jubran A, Laghi F. Misconceptions of pathophysiology of happy hypoxemia and implications for management of COVID-19. *Respir Res*. 2020;21:249, <http://dx.doi.org/10.1186/s12931-020-01520-y>.
- Dhont S, Derom E, Van Braeckel E, Depuydt P, Lambrecht BN. The pathophysiology of 'happy' hypoxemia in COVID-19. *Respir Res*. 2020;21:198, <http://dx.doi.org/10.1186/s12931-020-01462-5>.
- Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB, et al. Comparison of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio and the PaO<sub>2</sub>/FiO<sub>2</sub> ratio in patients with acute lung injury or ARDS. *Chest*. 2007;132:410–7, <http://dx.doi.org/10.1378/chest.07-0617>.
- Bilan N, Dastranji A, Behbahani AG. Comparison of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio and the PaO<sub>2</sub>/FiO<sub>2</sub> ratio in patients with acute lung injury or acute respiratory distress syndrome. *J Cardiovasc Thorac Res*. 2015;7:28–31, <http://dx.doi.org/10.15171/jcvtr.2014.06>.
- Rivello ED, Kiviri W, Twagirumugabe T, Mueller A, Banner-Goodspeed VM, Officer L, et al. Hospital incidence and outcomes of the acute respiratory distress syndrome using the Kigali modification of the Berlin definition. *Am J Respir Crit Care Med*. 2016;193:52–9, <http://dx.doi.org/10.1164/rccm.201503-0584OC>.
- Tobin MJ, Laghi F, Jubran A. Why COVID-19 silent hypoxemia is baffling to physicians. *Am J Respir Crit Care Med*. 2020;202:356–60, <http://dx.doi.org/10.1164/rccm.202006-2157CP>.
- Fukuda Y, Tanaka A, Homma T, Kaneko K, Uno T, Fujiwara A, et al. Utility of SpO<sub>2</sub>/FiO<sub>2</sub> ratio for acute hypoxemic respiratory failure with bilateral opacities in the ICU. *PLOS ONE*. 2021;16:e0245927, <http://dx.doi.org/10.1371/journal.pone.0245927>.
- Choi KJ, Hong HL, Kim EJ. The association between mortality and the oxygen saturation and fraction of inhaled oxygen in patients requiring oxygen therapy due to COVID-19-associated pneumonia. *Tuberc Respir Dis (Seoul)*. 2021;84:125–33, <http://dx.doi.org/10.4046/trd.2020.0126>.

A. Kumar<sup>a</sup>, R. Aggarwal<sup>b,\*</sup>, P. Khanna<sup>a</sup>, R. Kumar<sup>a</sup>, A.K. Singh<sup>a</sup>, K.D. Soni<sup>b</sup>, A. Trikha<sup>a</sup>

<sup>a</sup> Department of Anaesthesiology, Critical Care and Pain Medicine, AIIMS, New Delhi, India

<sup>b</sup> Critical and Intensive Care, JPNATC, AIIMS, India

\* Corresponding author.

E-mail address: [pathakricha@yahoo.co.in](mailto:pathakricha@yahoo.co.in) (R. Aggarwal).

0210-5691/ © 2021 Elsevier España, S.L.U. y SEMICYUC. All rights reserved.

## Heterogeneity of hypoxemia severity according to pulse oximetry and blood gas analysis in COVID-19 pneumonia



## Heterogeneidad de la severidad de hipoxemia de acuerdo a oximetría de pulso y gases arteriales en neumonía COVID-19

Dear Editor,

Pneumonia is the hallmark of severe COVID-19.<sup>1</sup> Strain in healthcare systems across the world has forced countless hospitals to conduct grueling triages to decide who gets to be admitted when healthcare saturation was rampant.<sup>2</sup> As these decisions are inherently complex, numerous risk scores and predictor factors have been described to aid the attending medical team.<sup>3–5</sup> These often include clinical and laboratory values.

One commonly utilized criteria to determine patient severity is the severity of hypoxemia.<sup>6</sup> This can be assessed with arterial oxygen pressure (PaO<sub>2</sub>), PaO<sub>2</sub> to inspired fraction of oxygen (FiO<sub>2</sub>) ratio, arterial oxygen saturation (SatO<sub>2</sub>), pulse oximeter oxygen saturation (SpO<sub>2</sub>), SatO<sub>2</sub> to FiO<sub>2</sub> ratio, SpO<sub>2</sub> to FiO<sub>2</sub> ratio, and the prescribed oxygen device.<sup>7</sup>

The use of these criteria for hypoxemia severity in non-intubated patients has been criticized given the expected high inter-patient variability in FiO<sub>2</sub>, shunt fraction, and physician's choice of oxygenation device and oxygen flow.<sup>7</sup> Therefore, relying on these criteria is suboptimal given the low comparability between different patients.

In this study, we aimed to compare the severity of hypoxemia in patients with severe COVID-19 according to oxygenation index arriving at an emergency department.

We performed a retrospective cohort study collecting information on every patient who arrived at the emergency department (ED) of a reference COVID-19 tertiary center between April 1st, 2020, and April 30th, 2021. At arrival, every patient had to go through a triage station where vital signs (including SpO<sub>2</sub>) were documented before entering the emergency department. Once in the emergency department, all patients who had low SpO<sub>2</sub> (usually < 92%) received supplemental oxygen. Only nasal cannula and non-rebreathing masks were available at our center. Arterial blood gas analysis was performed in all patients with suspected COVID-19. Generally, FiO<sub>2</sub> was estimated heuristically by the treating physician by adding to the baseline FiO<sub>2</sub> (21%) 3% for every extra liter of oxygen per minute.<sup>8</sup> For example, a patient receiving 2 l of minute of supplemental oxygen would have a calculated FiO<sub>2</sub> of 27% (21 + 3\*2). SpO<sub>2</sub> was obtained at ambient air, while arterial blood gas was obtained almost universally when patients received supplemental oxygen. Given the closeness between SpO<sub>2</sub> and