Platypnea-orthodeoxia Syndrome (POS) in Moderate COVID-19: An Uncommonly Common Bedside Sign?

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Abstract

Platypnoea-Orthodeoxia syndrome (POS) is the presence of postural hypoxaemia along with breathlessness in recumbent position. It is an uncommon syndrome with elusive pathophysiologic mechanisms. We observed POS in patients of moderate COVID-19 who required hospital admission to our indoor facility and oxygen supplementation when saturation was documented in sitting and supine positions for evaluation of platypnea.

Materials and methods: We conducted an observational, cross sectional, retrospective analysis of pulse oximetry readings of patients with stage 2 COVID-19 admitted in ward during the period from 15th May 2020 to 30th May 2020. The difference in the peripheral oxygen saturation in sitting and supine positions, documented as a routine standard of care, especially in patients with platypnea, was calculated and demographic details and co-morbidities were noted from indoor record forms.

Results: Of the 53 patients of stage 2 COVID-19 who were included in the study, 15 (28%) had platypnoea-orthodeoxia syndrome at the time of presentation and 18(33.9%) patients with platypnea had ≥ 3% desaturation in sitting position as compared to supine position. Rest of the 20 (37.7%) patients had neither platypnoea nor orthodeoxia. All the patients presenting with platypnoea-orthodeoxia required oxygen therapy during the course of treatment. Amongst the 33 patients who were hypoxic and required oxygen supplementation, 15 patients (45.4%) had oxygen saturation of ≥94% in the supine position at presentation.

Conclusion: Platypnoea-orthodeoxia syndrome is common in patients with stage 2 COVID-19 infection who require oxygen therapy. POS can be easily documented by using pulse oximeter without the need of any specialised equipment. Hence, we propose that documentation of POS at the time of admission in primary health care or resource depleted settings would help in successful triage of the patients needing oxygen therapy. We also propose that oxygen saturation in sitting position be documented as far as possible. Further clinical studies are necessary to validate this observation.

Introduction

Dyspnea is reported in COVID 19 patients as the third most common symptom.¹ Platypnea is shortness of breath that occurs when the patient is upright. Orthodeoxia is oxygen desaturation in recumbent position.

Platypnoea-orthodeoxia is a rare syndrome with an unclear pathophysiological mechanism. It has been reported in disorders involving the shunting of blood. It is defined as fall in peripheral oxygen saturation (SpO₂ > 5%) in sitting position as compared to supine position associated with breathlessness in sitting/standing position.²

POS can be demonstrated at the bedside by measurement of oxygen saturation in sitting and supine position during clinical examination of the patient. It requires only a pulse oximeter to document differences in oxygen saturation on changing position. Pulse oximetry is now annotated as the fifth vital sign of clinical examination.³ Portable pulse oximeters are widely available and bedside pulse oximetry is non-invasive and simple to perform.

At the Pulmonary Medicine department of a tertiary care Municipal general hospital, the presence of platypnea-orthodeoxia syndrome in COVID-19 patients was discovered serendipitously. We noted orthodeoxia in a patient with COVID-19 attending our outpatient clinic with a symptom of platypnea. We were curious about this finding and decided to review inpatient records to assess if it was present in other patients as well. This was furthered as many patients of COVID-19 were presenting with a symptom of platypnea and radiological findings of bibasilar and peripheral involvement.

Rationale

To evaluate the symptom of platypnea, that is, breathlessness in the standing/sitting position, oxygen saturation is checked in sitting/supine and recumbent positions to note any positional variation in oxygen saturation. In normal individuals, that is, physiologically, there is no statistically significant difference in the oxygen saturation in sitting and supine positions.⁴

A patient brought in the Casualty (Emergency Department) on a stretcher and examined in supine position
showing an oxygen saturation of $>94\%$ can get triaged as ‘mild’ prior to further investigations. However, in a patient with COVID-19 with a complaint of platypnea, measurement of oxygen saturation in sitting position may show a significant difference that is enough to classify the patient as ‘moderate’ and the oxygen saturation may drop, enough to make the patient eligible for triage to indoor facility for oxygen supplementation.

As a standard of care, oxygen saturation of COVID-19 patients were recorded in sitting and supine positions. Clinical data for all patients is stored in inpatient case records. These records are maintained for the entire duration of admission. Here, we describe the results of an observational, cross sectional, retrospective analysis of oxygen saturation measurements in the sitting and supine position in patients with moderate COVID-19.

