

# Capnography in Pediatric Critical Care Unit and Correlation of End-Tidal and Arterial Carbon Dioxide in Ventilated Children

Akhil Krishnamoorthy<sup>1</sup> Bijay Kumar Meher<sup>2</sup> Deepti Damayanty Pradhan<sup>3</sup> Saroj Kumar Satpathy<sup>4</sup>

<sup>1</sup>SVPPGIP, SCB Medical College, Cuttack, Odisha, India

<sup>2</sup>Bhima Bhoi Medical College and Hospital, Balangir, Odisha, India

<sup>3</sup>KIMS, Bhubaneswar, Odisha, India

<sup>4</sup>Department of Pediatrics, SVPPGIP, SCB Medical College, Cuttack, Odisha, India

Address for correspondence Bijay Kumar Meher, MD, Bhima Bhoi Medical College and Hospital, C/455, Sec-6, CDA, Cuttack 753014, Odisha, India (e-mail: bkmeher187@yahoo.co.in).

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## Abstract

Recording of end-tidal carbon dioxide (EtCO<sub>2</sub>) noninvasively reflects a real-time estimation of arterial carbon dioxide (PaCO<sub>2</sub> [partial pressure of CO<sub>2</sub>]). However, as the EtCO<sub>2</sub> is dependent on metabolism, perfusion, and ventilation, predicting PaCO<sub>2</sub> from EtCO<sub>2</sub> is not linear. The objective of the study was to find out the predictability of PaCO<sub>2</sub> from EtCO<sub>2</sub> in PICU and to evaluate the factors affecting the correlation of EtCO<sub>2</sub> and PaCO<sub>2</sub> in critically ill ventilated children. The design involved was prospective observational study. The setting discussed over here is that of pediatric intensive care unit (PICU) of tertiary care hospital. A total of 160 children between 1 month and 14 years received mechanical ventilation. EtCO<sub>2</sub>, PaCO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> (PF) ratio, oxygenation index (OI), and ventilation index (VI) are the factors involved in main outcome measures. A total of 535 pairs of EtCO<sub>2</sub> and PaCO<sub>2</sub> were recorded in 160 ventilated children during the stable hemodynamic state. Mean age and weight (Z-score) of patients were 31.15 ± 40.46 months and -2.10 ± 1.58, respectively. EtCO<sub>2</sub> and PaCO<sub>2</sub> differences were normal (2–5 mm of Hg) in 393 (73.5%) pairs. High gradient (>5 mm of Hg) was mostly found with children with pneumonia, prolonged ventilation, and pressure mode of ventilation (*p* < 0.05). EtCO<sub>2</sub> had a strong positive correlation with PaCO<sub>2</sub> (*r* = 0.723, 95% confidence interval [CI] = 0.68 and 0.76) and not significantly affected by PF ratio or OI. However, presence of pneumonia and high ventilation index (VI > 20) adversely affected the relationship with poor correlation coefficient (*r* = 0.449, 95% CI = 0.30, 0.58 and *r* = 0.227, 95% CI = 0.03, 0.41, respectively). EtCO<sub>2</sub> reading showed good validity to predict PaCO<sub>2</sub> and not affected by oxygenation parameters. The correlation was affected by the presence of pneumonia and high ventilation index; hence it is recommended to monitor PaCO<sub>2</sub> invasively in these patients till a good correlation is established.

## Keywords

- ▶ capnography
- ▶ end-tidal carbon dioxide
- ▶ PaCO<sub>2</sub>
- ▶ pediatric intensive care unit
- ▶ arterial blood gas

## Introduction

In the pediatric intensive care unit (PICU), to ensure proper patient care and professional credibility, monitoring of CO<sub>2</sub> and O<sub>2</sub> is the recommended “minimum guidelines and levels

of care” by American Academy of Pediatrics. Arterial blood gas (ABG) analysis is considered the gold standard in monitoring sick children on a mechanical ventilator. ABG sampling is costly, time-consuming, needs training, invasive with a risk of infection, and provides a snapshot view into the condition

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of the patient. Pulse oximetry and capnography provide noninvasive and real-time monitoring in PICU. Pulse oximetry provides predictable information about oxygenation. As capnography is dependent on metabolism, perfusion, and ventilation of the patient, it does not provide reliable information on ventilation during hemodynamic instability. Also, in conditions with increased physiological dead space (VD or dead space ventilation), the arterial carbon dioxide (PaCO<sub>2</sub> or partial pressure of CO<sub>2</sub>) and end-tidal carbon dioxide (EtCO<sub>2</sub>) gradients are increased, and the correlation is affected.<sup>1</sup>

EtCO<sub>2</sub> monitoring is the standard of care during procedures such as intubations and sedations and also used in a variety of clinical situations. However, EtCO<sub>2</sub> may be underused in pediatric settings.<sup>2</sup> There is insufficient data for the use of capnography in PICU as a substitute for repeated ABG sampling in resource-poor settings and parameters affecting noncorrelation of EtCO<sub>2</sub> with PaCO<sub>2</sub>. Hence, this study was designed to assess how reliably EtCO<sub>2</sub> predicts PaCO<sub>2</sub> in critically sick ventilated infants and children in PICU and, to find out the different parameters which may affect the correlation.

