*Available online at* www.scientiaresearchlibrary.com

**Scientia Research Library**

**ISSN 2348-0416**
**USA CODEN: JASRHB**

**Journal of Applied Science And Research, 2021, 9 (3):6-11**

(*http://www.scientiaresearchlibrary.com/arhcive.php*)

# HAPPY HYPOXIA

**MRS. NANCY THOMAS**
*ASST.PROFESSOR, MEDICAL SURGICAL NURSING, SANJAY GANDHI COLLEGE OF NURSING, BENGALURU*

## ABSTRACT

*The pandemic COVID-19added to the misery in the life of the people. The destiny of the world after this unremitting pandemic remains as mystery.In spiteof practisingall the safety measures including frequent handwashing, staying indoors, imposing curbs in society, maintaining social distancing and ongoing vaccination drive,the contagious infection still grabs the earth.The symptoms ofCOVID-19include fever, dry cough, tiredness,shortness of breath, chest pain or pressure,sore throat, headache, diarrhoea, loss of smell and taste, rashes on skinetc. The latest symptom to get included inCOVID-19list is 'happy hypoxia'.Normally,our body shows symptoms of less oxygen saturationsuch as headache, breathlessness, increased heart rate, confusion, bluish colour in skin, fingernails, and lips. But, doctors who treat COVID-19 have noticed that the even after the oxygen levels dip to a very dangerous level, patients do not get any breathing difficulty and seems to be alright. Many patients may have arterial hypoxemia without any signs of respiratory distress. This entity is described as silent or 'happy' hypoxemia.[1]Although some clinicians call this condition 'Happy Hypoxia' colloquially, the proper medical term is 'Silent Hypoxia.[3]Understanding the essentialpathology and symptoms of happy hypoxia may help us nurses to educate the general public regarding the dangers of this entity and thus save the lives of many people around us. This article focuses on various mechanisms involved in hypoxemia in the human body.*

**Keywords :** ***COVID-19:***Coronavirus Disease 2019

***SARS-CoV-2:***Severe Acute Respiratory Syndrome Coronavirus 2

***$SpO_2$ :***Oxygen saturation measured by pulse oximetry

***$PaO_2$ :*** Partial gas pressure of dissolved oxygen in the blood

***$PaCO_2$ :*** Partial gas pressure of dissolved carbon dioxide in the blood

***V/Q:***Ventilation/Perfusion

***$F_iO_2$:*** Fraction of inspired oxygen

***$P(A\text{-}a)O_2$ gradient:*** the alveolar to arterial oxygen gradient

## INTRODUCTION

Hypoxemia is defined as the decrease in the partial pressure of oxygen in the blood, and Hypoxia is defined as reduced level of tissue oxygenation.[2] While hypoxemia can cause hypoxia, the word "hypoxia" is usuallyused interchangeably to explain both the problems.[3]Happy or silent hypoxemiaisn't exclusively seen in COVID-19, but may also occur in conditions likeatelectasis, intrapulmonary shunt (i.e. arterio-venous malformations) or right-to-left intracardiac shunt.[1]

Diseases that interfere with adequate oxygen transfer results inhypoxemia**.**Thiscauses a decrease in arterial oxygen (PaO2) and saturation (SaO2).[4]Arterial oxygen tension ($PaO_2$) is the partial pressure of oxygen that indicates the dissolved oxygen in the plasma and not the oxygen bound to haemoglobin.The normal $PaO_2$ level ranges from 80 to 100 mmHg. It is measured by arterial blood gas analyser.[2]Arterial oxygen saturation ($SaO_2$) is defined as the percentage of haemoglobin saturated with oxygen. It can be measured by both pulse oximetry and arterial blood gas analysis.[2] The abbreviation SpO2 is used to indicate the oxygen saturation of haemoglobin as measured by pulse oximetry.[4]The normal oxygen levels in a pulse oximeter usually range from 95% to 100%.Blood oxygen levels below 90% are considered low (hypoxemia).[7]Arterial blood gases (ABGs) are used to assess changes in pH, PaO2, PaCO2, bicarbonate, and SaO2. Pulse oximetry is used tofind out the arterial O2 saturation (SpO2).[4]

