Correlations between intradialytic hypoxemia and complications in patients undergoing regular hemodialysis

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Correlations Between Intradialytic Hypoxemia and Complications in Patients Undergoing Regular Hemodialysis

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Abstract

Background: Dialysis is a replacement of renal functioning in patients with end-stage renal disease. Approximately 10% of chronic regular hemodialysis (HD) patients have arterial oxygen saturation of less than 90% for more than one-third of their dialysis session, which was associated with increased rates of hospitalization and mortality.

Aim: This current study aims to assess the effect of intradialytic hypoxemia as a complication that may occur during HD sessions and its impact on clinical and laboratory parameters of patients with end-stage renal disease undergoing regular HD.

Patients and methods: The current work is a hospital-based cross-sectional study. A total of 60 Egyptian patients with chronic kidney disease on regular HD were selected from patients attending the dialysis unit at New Cairo Hospital from September 2021 to December 2021. They were divided into two groups: group I, the nonhypoxic group (n = 20) and group II, the hypoxic group (n = 40).

Results: Oxygen saturation at the end of HD (89.9 ± 5.1) was significantly correlated to the development of intradialytic hypotension with a P value of 0.048.

Conclusion: Hypoxia is a predictive factor for the development of intradialytic complications.

Keywords: Hemodialysis, Hypoxia, Intradialytic hypotension

1. Introduction

Chronic renal disease occurs when the kidney damage or an estimated glomerular filtration rate of less than 60 ml/min/1.73 m² persists for more than 3 months. That is a condition in which kidney function gradually decreases, and eventually necessitating renal replacement therapy in the form of transplantation or dialysis, which may be hemodialysis (HD) or peritoneal dialysis.1

Therefore, the condition of end-stage renal disease (ESRD) can be defined as the function of the kidneys has significantly worsened to the place where renal replacement therapies are required to preserve survival. A glomerular filtration rate of less than 15 ml/min correlates with end-stage kidney failure.2 The peritoneal dialysis, continuous renal replacement therapy, and also HD are the three primary forms of dialysis.3

In those with end-stage renal failure, HD sessions are an alternative to preserve kidney function, but they have numerous impacts on psychological, social, and also physical aspects, such as exhaustion, dyspnea, anxiety, bone aches, and also depression.4

One of the complications associated with HD treatment is intradialytic hypoxemia, characterized by low arterial oxygen saturation and central venous oxygen saturation. This condition arises due to an imbalance between systemic oxygen supply and demand and is known to be associated with higher mortality rates.5

Approximately 10% of chronic regular HD patients had arterial oxygen saturation beneath 90% for more than one-third of treatment session, which
made the patients more susceptible to increased hospitalization and higher rate of mortality. Fluid overflow, impaired respiration, as well as an imbalance between ventilation and perfusion are all risk factors for the occurrence of intradialytic hypoxemia.\(^6\)

Hypoxia is a condition in which tissues receive an insufficient amount of oxygen caused by inadequate blood flow or oxygen levels in the body (known as hypoxemia). This makes it difficult to maintain appropriate homeostasis.\(^7\)

### 2. Patients and methods

This study was a hospital-based cross-sectional study. A total of 60 Egyptian patients with chronic kidney disease on regular HD were selected from patients attending the Dialysis Unit at New Cairo Hospital from September 2021 till December 2021. An informed consent was obtained from each patient before enrollment to the study after explaining the content and implication of the study. The patients had the right to withdraw from the study at any time without giving any reasons. The study was reviewed and approved by the ethics committee of the Faculty of Medicine for Girls, Al-Azhar University.

Patients with the following criteria were excluded from the study: patients who had Hb\% less than 10.5 g, patients with lung diseases, patients with heart failure, and patients with active infection requiring ongoing antibiotics or antiviral.

The included patients were classified into two groups: group I: the nonhypoxic group included 20 patients with ESRD on regular HD and group II: the hypoxic group included 40 patients with ESRD on regular HD.

All participants were subjected to the following.

- Full medical history including: personal history, history of medical disorders, past history of drug or alcohol intake, blood transfusion, and history of surgical operations.
- Complete physical examination: complete physical examination was performed on the patients including heart rate, pulse, temperature, blood pressure, and oxygen saturation by peripheral pulse oximeter every hour.
- The following laboratory investigations were collected from all studied population: complete blood pictures, C-reactive protein, liver function tests (serum albumin, alanine transaminases and aspartate transaminase), and kidney function tests including serum urea, creatinine, calcium, potassium, Na, and phosphorus and parathyroid hormone.

### 2.1. Specific investigations

Arterial blood gas at the beginning of a dialysis session and after 2 h of the session.

### 2.2. Radiological investigations

Included 12-lead surface ECG and transthoracic echocardiographic examination.

