Clinical Infectious Diseases
CORRESPONDENCE

Severe Hypoxemia With Normal Heart and Respiratory Rate in Early-stage Coronavirus Disease 2019 Patients: The "Happy Hypoxemia Phenomenon"

To the Editor—To reach a wide audience of colleagues and patients, we used social media and repeatedly posted an image showing oxygen saturation measured in coronavirus disease 2019 (COVID-19) outpatients. One Instagram follower showed this device's reading for a COVID-19 patient with a normal heart rate despite low oxygen saturation (Figure 1A). Since the beginning of the COVID-19 pandemic, some of us have used digital oximeters as a routine screening tool for hypoxemia. These devices show oxygen saturation and heart rate simultaneously, are inexpensive, and lay people can use them with minor guidance. Curiously, COVID-19 patients often show a low oxygen saturation while presenting clinically well: an unexpected presentation for this new disease when compared with other common acute respiratory distress syndromes [1]. This is sometimes referred to as "happy hypoxemia" [1].

The Instagram comment made us realize that in patients with confirmed COVID-19 at early stages who are breathing room air, the detection of hypoxia (oxygen saturation lower than 94%) is often not clinically followed by a corresponding increase in heart or respiratory rates. As a consequence, many patients with silent hypoxemia do not seek medical care, which might explain the high lethality observed during the first wave of the disease in many continents when the recommendation was to seek medical care only in case of dyspnea [2]. In COVID-19, when respiratory discomfort begins, hypoxemia has presumably lasted for several days, and patients have severe illness and are hospitalized with more advanced lung disease, leading to poor outcomes [3]. When patients start to desaturate (oxygen saturation <94%), they benefit from supplementary oxygen [4] and the use of steroids for 10 days [5]. Actually, corticoid administration before the need for supplementary oxygen seems to be associated with increased lethality [6].

We analyzed the dataset derived from admission records of participants with COVID-19 recruited into our Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With COVID-19 (Metcovid) trial [7], and focused on those with oxygen saturation higher than 80% and not regularly using drugs that could lead to reduced heart rate. We found that peripheral oxygen saturation was poorly correlated with heart and/or respiratory rates (Figure 1B and C). In the dots representing individual cases, one sees that many patients had hypoxia with heart rates lower than 100 beats per minute and respiratory rates below 20 incursions per minute. The correlation between these 2 variables is expected to be linear, as per physiological compensation mechanisms [8].

COVID-19–related acute respiratory distress syndrome is often not accompanied by typical features of the syndrome, as has been recognized before. A combination of factors including low P/F ratios, high A-a gradient, relatively preserved lung mechanics, and normal pulmonary pressure may indicate a process occurring on the vascular side of the alveolar-capillary unit. The scant pathophysiology data available indicate the relative dominance of intrapulmonary shunting or dead space in different studies [9]. This might also explain why endotracheal intubation is generally postponed in such patients, unless they

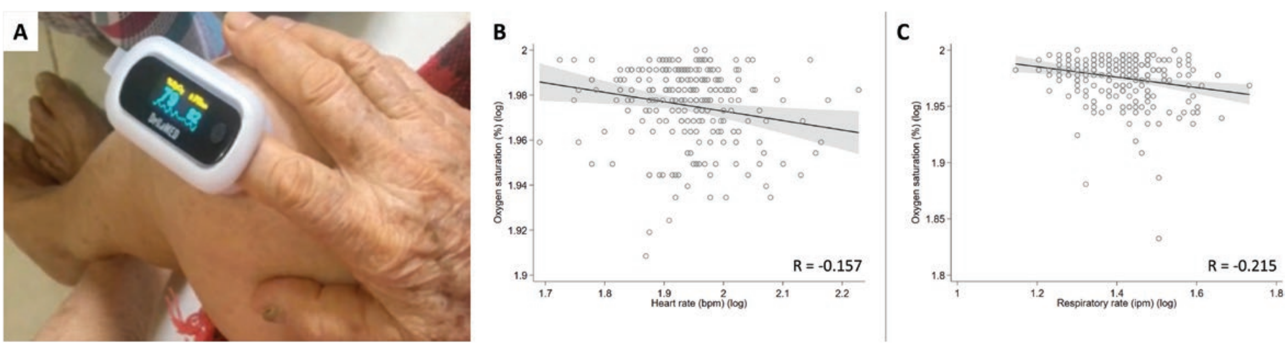

Figure 1. Low oxygen saturation without increased heart rate (*A*) in a COVID-19 outpatient and (*B* and *C*) weak correlation between peripheral oxygen saturation and heart rate in COVID-19 patients. Oxygen saturation measured with a digital oximeter in a 74-year-old female outpatient with confirmed COVID-19 without any respiratory complaints shows a normal heart rate (82 beats/min), despite low oxygen saturation (79%). The patient was immediately transferred to a reference hospital, where she received noninvasive ventilation and recovered 10 days after being hospitalized. Logarithmical correlations are shown between (*B*) peripheral oxygen saturation (%) and heart rate (beats per minute) and (*C*) peripheral oxygen saturation (%) and respiratory rate (incursions per minute) on admission, in hospitalized patients with confirmed COVID-19 by RT-PCR. The Pearson test was used (n = 252). Abbreviations: COVID-19, coronavirus disease 2019; RT-PCR, reverse transcription polymerase chain reaction.

present with clinical signs of excessive inspiratory efforts, in which case mechanical ventilation is prioritized to avoid excessive intrathoracic negative pressures and self-inflicted lung injury [10].

The early clinical evaluation of patients with mild/moderate symptoms using an oximeter rather than respiratory discomfort as a triaging warning sign is recommended to guide hospitalization because it might contribute to detecting those with inadvertent hypoxemia and thus lead to a more favorable outcome. Such strategy may work better than the early use of drug interventions, which to date have failed to show a significant impact.

More emphasis should be given to the importance and usefulness of digital oximetry in the risk-stratification of outpatients with COVID-19 as a cost-effective measure with potential impact on public health in times of this global pandemic. Clinical symptoms of respiratory discomfort, triggered by an increase in heart and respiratory rates, are not good markers for a timely diagnosis of this unique "silent/happy hypoxemia" seen in COVID-19. Early detection of hypoxemia with the use of low-cost household oximeters may save lives, allowing for timely hospitalization and the use of evidence-based treatment with oxygen supplementation and steroids.

Notes

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