When arterial $P_aO_2$ drops below 40 mmHg, dyspneamay occur. When hypoxemia occurs, there is an increase in the tidal volume and respiratory rate. Not the dyspnoea, but the increased respiratory rate (tachypnea) and tidal volume (hyperpnea) are the foremost clinical signs of impending hypoxemic respiratory failure.[1]The air sacs in COVID-19 patients' lungs do not fill with fluid or pus as in normal pneumonia infections but rather the virus only causes the air sacs to collapse, thereby reducing the oxygen levels that lead to hypoxia in these patients but still maintains the lungs' normal ability to expel carbon dioxide. Consequently, the still-efficient removal of carbon dioxide is the reason why COVID-19 patients do not feel shortness of breath in the initial stages of COVID-19 pneumonia.[8]Hypoxia is a serious warning call given by our body for impending failure of body organs and is generally accompanied by severe breathlessness. But, silent or happy hypoxia does not show any noticeable external symptoms and patient seems to be normal outside. Patients may have severe hypoxaemia without proportional features of respiratory distress.In the initial stages of sickness,the COVID-19 infected patient seems to be fineand 'happy' on the outside. The patients don't realize that they are being bereft of oxygen and their health would be deteriorated critically by the time when they realize the ill-health and seek medical advice.[3]The prognosis for silent hypoxia is generally poor, as oxygen levels in the blood can drop below 50 percent without being noticed.[8]

### Substantive factors associated with silent hypoxia in COVID-19 patients

Research findings revealed that the possible reasons for lack of dyspnoea in silent hypoxic COVID-19 patientsmay include the following: (i)silent hypoxic COVID-19 patients having a slightly increased level of carbon dioxide (~ 34–41 mm Hg, while the normal blood carbon dioxide concentration is ~ 22–29 mm Hg). The alteration in carbon dioxide level triggers a hypoxia threshold resulting in precipitation of the lung damage indicator of dyspnoea symptoms.

In normal hypoxic conditions, even minute imbalance in the $PaCO_2$ levels rapidly evokes large increases in minute ventilation and brief respiratory alkalosis, which provokes dyspnoea. However, normal hypoxia-induced dyspnoea does not evoke a stronger and excessive volume like hypercapnia does. This might be the reason for COVID-19 patients not showing any sign of distress even during the low oxygen saturation level; (ii) the virus having an impact on the brain and nervous system; altering the mechanisms in our brain responsible for regulating respiration; (iii) the

virus having an effect on blood vessels and causing "lack of hypoxic vasoconstriction". (iv) Besides, the condition can further contribute to the mechanism of "cytokine storm" by recruiting different mediators of inflammation. (iv) silent hypoxia can cause serious endothelial damage through NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells)transcription factor activation. (v) Silent hypoxia can also signal a different immune-metabolism pathway and cause secondary organ damage. All these factors lead to the critical condition of patients along with an increased mortality rate among COVID-19 patients.[9]

**Mechanismof hypoxemia in COVID-19**

Ventilation-Perfusion Mismatch. In normal lungs, the volumeof blood perfusing the lungs each minute is approximately equal to the amount of gas that reaches the alveoli each minute. In a perfectly matched system, each portion of the lung would receive 1 mL of air (ventilation) for every 1 mLof blood flow (perfusion). This match of ventilation and perfusionwould result in a V/Q ratio of 1:1, which is expressed asV/Q = 1. When the match is not 1:1, a V/Q mismatch may occur.[4]

V/Q mismatch occurs in many diseases in which increased secretionsare present in the airways such as chronic obstructive pulmonarydisease or alveoli (pneumonia), inwhich bronchospasm is present (asthma) and with alveolar collapse (atelectasis). All these conditions resultin limited airflow (ventilation) to alveoli but have no effect onblood flow (perfusion) to the gas exchange units.A pulmonary embolus affects the perfusion portion of theV/Q relationship. The embolus limits blood flow but has noeffect on airflow to the alveoli, again causing V/Q mismatch.[4]

Arterial hypoxemia early in SARS-CoV-2 infection is mainly caused by V/Q mismatch and the pulmonary arterial blood flow to non-ventilated alveoli.[1]

**Intrapulmonary shunting**

An intrapulmonary shuntoccurs when blood flows through thepulmonary capillaries without participating in gas exchange.Intrapulmonary shunt is seen in conditions in which the alveoli

fill with fluid such as acute respiratory distress syndrome,pneumonia.[4]

Patients with shunt are usually more hypoxemic than patients with V/Q mismatch. Oxygen therapy alone is usually ineffective in increasing the PaO2if hypoxemia is due to shunt. They oftenrequire mechanical ventilation and a high fraction of inspiredO2 (FIO2) to improve the gas exchange.[4]

Due to increased lung edema (leading to ground-glass opacities and consolidation on chest imaging), loss of surfactant and superimposed pressure, alveolar collapse occurs and a significant fraction of the cardiac output is perfusing non-aerated lung tissue, resulting in intrapulmonary shunting.[1]