### 2.3. Statistical analysis

Statistical analysis was conducted using SPSS (Cairo, Egypt) 22nd edition; continuous variables were presented in mean ± SD, and compared using Mann–Whitney U test. Categorical variables were presented in frequency and percentage and were compared using \(\chi^2\) test. Logistic regression model was conducted to assess the risk of development of intradialytic complications in the form of hypotension and muscle cramps due to hypoxia. Any \(P\) value less than 0.05 was considered significant.

### 3. Results

This study was conducted on 60 chronic kidney disease patients on regular HD, three sessions/week each session of 4 h with high flux filter FX100, surface area 2.2 m\(^2\), dialysate flow 500 ml/min, bicarbonate +3 mmol/l, and blood bump average of 350 ml/min from arteriovenous shunt were eligible for inclusion in our final analysis.

#### 3.1. Patient’s classifications

They were divided into two groups according to the development of hypoxia: group I: the nonhypoxic group included 20 patients and group II: the hypoxic group included 40 patients.

Comparison of demographics and comorbidities between groups showed that there was no statistically significant difference in age, sex, prevalence of diabetes mellitus and hypertension with \(P\) values more than 0.05 each.

Comparison of baseline laboratory findings between groups showed that hypoxic groups had a significantly elevated serum urea and creatinine with \(P\) values of 0.0001 and 0.0001.

Hypoxic group had a significantly higher potassium level \((P = 0.0001)\), higher phosphorus \((P = 0.0001)\), higher serum cholesterol level \((P = 0.007)\), and lower calcium level \((P = 0.0001)\) when compared with the nonhypoxic group (Table 1, Figs. 1–10).
Comparison of incidence of intradialytic complications such as hypotension and muscle cramps between groups showed that there was a significantly higher incidence of hypotension among the hypoxic group when compared with the nonhypoxic group with a P value of 0.028, while there was no difference in the incidence of muscle cramps between groups with a P value of 0.71 (Table 2).

Regarding vital signs, heart rate, mean arterial pressure, and pH predialytic and intradialytic, there was no significant difference between groups. However, oxygen saturation was significantly lower among the hypoxic group, as the mean ± SD oxygen saturation baseline was 98.4 ± 1.0 % in the nonhypoxic group versus 92.7 ± 4.8 in the hypoxic group with a P value of 0.04.

Comparison of arterial pH and oxygen saturation between groups showed that the mean ± SD oxygen saturation after 1 h was 97.9 ± 1.3 in the nonhypoxic group versus 93.9 ± 4.6 in the hypoxic group with a P value of 0.003, while the mean ± SD oxygen saturation after 2 h was 98 ± 1.3 in the nonhypoxic group versus 91.6 ± 5.3 in the hypoxic group with a P value of 0.0001 and the mean ± SD oxygen saturation at the end of the session was 97.1 ± 3 in the nonhypoxic versus 91.4 ± 5.3 in the hypoxic group with a P value of 0.0001 (Table 3).

Correlations between laboratory findings and incidence of intradialytic hypotension showed that baseline laboratory findings were not associated with the development of intradialytic hypotension including kidney function tests, lipid profile, electrolytes, complete blood picture, and liver function tests with a P value of more than 0.05 (Table 4).

Logistic regression model assessing the timing of hypoxia as a risk factor for intradialytic hypotension showed that the development of hypoxia at the end of the dialysis session was an independent predictive factor for the development of intradialytic hypotension with an odds ratio of 2.48 (95 % confidence interval 0.363–6.072 and P = 0.038), which means that hypoxic patients are susceptible to hypotension 2.48 times more than nonhypoxic patients (Table 5).

Correlations between laboratory findings and incidence of intradialytic muscle cramp showed that

