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Association Between PaCO2 and Optic Nerve Sheath Diameter in Acute Hypercarbic Respiratory Failure

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ABSTRACT

Objective: To investigate the relationship between changes in Optic Nerve Sheath Diameter (ONSD), Partial arterial carbon dioxide pressure (PaCO2) and pH in Arterial blood gases (ABGs) in Chronic Obstructive Pulmonary Disease (COPD) patients presenting with acute hypercarbic respiratory failure (AHRF) receiving Non Invasive mechanical ventilation (NIMV).

Study Design: Quasi Experimental Study.

Place and Duration of study: Department of Critical Care Medicine, Pakistan Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from Jan to Jun 2025.

Methodology: One Hundred patients with COPD were recruited in study having Acute Hypercarbic Respiratory Failure on ABGs requiring Noninvasive mechanical ventilation. Demographic variables, vital signs, conscious level, PaCO2, pH and ONSD were measured prior to initiation of NIMV and in second hour of NIMV.

Results: A total of 100 patients with acute hypercarbic respiratory failure were analyzed. After 1 hour of non-invasive ventilation, median $PaCO_2$ significantly decreased from 64.00 (66.00 – 62.00) mmHg to 50.00 (53.00 – 48.00) mmHg showing a 21.9% reduction (p<0.001), while arterial pH improved from 7.28 (7.31–7.25) to 7.34 (7.37–7.30) as p-value <0.001. The overall median ONSD demonstrated a 10.3% reduction following treatment. A significant positive correlation was observed between baseline $PaCO_2$ and mean ONSD (r value = 0.58, p-value <0.001), as well as between changes in $PaCO_2$ and changes in ONSD (r value = 0.60, p-value <0.001).

Conclusion: Optic Nerve Sheath Diameter and Partial arterial carbon dioxide pressure changes were positively correlated with each other.

Keywords: Acute Hypercarbic Respiratory Failure, Hypercapnia, Ocular Ultrasound, Optic Nerve Sheath Diameter.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an advancing and inflammatory lung disease associated with significant morbidity and mortality leading to reduced life expectancy.[1] Prevalence based studies show heterogeneity in disease in different parts of world which can be explained on basis of difference in diagnostic criteria and assessment method. Prevalence of COPD is 4-6% in Europe.[2] COPD is a burdensome illness that makes 96% of all of chronic respiratory disease related deaths in China. In COPD, acute exacerbations may be associated with Acute hypercarbic respiratory failure(AHRF) requiring non mechanical ventilation(NIV).[2] Acute hypercarbic failure is caused by retention of CO2 which is a potent vasodilator leading to an increase in intracranial pressure (ICP). A study conducted by Bhide et al in India suggested that instead of frequent Arterial Blood Gases (ABGs) measurements, one can opt for a noninvasive comparable method to reflect increases in ICP.[3]

Due to progress in science and technology, numerous invasive and non-invasive methods for ICP monitoring have emerged. Invasive methods, including lumbar puncture and devices linked to the extra-ventricular drainage, continue to be the benchmark for ICP monitoring,[1,4] ICP monitoring in medical intensive care units is otherwise challenging as most patients are unfit for invasive intracranial pressure (ICP) modalities or unstable to transport for imaging,[5,6] Two separate studies conducted in China and Korea showed that these changes in arterial CO2 levels can be surrogate measured by ONSD and correlates well with PaCO2 levels.[6,7]

Our goal is to measure difference in PaCO2 values and their relationship with ONSD measurements which are a surrogate for ICP measurements. So far, no such study is conducted in critical care in Pakistan, and it can pave a way for shift

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to noninvasive frequent monitoring in this cohort of patients.

METHODOLOGY

This qausi experimental study was conducted at Medical ITC Department, Pakistan Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from Jan 2025 to Jun 2025. Approval for the Study was sanctioned by Ethical Review Board of our Institute (with reference no A/28/20/12/24 on 20 Dec 2024). Patient flow diagram is added as below (Figure-1). Sample size was calculated using WHO sample size calculator taking confidence level 95%, margin of error 5%, correlation (r=0.94) between the mean ONSD and PaCO2[1].