The tidal volume increases during the disease course leading to rising negative inspiratory intrathoracic pressure. The latter, along with increased lung permeability due to inflammation, will eventually lead to progressive edema, alveolar flooding, and patient self-inflicted lung injury. Gradually, the increased edema will further enhance lung weight, alveolar collapse, and dependent atelectasis, resulting in progressively increasing shunt fraction and further decline of oxygenation which cannot completely be corrected by increasing $F_iO_2$.[1]

**Loss of lung perfusion regulation**

The persistence of high pulmonary blood flow to non-aerated lung alveoli appears to be caused by the relative failure of the hypoxic pulmonary vasoconstriction mechanism (constriction of small intrapulmonary arteries in response to alveolar hypoxia) during SARS-CoV-2 infection, as recently

illustrated by Lang et al. using dual-energy CT.[1]

**Intravascular microthrombi**

Endothelial injury is emerging as a central hallmark of COVID-19 pathogenesis. Intravascular microthrombi occurs due to an imbalance between procoagulant and fibrinolytic activity in the presence of acute inflammation and endothelial injury.

Diffuse intravascular coagulation (DIC) is also seen in patients with severe COVID-19, mediated via endothelial release of tissue factor and activation of clotting factor VII and XI. Many patients with COVID-19 develop elevated D-dimers suggesting the formation of blood clots. D-dimer levels on admission are used to predict in-hospital mortality in COVID-19.

Autopsy of the lungs after severe disease showed fibrin deposition, diffuse alveolar damage, vascular wall thickening, and frequently occurring complement-rich microthrombi occluding lung capillaries and larger thrombi causing pulmonary artery thrombosis and embolism. Hypercoagulable state ends up in further deterioration in V/Q mismatch and lung tissue damage. Coagulation is also modulated by activating C-reactive protein and resulting complement activation and hepatic synthesis of fibrinogen as an acute phase protein in COVID-19.[1]

**Impaired diffusion capacity or diffusion limitation.**

Diffusion limitation occurs when gasexchange across the alveolar-capillary interface is compromisedby a process that thickens, damages, or destroys the alveolarmembrane or affects blood flow through the pulmonary capillaries. Diffusion limitation is worsened by diseasestates affecting the pulmonary vascular bed such as severeCOPD (chronic obstructive pulmonary disease)or recurrent pulmonary emboli. Some disease statescause the alveolar-capillary interface to become thicker(fibrotic), which slows gas transport. These include pulmonaryfibrosis, interstitial lung disease, and ARDS (acute respiratory distress syndrome).The classic sign of diffusion limitation is hypoxemia that ispresent during exercise but not at rest. During exercise, bloodmoves more rapidly through the lungs, decreasing the time fordiffusion of O2 across the alveolar-capillary interface.[4]

SARS-CoV-2 propagates within alveolar type II cells, where a large number of viral particles will be produced and released, followed by immune response mediated destruction ofinfected cells. Loss of alveolar epithelial cells and a pro-coagulant state cause the denuded basement membrane to be covered with debris, consisting of fibrin, dead cells, and complement activation products, collectively referred to as hyaline membranes.[1]

With incremental exercise and in the state of absent hypoxic vasoconstriction in COVID-19, a hyperdynamic pulmonary circulation might not allow sufficient time for red blood cells to equilibrate their oxygen uptake. A diffusion limitation may, therefore, occur in COVID-19 leading to a raised $P(A\text{-}a)O_2$ gradient and exercise-induced arterial hypoxemia (EIAH).[1]

The A-a oxygen gradient indicates the integrity of the alveolocapillary membrane and effectiveness of gas exchange.[2] The A-a gradient, or the alveolar-arterial gradient, measures the difference between the oxygen concentration in the alveoli and arterial system. In a perfect system, no A-a gradient would exist: oxygen would diffuse and equalize across the capillary membrane, and the pressures in the arterial system and alveoli would be equal (resulting in an A-a gradient of zero).The A-a gradient has important clinical utility as it can help narrow the differential diagnosis for hypoxemia.[6]

**Early Detection of Silent Hypoxia in COVID-19**

The patients who have minor COVID-19 symptoms like sore throat, cough, fever, headaches, without any noticeable breathing difficulty should monitor their oxygen level by using pulse oximeter at home. Seek medical attention immediately if the oxygen value drops less than 94 percent.[3]