Table 1. Comparison of baseline laboratory findings between groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group I (N = 20)</th>
<th>Group II (N = 40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mg/dl)</td>
<td>101.5 ± 4.8</td>
<td>206.1 ± 67.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>3.98 ± 1.6</td>
<td>5.48 ± 0.65</td>
<td>0.0001</td>
</tr>
<tr>
<td>Na (mmol/ml)</td>
<td>134.7 ± 0.9</td>
<td>135.0 ± 2.2</td>
<td>0.59</td>
</tr>
<tr>
<td>K (mmol/ml)</td>
<td>4.0 ± 0.7</td>
<td>5.4 ± 0.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>1.1 ± 0.48</td>
<td>0.8 ± 0.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>PO4 (mg/dl)</td>
<td>3.54 ± 0.61</td>
<td>5.33 ± 1.39</td>
<td>0.0001</td>
</tr>
<tr>
<td>PTH (ng/dl)</td>
<td>200.3 ± 120.6</td>
<td>608.1 ± 208.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4.30 ± 0.62</td>
<td>4.05 ± 0.45</td>
<td>0.15</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>11.6 ± 4.2</td>
<td>11.7 ± 1.1</td>
<td>0.22</td>
</tr>
<tr>
<td>WBC (10^9/ml)</td>
<td>5.9 ± 0.9</td>
<td>7.0 ± 1.7</td>
<td>0.08</td>
</tr>
<tr>
<td>PLT (10^9/ml)</td>
<td>228.3 ± 64.6</td>
<td>239.6 ± 75.3</td>
<td>0.67</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>112.3 ± 25.7</td>
<td>114.5 ± 44.7</td>
<td>0.92</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>113.2 ± 31.6</td>
<td>142.0 ± 41.7</td>
<td>0.007</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>48.0 ± 12.1</td>
<td>50.2 ± 15.8</td>
<td>0.70</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>85.7 ± 15.7</td>
<td>94.4 ± 21.3</td>
<td>0.12</td>
</tr>
<tr>
<td>UF (l)</td>
<td>4.1 ± 0.7</td>
<td>4.0 ± 0.8</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PTH, parathyroid hormone; PLT, platelet; WBC, white blood cell.
Fig. 2. Box plot showing heart rate variations throughout the HD session among participants. HD, hemodialysis.

Fig. 3. Box plot showing mean blood pressure variations throughout the HD session among participants. HD, hemodialysis.
Fig. 4. Bar chart showing mean ultrafiltration based on the development of intradialytic hypotension.

Fig. 5. Box plot showing oxygen saturation at the end of the session based on the development of hypotension.
the serum calcium level was significantly associated with the development of muscle cramps, as patients who developed muscle cramps were more commonly hypocalcemia with a $P$ value of less than 0.0001. The parathormone level was significantly associated with a higher incidence of muscle cramps during the HD session as higher parathormone levels were associated with a higher incidence of muscle cramps with a $P$ value of less than 0.0001 (Table 6).

Logistic regression model assessing the timing of hypoxia as a risk factor for intradialytic muscle cramps showed that hypoxia at any time of dialysis session was not associated with incidence of muscle cramps with a $P$ value of more than 0.05 (Table 7). Correlations between laboratory findings and incidence of intradialytic hypoxia showed that the HDL level was significantly lower among the hypoxic group with a $P$ value of 0.012; however, the rest of the laboratory findings was not associated with the development of intradialytic hypoxia (Table 8).

4. Discussion

Our study showed that the development of hypoxia at the end of a dialysis session was an independent predictive factor for the development of intradialytic hypotension with an odds ratio of 2.48 (95% confidence interval 0.363–6.072 and $P = 0.038$). Thus, hypoxic patients are susceptible to hypotension 2.48 times more than nonhypoxic patients. The finding was consistent with the study conducted by Mancini, which was a prospective observational multicenter trial carried out on 18 public dialysis centers in Italy using an open-label design. The study lasted 3 months for each patient, and there were no changes in the usual dialysis sessions prescriptions. They found that $SO_2$ saturation variability would seem to stand confirmed as a parameter associated with decreased blood pressure events during a HD session.

This was in contrast to a study by Meyring-Wösten et al., which retrospectively analyzed peridialytic systolic blood pressure change and
Fig. 7. Bar chart showing mean parathormone level based on the incidence of muscle cramps.

Fig. 8. Box plot showing baseline arterial pH based on the incidence of muscle cramps.
intradialytic SaO₂ in a cohort of 983 chronic HD patients with arteriovenous vascular access. Their study revealed a significant association between intradialytic hypertension and low arterial oxygen saturation during the dialysis session.

Our present study showed that hypoxic groups had a significantly elevated serum urea and creatinine with \( P \) values of 0.0001 and 0.0001. This was in contrast to Zhang et al.\(^{10}\) who showed that there is no statistically significant difference in laboratory data between the two groups. It was a 6-month retrospective cohort study conducted on 232 maintenance HD patients with central venous catheters as vascular access.

The hypoxic patient group had a significantly higher potassium level (\( P = 0.0001 \)), lower calcium

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**Fig. 9. Bar chart showing prevalence of chronic illnesses based on the incidence of intradialytic hypoxia.**

![Bar chart showing prevalence of chronic illnesses based on the incidence of intradialytic hypoxia.](image)

**Fig. 10. Box plot showing HDL level among patients with intradialytic hypoxia. HDL, high-density lipoprotein.**

![Box plot showing HDL level among patients with intradialytic hypoxia.](image)
level (P = 0.0001), higher phosphorus (P = 0.0001), and higher serum cholesterol level (P = 0.007) when compared with the nonhypoxic group in our present study.