**Materials and Methods**

The study was conducted by the Department of Pulmonary Medicine and Environmental Pollution Research Centre (EPRC) at Seth G S Medical College and KEM Hospital, Parel. The study had prior approval of the Institutional Ethics Committee and a waiver of consent was granted. The study was registered in the ICMR clinical trial registry (CTRI/2020/08/027104).

This study was designed as a retrospective, cross sectional, observational analysis. It involved an analysis of daily parameter charts of patients admitted to COVID-19 ward managed by Pulmonary Medicine department at our institute. Records of indoor patients between 15th May 2020 and 30th May 2020 were included in the analysis. All the patients were diagnosed with stage 2 COVID-19. Stage 2 disease was classified as moderate, with findings of pneumonia with no signs of severe disease; in adolescents or adults, with presence of clinical features of dyspnea and/or hypoxia, fever, cough, including SpO2≤94\%(range 90-94\%) on room air; respiratory rate more or equal to 24 per minute. The patients who required ICU admission were excluded.

Oxygen saturation in sitting and supine positions are recorded as standard of care in Pulmonary Medicine ward, as we maintain a high index of suspicion for unrecognised orthodeoxia, which although very uncommon, can provide an early clinical suspicion in certain cases. Pulse oximetry is performed using a standard portable pulse oximeter (POX17, Vissco Rehabilitation Aids Pvt. Ltd., Umbergaon, Gujarat) and readings with good pulse signal strength are recorded. Platypnea-Orthodeoxia syndrome was identified by the presence of a complaint of platypnea along with oxygen saturation in the sitting position that was $>5\%$ lower than the value recorded in supine position.

**Statistical analysis:** Categorical values were described as count with percentages. Continuous variables were summarized using median and interquartile range (IQR) values. We used ‘t’ test to compare the means of differences in oxygen saturation in sitting and supine positions in patients who required oxygen supplementation during the course of their hospital admission with those who did not. ANOVA test was used to test the statistical difference in the three groups- patients with platypnea-orthodeoxia, all of whom had required oxygen supplementation at some point of their hospital course, patients who required oxygen supplementation but did not fit into the criteria for defining orthodeoxia, and patients who were not hypoxic and therefore did not require oxygen supplementation. A p value of $<0.05$ was considered to be statistically significant.

**Results**

Retrospective data over a period of 15 days was analysed. There were 45 beds in the COVID-19 ward under the care of Department of Pulmonary Medicine & EPRC and records of all the 53 patients admitted to the ward over the study period were included for retrospective, cross sectional, observational study. All the patients had pulmonary involvement and had been categorised to have stage 2 COVID-19.

The demographic data and comorbidities of these 53 patients are summarised in Table 1.

15 out of 53 patients met the definition criteria for POS at presentation. All the 15 patients were hypoxic in sitting position and required oxygen supplementation.

Platypnea-orthodeoxia syndrome was reversible in these patients as at discharge there was resolution of platypnea and no change in oxygen saturation was evident on changing position from supine to sitting. Although the objective was to study the presence of platypnea-orthodeoxia at presentation, the resolution of POS at discharge indirectly eliminates possibilities of cardiac causes like ASD, patent foramen ovale etc as the causes responsible for POS.

The median desaturation was 6\% in the POS group and 4\% in the platypnoea group who did not meet the criterion of orthodeoxia.

Amongst the 33 patients who were hypoxic and required oxygen supplementation at some point of their course in the hospital, 15 patients had oxygen saturation of $>94\%$ in the supine position at presentation and would not have been triaged as hypoxic if examined only in the supine position.

Figure 2 depicts the correlation between sitting oxygen saturation and oxygen requirement in L/min ($r=0.85$, $p<0.0001$). This brings us to the conclusion that during triage, if we need to choose one position, it should be sitting to check the initial oxygen saturation in patients attending outpatient clinics.

There was a significant difference in the positional changes in oxygen saturation in the three groups: patients with POS, patients with platypnea who did not meet criterion of orthodeoxia, and patients who neither complained of platypnea nor required oxygen supplementation. ANOVA test (6.53 ±0.99 v/s 4.22 ± 0.65 v/s 0.6± 0.94; $p<0.01$).

Mean increase in oxygen saturation in supine position in patients requiring oxygen therapy was significantly higher than in patients not requiring oxygen therapy ($5.27\%$ v/s $0.6\%$; $p<0.01$).

Table 2 summarises data observed in the study.