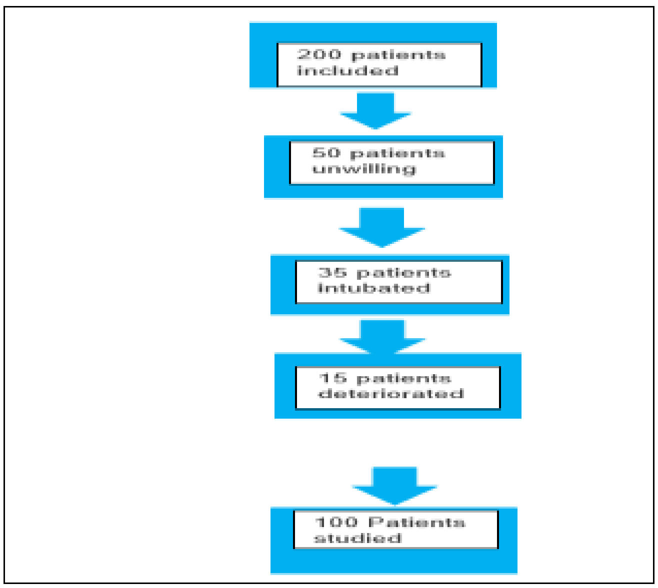

Figure-1: Patient flow diagram

Inclusion Criteria: Patients with age ≥ 18 years, patients experiencing acute exacerbation of COPD complicated by hypercapnic acidosis (PaCO2>45 mmHg and pH<7.35) and patients indicated NIV.

Exclusion Criteria: Patients with NIV contraindications like Facial trauma involving eyeballs, a prior eye condition impacting the optic nerve and/or the cavity of the optic globe, alternative clinical reasons for elevated ICP include endocrinopathies, metabolic imbalances, infectious and immunological conditions, trauma and cancer, clear indication for intubation, deterioration of awareness during the therapy and occurrence of cardiac or respiratory arrest during the monitoring in the ITC were excluded.

Written informed consent was attained from patient or next of kin if patient could not consent for any reason. Data such as Age, gender, BMI, smoking status, vitals, conscious level, pH, PaCO2 and ONSD were noted in all patients prior to initiation of NIMV and in second hour of NIMV treatment. ABGs Analyzer: Nova medical pHOx plus C. US Probe: Prime Acuson 2000 9L4 probe 2.6-9.6 MHz frequency.

For measurement of ONSD, linear transducer probes of 2.6-9.6 MHz in ocular Mode of Acuson SC2000 brand were employed. Patients in the critical care were taught to wait for 1 minute in an upright position (20-30°) to circumvent putting pressure on globe. Participants were instructed to gaze ahead with their eyes shut to prevent eye movement. A sterile gel was put in eye and midline view was obtained gently without exerting pressure. The globe and optic nerve sheath were examined in the transverse plane. ONSD was assessed transversely from each eye consistently. Optic Nerve entering the globe is the point where display is frozen and is measured in transverse plane 3 mm inferior to optic nerve sheath entry point of globe as shown in Figure-2. Observations were recorded and their statistical analysis was performed.

Figure-2: The Diameter of the Optic Nerve Sheath; Assessed 3mm away from the Optic disc on the Transverse Plane

Observations were carried out by critical care medicine fellows who were given training sessions by consultant radiologist. It consisted of both theoretical and hands on training of 2 hours' sessions each. An independent evaluation was carried out afterwards by 2 unbiased Consultant radiologists who were not involved in training. Physicians with Consecutive 25 accurate measurements were considered qualified. Data images were scanned. Low quality and false data images were discarded. No sedation or anesthetic agent was administered to any patient at any stage.

Noninvasive mode with Bi PAP settings was selected and pressure support was of 15 cmH20 and PEEP of 5cmH20 was initiated on Ventilator model Mindray SV300 Model. Patients were sitting up in bed with CPAP mask snugly fit to them. Tidal volume leak was ensured to be minimal. Short-acting beta-2 agonists (Salbutamol) and anticholinergics (Ipratropium) were given in the first hour using a nebulizer, three times at 20-minute intervals. The maintenance dose was adjusted according to each patient's needs. Intravenous administration of par-enteral corticosteroids (Hydrocortisone) was given at a dose of 0.5-1mg/kg.

In COPD patients diagnosed with AHRF requiring NIV, ONSD, pH and PaCO2 were measured before and 1 hour after initiation of NIV. A structured questionnaire was designed and observations were collected accordingly.

Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Quantitative variables including age, systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, $PaCO_2$, arterial pH, and optic nerve sheath diameter (ONSD) were assessed for normality using the Shapiro–Wilk test. As all of continuous variables were not normally distributed, they were summarized as median and interquartile range (IQR), while categorical variables were presented as frequencies and percentages. For comparison of pre- and post-treatment measurements ($PaCO_2$, pH, right ONSD, left ONSD, and mean ONSD), the Wilcoxon signed-rank test was applied. Correlation between $PaCO_2$ and ONSD was assessed using Spearman's rank correlation coefficient. A p-value of ≤0.05 was considered statistically significant.

RESULTS

Of the 100 patients studied and diagnosed with AHRF included, 28.0% were female and 72.0% were men. Median age was 62.00 (66.75 – 58.00) years range from 49 to 89 years. The median SBP was 155.00 (164.00 – 136.00) and the median DBP was 77.00 (85.00 – 76.00) mmHg. The median pulse rate was 74.00 (67.00–85.00) bpm beats per minute, while the median respiratory rate was 24.00 (27.00 – 19.00) breaths per minute. Median SpO2 was 84.00 (87.00 – 79.00) % and GCS was 15.00(15.00 – 15.00) shown in Table-I. There was a statistically significant reduction in $PaCO_2$ after 1 hour of non-invasive ventilation, with median values decreasing from 64.00 (66.00 – 62.00) mmHg 50.00 (53.00 -48.00) mmHg (p-value<0.001). Arterial pH showed significant improvement from 7.28 (7.31 – 7.25) to 7.34 (7.37 – 7.30) (p-value <0.001).Similarly, both right and left optic nerve sheath diameters demonstrated significant reductions following treatment, and the overall median ONSD decreased from 5.80 (6.10 – 5.55) mm to 5.20 (5.45 – 4.95)mm as p-value <0.001 shown in Table-II. There was a moderate to strong positive correlation between baseline $PaCO_2$ and mean optic nerve sheath diameter (r value = 0.58, p-value<0.001). Similar significant positive correlations were observed between $PaCO_2$ and both right (r value= 0.56, p-value< 0.001) and left ONSD (r value= 0.54, p-value<0.001). Furthermore, the change in $PaCO_2$ showed a significant positive correlation with the change in mean ONSD (r value=0.60, p-value< 0.001) shown in Table-III.

Table-I: Descriptive characteristics of study Participants (n=100)

Characteristic(s)	Group	Percentage
Gender	Female	28%
	Male	72%
	Range (Min-Max)	Median (IQR)
Age(years)	49 – 89	62.00 (66.75 – 58.00)
Systolic blood pressure (mmHg)	125 – 178	155.00 (164.00 – 136.00)
Diastolic blood pressure (mmHg)	65 – 93	77.00 (85.00 – 76.00)
Pulse (/min)	56 – 110	74.00 (67.00–85.00
Respiratory rate (/min)	15 - 30	24.00 (27.00 – 19.00
SpO2	68 - 92	84.00 (87.00 – 79.00)
GCS	14 – 15	15.00 (15.00 – 15.00)

GCS: Glasgow Coma Scale

Table-II: Evaluation of Difference in pH, Partial Arterial Carbon-dioxide (PaCO2) and Optic nerve Sheath Diameter (ONSD) Before and After Treatment (n=100)

Variable(s)	Pre Treatment Median (IQR)	After treatment Median (IQR)	p-value
PaCO2	64.00 (66.00 – 62.00)	50.00 (53.00 -48.00)	< 0.001
pH	7.28 (7.31 – 7.25)	7.34 (7.37 – 7.30)	< 0.001
ONSD Right (mm)	5.82 (6.12 - 5.58)	5.22 (5.47 – 4.98)	< 0.001
ONSD Left (mm)	5.78 (6.08 – 5.52)	5.18 (5.42 – 4.92)	< 0.001
Mean ONSD	5.80 (6.10 – 5.55)	5.20 (5.45 – 4.95)	< 0.001

ONSD: Optic Nerve Sheath Diameter

Table-III: Correlation Between $PaCO_2$ and ONSD (n = 100)

Variable(s)	Spearman's r value	p-value
Baseline $PaCO_2$ vs Mean ONSD	0.58	< 0.001
Baseline $PaCO_2$ vs Right ONSD	0.56	< 0.001
Baseline $PaCO_2$ vs Left ONSD	0.54	< 0.001
$\Delta PaCO_2$ vs ΔMean ONSD	0.60	< 0.001

ONSD: Optic Nerve Sheath Diameter

DISCUSSION

As per findings of this study, there is a positive correlation to Optic nerve sheath diameter and Partial arterial carbon dioxide pressure (PaCO2) and negative correlation between Optic nerve sheath diameter and pH hence establishing Optic nerve sheath diameter is an acceptable, non-invasive surrogate measure of PaCO2.