This is in partial agreement with Meyring-Wösten et al. who found that there was only significant difference between groups regarding serum calcium level with a P value of 0.01.
Our study showed a statistically significant higher incidence of hypotension among the hypoxic group when compared with the nonhypoxic group with a \( P \) value of 0.028.

This was in agreement with Mancini,\(^8\) who found the variations in the SO\(_2\) which measured on the extracorporeal blood during HD session are associated with IDH and could have predictive value for its onset, especially in patients with a highly arterialized fistula (SO\(_2\)>95\%).

In our study, oxygen saturation was significantly lower among the hypoxic group, as the mean ± SD oxygen saturation baseline was 98.4 ± 1.0 % in the nonhypoxic group versus 92.7 ± 4.8 in the hypoxic group with a \( P \) value of 0.04.

This was in agreement with Meyring-Wosten et al.\(^9\) who found that 10.2 % of patients had prolonged intradialytic hypoxemia (PIH). These patients had significantly lower mean SaO\(_2\) values and spent, on average, 58 and 20 % of their treatment time at SaO\(_2\) levels of less than or equal to 90 % and less than or equal to 87 %, respectively.

Moreover, it has been Meyring-Wosten et al.\(^9\) found that the variability of SaO\(_2\) levels was significantly higher in patients with PIH. SaO\(_2\) decreased after starting dialysis in both patients with PIH and patients without PIH, with SaO\(_2\) after around 40 min SaO\(_2\) decreased by 0.3 % points in controls and 0.5 % points in patients with PIH.

While in our study the mean ± SD oxygen saturation after 1 h was 97.9 ± 1.3 in the nonhypoxic versus 93.9 ± 4.6 in the hypoxic group with a \( P \) value of 0.003, the mean ± SD oxygen saturation after 2 h was 98 ± 1.3 in the nonhypoxic group versus 91.6 ± 5.3 in the hypoxic group with a \( P \) value of 0.0001.

Our present study showed that the mean ± SD oxygen saturation at the end of the session was 97.1 ± 3 in the nonhypoxic versus 91.4 ± 5.3 in the hypoxic group with a \( P \) value of 0.0001.
In agreement with Harrison et al.\textsuperscript{11} a pilot study on 18 prevalent regular HD patients studied during their routine session it has been found that pre-dialysis ScvO\textsubscript{2} was 63.5 ± 13 % and decreased significantly to 56.4 ± 8 % at the end of the dialysis session ($P = 0.046$).

In contrast the Meyring-Wosten et al.\textsuperscript{9} study found that SaO\textsubscript{2} increased from 92.6 ± 1.9 % at the beginning of the session to 93.2 ± 61.8 % at the end. At the end of the dialysis session SaO\textsubscript{2} was above starting levels. Ultrafiltration has no significant difference between the groups.

This finding contrasts with that of the study by Zhang et al.\textsuperscript{10} who reported that higher cUFV volumes are linked to more significant declines in intradialytic ScvO\textsubscript{2}.

This also goes in contrast with the study by Meyring-Wosten et al.\textsuperscript{9} who found that patients with PIH had a slightly higher intradialytic weight gain, pointing toward fluid status as a factor affecting SaO\textsubscript{2}.

This also goes in contrast with the study by Harrison et al.\textsuperscript{11} who found that there was a strong inverse correlation between ultrafiltration volume and ScvO\textsubscript{2} HD end.

UF was significantly more common among those who developed hypotension with a $P$ value of 0.036.

This goes in agreement with the retrospective cohort study by Yu et al.\textsuperscript{12} which collected clinical and echocardiographic data. Patients were enrolled from January 2014 to March 2014 and were followed-up for 5 years. Those who suffered from more than four hypotensive events during 3 months (10 % of dialysis treatments) were defined as the IDH group. They found that a high UF rate induced intradialytic hypotension.

This is also consistent with the findings of Thongdee et al.\textsuperscript{13} which used a retrospective case--control design was conducted. Patient data were gathered from four HD units from January to December 2017. A total of 108 patients were included in the study. They discovered that the UF rate should be limited to 12 ml/kg/h and if a higher rate of fluid removal was indicated, it should not exceed 16 ml/kg/h to avoid the occurrence of IDH.

This also goes in agreement with a retrospective study by Deng et al.\textsuperscript{14} which was performed on 312 regular HD patients. IDH commonly occurs during HD sessions in Chinese patients, often associated with the process of ultrafiltration.

### 4.1. Conclusion

Chronic HD patients have an SaO\textsubscript{2} of less than 90 % for more than one-third of their treatment time. Hypoxia is a predictive factor for the development of intradialytic complications. Hypoxic patients are susceptible to hypotension 2.48 times more than nonhypoxic patients.

### Conflicts of interest

There are no conflicts of interest.

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