In the 18 patients who did not fulfill the criterion for orthodeoxia (a fall in oxygen saturation $>5\%$ in the sitting position), but had platypnea as a complaint, the mean increase on change of position from sitting to supine was 4.22\% (95% CI 3.92-4.52). This difference was significantly greater that in patients who did not require oxygen supplementation.
Platypnea-orthodeoxia syndrome is a rare clinical entity. To the best of our knowledge, this is the first study that identifies this syndrome in patients of moderate COVID-19 at presentation. Reversible platypnea-orthodeoxia has been previously described in patients with COVID-19 who recovered from severe ARDS. ⁶

Multiple mechanisms have been proposed for orthodeoxia. Although intracardiac causes are the commonest cause responsible for this syndrome, lungs are the commonest site of pathology in extracardiac causes. Pulmonary arteriovenous malformations have been found to be an important cause as these create a ‘shunt physiology’ in the lungs. Figure 3 summarizes proposed mechanisms of POS. ²

Platypnea-orthodeoxia has been reported in cases of pneumocystis and cytomegalovirus pneumonia, in patients with idiopathic pulmonary fibrosis and is an important, and at times, a debilitating feature of hepatopulmonary syndrome. This finding has also been reported in a case of bilateral lower lobe pulmonary emboli. ⁷⁻¹⁰

**Table 1: Demographic profile of 53 patients included in the study (POS: platypnea-orthodeoxia syndrome); percentages given in parentheses**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total (n=53)</th>
<th>Platypnea-orthodeoxia syndrome (n=15)</th>
<th>Platypnea-orthodeoxia syndrome ≤ 5% positional difference in O₂ saturation (n=18)</th>
<th>No platypnea-orthodeoxia (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median years)</td>
<td>54</td>
<td>46</td>
<td>52</td>
<td>60</td>
</tr>
<tr>
<td>Total individuals</td>
<td>53</td>
<td>15</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Gender- number of females(%females)</td>
<td>22 (41.5%)</td>
<td>1 (6.6%)</td>
<td>10 (55.5%)</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>No known comorbidities(%)</td>
<td>21 (39.6%)</td>
<td>6 (40%)</td>
<td>3 (16.6%)</td>
<td>12 (60%)</td>
</tr>
<tr>
<td>Diabetes(%)</td>
<td>26 (49%)</td>
<td>8 (53.3%)</td>
<td>13 (72.2%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Hypertension(%)</td>
<td>15 (28.3%)</td>
<td>2 (13.3%)</td>
<td>9 (45%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Epilepsy(%)</td>
<td>2 (3.7%)</td>
<td>1 (6.6%)</td>
<td>1 (5.5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Acute kidney injury(%)</td>
<td>1 (1.8%)</td>
<td>0 (0%)</td>
<td>1 (5.5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Acute Pulmonary embolism(%)</td>
<td>1 (1.8%)</td>
<td>1 (6.6%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Abdominal tuberculosis</td>
<td>1 (1.8%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>

Table 2: Results of retrospective analysis of clinical data. (p<0.05 is considered significant)

<table>
<thead>
<tr>
<th>Patients requiring oxygen supplementation in hospital course (n=33)</th>
<th>Patients with platypnea-orthodeoxia (n=15)</th>
<th>Patients with platypnea without defined orthodeoxia (n=18)</th>
<th>Patients with neither platypnea nor orthodeoxia (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO₂% at presentation≥94 (n)</td>
<td>7 (46.6%)</td>
<td>8 (44.4%)</td>
<td>19 (95%)</td>
</tr>
<tr>
<td>% desaturation with position change mean ± SD</td>
<td>6.53 ±0.99</td>
<td>4.22 ± 0.65</td>
<td>0.6± 0.94</td>
</tr>
<tr>
<td>P value</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Median drop in SpO₂</td>
<td>6</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Resolution of POS on recovery/discharge (%)</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

While the commonest mechanism of platypnea-orthodeoxia in cardiac pathologies is an interatrial communication, the pathophysiology of respiratory disorders differs significantly. The predominant mechanism responsible for orthodeoxia and resulting platypnea in lung disease is the creation of zone one phenomenon in the diseased lung, that is, more blood supply to diseased and underventilated lung bases.¹¹

This results in a ventilation-perfusion mismatch and impairs adequate and efficient oxygenation in the lungs. This is evident from the various case reports identifying presence of orthodeoxia in patients with respiratory disease predominantly involving the lung bases. With reduced ventilation in the lung bases, efficiency of oxygenation reduces significantly. When there is a gravity dependent increase in the blood flow to the lung bases in the upright position, the fraction of blood remaining deoxygenated is accentuated, ultimately resulting in orthodeoxia.