The average age of the patients examined was 63 years, while the median age was 62 years. The youngest patient was 49 years and oldest was 89 years old. As COPD prevalence is more in older individuals, mean age is therefore higher in our study. In our study population, 28% females and 72% males were having COPD with AHRF. The Glasgow coma scale (GCS) was used assess to consciousness level of patients in the study. Of the 100 patients, 18 (18%) patients had GCS of 14 and 82 (82%) had GCS of 15. The brain has the capability to auto regulate its blood supply physiologically. This ability ensures adequate cerebral blood flow despite variations in cerebral perfusion pressure (CPP) (CPP = MAP – ICP). This ICP varies with changes in level of PaCO2. The raised levels of PaCO2 are associated with increased ICP. These changes in arterial CO2 levels can be surrogate measured by ONSD and correlates well with PaCO2 levels.[6,7] Bala *et al*. studied this correlation during general anesthesia in different types of surgeries and concluded that there are sharp and evolving changes in ONSD due to hyperventilation and the presence of PEEP in patients under anesthesia.[8]

Monitoring intracranial pressure (ICP) is crucial for liver transplant patients.[9] Invasive ICP monitoring is recognized as a gold standard technique, yet it may lead to bleeding and infection, making its application a contentious topic. Research indicates that an ONSD greater than 5 mm measured by OUS effectively assesses ICP exceeding 20 mmHg noninvasively across various clinical scenarios. ONSD measurement with ultrasound is a non-invasive procedure, avoiding the risks associated with invasive ICP monitoring. It can be performed at the bedside, quick and relatively easy to learn and useful for detecting increased ICP in critical scenarios like TBI where raised ICP can lead to critical decision making like decompressive craniectomy for TBI.

Various studies conducted independently established the relationship between ONSD and increased ICP. Omur *et al*. showed that ONSD increased in relation to Trendelenburg position and pneumoperitoneum. They suggested ONSD measurements to be used for in patients requiring ICP measurement.[10] Similarly, another trial showed that Dexmedetomidine attenuates ONSD increase while performing Robot-assisted Laparoscopic Prostatectomy with pneumoperitoneum in an inclined Trendelenburg position.[11] This claim of effect of position has been contradicted in a study done in another Korean study.[12] Legrand *et al*. supported use of ONSD as preferred method of noninvasive ICP Monitoring as well as a screening tool.[13] Similarly, other studies established ONSD measurements as dynamic real time assessment of ICP.[14-15]

The applications of ONSD have wider applications and multiple studies have been done in this regard world over. Park *et al*. studied that mild hypercapnia during Lung protective ventilation (LPV) may not worsen the rise in ONSD during CO2 pneumoperitoneum in the Trendelenburg position and might enhance the regional cerebral oxygen saturation (rSO2) relative to normocapnia in patients receiving TIVA during gynecological laparoscopy16. Ray *et al*.[17] observed Laparoscopic surgeries in children can cause significant increases in ICP related to creation of pneumoperitoneum as measured by the ONSD. Studies from previous literature suggested Validity and reliability of optic nerve sheath diameter by pocket size devices compared to standard ultrasound devices and is preferred for use in emergency medicine and critical care.[18-20]

LIMITATIONS OF STUDY

Limitations of the study include the patients of specific group with COPD & AHRF manageable by NIMV only so cannot be generalized or applied on wider groups. Additionally, there is an absence of a recognized standardized framework for training physicians and other healthcare practitioners in ultrasound ONSD assessment.

CONCLUSION

As per findings of this study, there is a positive correlation to Optic nerve sheath diameter and Partial arterial carbon dioxide pressure (PaCO2) and negative correlation between Optic nerve sheath diameter and pH hence establishing Optic nerve sheath diameter is an acceptable, non-invasive surrogate measure of PaCO2.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AAM & AR: Data acquisition, data analysis, critical review, approval of the final version to be published.

AMK & KK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AH & SH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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