## CONCLUSION

According to the existing knowledge, it is still unclear why silent hypoxia occurs in a COVID-19 patient. The available data suggest that the virus may be affecting the brain and nervous system, or there might be a lack of hypoxic vasoconstriction in such patients. Some studies suggest that hyper-fusion and normal carbon dioxide level even at the time of low oxygen saturation could be potential reasons behind this phenomenon. The clinicians are working to draw a solid conclusion on this matter.[9]In COVID-19 patients with comorbidity, the absence of shortness of breath should not be considered as a good sign of well-being. In these patients, pulse oximetry is an important mean to predict the outcome along with LDCT scanner(low-dose computed tomography).[5]The key factorto prevent complication is to detect this initial drop in oxygen saturation levels to prevent the lungs from deteriorating further.[8]Understanding of silent hypoxemia and its pathology would help the health care team including nurses to do meticulous monitoringof respiratory rate, signs of hyperventilation, oxygen saturation. Early detection of COVID-19 pneumonia can prevent patients from having to be treated with highly invasive procedures such as intubation and mechanical ventilation, a procedure which currently results in an 80% mortality rate for COVID-19 patients.[8]

COVID-19 patients should be educated to regularly check their oxygen levels using an oximeter and be responsive to immediately track any variation. If value drops below 94 per cent, immediate hospitalization with oxygen administration is critical to forestallfurther complications.This unusual clinical picture of hypoxia out of proportion to the respiratory distress should be discussed with the health care team so that they can they can identify the subtle clinical signs in the community[10].Nurses, being the front-line health workers can educatethe public regarding symptoms of happy hypoxia and save the life of people.

## REFERENCE

[1] SebastiaanDhont, Eric Derom, Eva Van Braeckel, Pieter Depuydt& Bart N. Lambrecht. The pathophysiology of ‘happy’ hypoxemia in COVID-19. Respiratory Research volume 21, Article number: 198 (2020). [cited 2021June 11].Available from:URL: https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-020-01462-5

[2] Malay Sarkar, N Niranjan and PK Banyal Mechanisms of hypoxemia. Lung India. 2017 Jan-Feb; 34(1): 47–60.doi: 10.4103/0970-2113.197116. PMID: 28144061. [cited 2021June 11]. Available from: URL:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5234199/

[3] Silent Hypoxia or Happy Hypoxia in COVID-19 Patients. [cited 2021June 11]Available from: URL:https://healthlibrary.askapollo.com/silent-hypoxia-or-happy-hypoxia-in-COVID-19-patients/

[4] Lewis, Heitkemper, Dirksen Bucher. Medical surgical nursing- assessment and management of clinical problems. 9th ed.ElsevierMosby, Missouri; 2014.p. 1654-7.

[5] Philippe Brouqui, Sophie Amrane, Matthieu Million, Sébastien Cortaredona, Philippe Parola, Jean-Christophe Lagier,Didier Raoult. Asymptomatic hypoxia in COVID-19 is associated with poor outcome. International Journal of Infectious Diseases.Volume 102, P233-238, January 01, 2021. [cited 2021June 11]. DOI:https://doi.org/10.1016/j.ijid.2020.10.067. Available from: URL: https://www.ijidonline.com/article/S1201-9712(20)32271-2/fulltext.

[6] Paris J. Hantzidiamantis; Eric Amaro. Physiology, Alveolar to Arterial Oxygen Gradient. [cited 2021June 18]. Available from:URL: https://www.ncbi.nlm.nih.gov/books/NBK545153/

[7] Dr. Jasmine Shaikh. What Are Blood Oxygen Levels? Chart. [cited 2021June 18]. Available from: URL:https://www.medicinenet.com/what_are_blood_oxygen_levels/article.htm

[8] Jason Teo. Early Detection of Silent Hypoxia in COVID-19 Pneumonia Using Smartphone Pulse Oximetry. J Med Syst. 2020; 44(8): 134.doi: 10.1007/s10916-020-01587-6. [cited 2021June 19]. Available from: URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7305055/

[9] Ahsab Rahman, Tahani Tabassum, YushaAraf, Abdullah Al Nahid, Md. Asad Ullah & Mohammad Jakir Hosen.Silent hypoxia in COVID-19: pathomechanism and possible management strategy.Molecular Biology Reports volume 48, pages 3863–3869 (2021). [cited 2021June 11]. Available from: URL: *https://link.springer.com/article/10.1007/s11033-021-06358-1*

[10] Atanu Chandra, Uddalak Chakraborty, Jyotirmoy Pal and ParthasarathiKarmakar. *Silent hypoxia: a frequently overlooked clinical entity in patients with COVID-19.* [cited 2021June 11]. Available from: URL: https://casereports.bmj.com/content/13/9/e237207