Prothrombotic nature of COVID-19 has been widely studied. Microvascular thromboses seen in patients with COVID-19 play a major role in the clinical manifestations of this disease. SARS-CoV-2 affects the circulatory system in multiple ways that includes endothelial damage and lymphocyte recruitment. Anticoagulation forms the basis of most treatment protocols for patients with
COVID-19 demonstrating evidence of microthrombi in the form of clinical, radiological signs or derangements in laboratory parameters.\textsuperscript{12}

A mathematical model, evolved to assess the mechanism of silent hypoxia in early stages of COVID-19 suggested that a combination of pulmonary embolism, ventilation-perfusion mismatch in the non-injured lung and normal perfusion in the small fraction of lung with alveolar injury, explain the large amount of pulmonary venous admixture.\textsuperscript{13}

Reversible platypnea-orthodeoxia syndrome has been described in COVID-19 by Tan et al. where the authors observed POS in 5/20 cases of severe COVID-19. The median drop in saturation noted by them was 8% whereas in our group we noted median drop oxygen saturation of 6%.\textsuperscript{6}

This discrepancy in median drop in oxygen saturation in patients with POS can be attributed to larger sample size of our study (5 patients v/s 15 patients). The group studied by Tan et al. had severe COVID-19 whereas our group had moderate COVID-19.

All 15 patients with platypnea-orthodeoxia syndrome required oxygen supplementation at some point of their course in the hospital. 7 out of the 15 patients had an oxygen saturation reading of \(>94\%\) at presentation in supine position, which is often how patients present in the emergency triage area.

This observation can be of help in resource limited settings for successful triage of patients where CT-Scan and inflammatory markers may not be available. The demonstration of POS requires a couple of things- a pulse oximeter which is readily available everywhere and willingness of the clinician to document oxygen saturation in supine as well as sitting positions. However, larger studies are required to validate the proposal to incorporate this as a routine protocol."

With 15 cases of moderate COVID-19 fulfilling the criteria of POS this is the largest documented study of POS in respiratory disorders, especially in COVID-19, to the best of our knowledge.

**Conclusion**

Our study observes that platypnea-orthodeoxia is a common presentation of moderate COVID-19 requiring oxygen supplementation therapy. The oxygen saturation in sitting position correlates with requirement of oxygen supplementation in patients of moderate COVID-19. Patients of moderate COVID-19 who require oxygen supplementation have a greater difference in positional oxygen saturation and a larger drop in oxygen saturation on assuming sitting from supine position as compared to patients who do not require oxygen supplementation.

It is prudent to monitor the oxygen saturation in sitting position in all patients as hypoxia may be missed if oxygen saturation is documented only in the supine position, which is how patients are often examined.

**Limitations**

The limitations of our study include the absence of cardiac evaluation for ruling out other causes of platypnea-orthodeoxia including an intracardiac shunt physiology. The study is a retrospective one. We have purposely limited our analysis to pulse oximetry records as we propose that this be a ‘clinical sign’ which will aid in initial triaging and management of COVID-19 patients at presentation. The accurate pathophysiology behind this phenomenon shall have to be studied elsewhere and is an area of research by itself.

Larger population-based studies are required to validate our claims and implement them in the national program and incorporate drop in oxygen saturation in sitting position as one of the clinical signs of mild to moderate COVID-19 patients who require oxygen therapy.

**Value added by our study**

Medical diagnosis has largely relied on a thorough history and complete physical examination with laboratory examination contributing to the confirmation. However, this pandemic has ensured that we rely on complex genotypic tests for confirmation of diagnosis.

Pulse oximetry is widely available and is being used by almost all public health initiatives across the country. We propose that positional oxygen saturation be documented in all cases of COVID-19 as the presence of a reversed gradient may be the initial, and in community health care settings, the only sign of possible hypoxia and complications.

In our study, 15 of the 33 patients who eventually required supplemental oxygen had oxygen saturations of \(\geq94\%\) at presentation and had a drop in saturation level on assuming the sitting position. This highlights the need for recording oxygen saturation in patients in the sitting and supine positions as patients present in the emergency triage area.

**Fig. 3: Proposed mechanisms of platypnea-orthodeoxia syndrome. (RA: right atrium, V/Q: ventilation-perfusion)**
a seemingly normal value of oxygen saturation in the supine position may still manifest orthodeoxia.

We propose careful examination of mild to moderate COVID cases to identify POS. Even a fall in oxygen saturation in sitting position as compared to supine position can predict the need for oxygen therapy during treatment.

We propose that documentation of oxygen saturation in sitting and supine positions be adopted at the grass root level while evaluating patients of COVID-19 as this shall contribute to more accurate triaging even in resource limited settings.

References