## Methods

### Study Design

This was a prospective study done at PICU of a tertiary care hospital in India. Approval was obtained from the Institutional Ethical Committee. Informed consent was obtained from the parents before enrolling in the study.

### Participants

All critically ill children from 1 month to 14 years admitted to PICU and requiring mechanical ventilation were included for the study. Patients diagnosed with or suspected of congenital cyanotic heart disease were excluded from the study as intracardiac shunting is likely to cause an obligatory difference between arterial and EtCO<sub>2</sub>.

### Data Collection

After obtaining informed written consent from the parents, mechanically ventilated patients were selected from PICU according to inclusion and exclusion criteria. The patients were intubated with appropriate size endotracheal tube and ventilated using Puritan Bennet 840 Ventilator or Maquet (servo-I) ventilator in various modes like synchronized intermittent mandatory ventilation (SIMV) or assist-control modes. Humidifier (Fisher and Paykel M 850/heat and moisture exchanger[HME] filter) was used for all patients whenever available. Uncuffed endotracheal tubes were used in infants and cuffed tubes in older children. Continuous mainstream EtCO<sub>2</sub> monitoring probe, IRMA MAXIMO gas analyzer was attached to the endotracheal tube end for recording the EtCO<sub>2</sub>.<sup>3</sup> Capnography and EtCO<sub>2</sub> values were obtained using a multiparameter monitor (Truscope II; 12" Multi-parameter Monitor, Schiller).

Demographic data like age, sex, socioeconomic status were recorded. Anthropometric details were obtained. History and physical findings of each patient were recorded with relevant investigations at the time of admission and progress

throughout ICU stay. The disease of the patient, major organ systems involved, indication for ICU admission, and that of mechanical ventilation were noted. The patients were resuscitated by the ICU team and managed as per ICU protocols. Hemodynamic instability was defined as perfusion failure represented by clinical features of circulatory shock and advanced heart failure.<sup>4</sup> In the present study, hemodynamic stability was based on the measurement of vital signs irrespective of the use of vasopressor and ventilatory support. When the baby was hemodynamically stable on the ventilator, ABG was done, and simultaneously EtCO<sub>2</sub> values were noted. The mode of ventilation, humidification used, oxygenation, and ventilator parameters were recorded at each measurement of ABG. Due to the risk of an increase in dead space in infants and young children with the use of HME filter, it was used only in older children and adolescents.<sup>5</sup> A maximum of five ABGs (minimum one ABG) was taken for each patient at an interval of at least 12 hours ensuring stable hemodynamic state. Oxygenation parameters were fractional inspired oxygen concentration (FiO<sub>2</sub>), PaO<sub>2</sub>, PF ratio, and oxygenation index (OI). PF ratio was calculated using the formula PaO<sub>2</sub>/FiO<sub>2</sub>, and OI was calculated using the formula (FiO<sub>2</sub> × MAP [mean airway pressure])/PaO<sub>2</sub>. Ventilation parameters were respiratory rate (RR), peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), tidal volume (Tv), and ventilation index (VI). VI is a calculation used to determine the severity of respiratory illness (acute lung injury and/or respiratory distress syndrome) in critically ill patients. It was calculated in pressure mode of ventilation using the formula  $[RR \times (PIP - PEEP) \times PaCO_2] / 1,000$ , whereas RR is the input ventilator respiratory rate.<sup>6</sup>

**Laboratory procedures:** For ABG analysis, 0.1 mL of arterial blood was collected from radial artery puncture using 1-mL heparinized syringe (flushed with 20 IU/mL heparin solution) and analysis was done within 15 minutes of collection using Instrumentation Laboratory Worldwide (GEM Premier 3000) or Eschweiler Gas analyzer.<sup>7,8</sup>

### Outcomes

The outcome variable was EtCO<sub>2</sub>, arterial PaCO<sub>2</sub>, PF ratio, OI, and VI.

## Statistics

### Sample Size

Assuming a confidence level  $1 - \alpha(\alpha)$  of 95%, anticipated population proportions (*P*) of 50% and absolute precision (*d*) of 8%, the minimum sample size required was computed to be 150. A total of 223 patients were mechanically ventilated during the study period, 160 patients meeting the inclusion criteria were included for the study during hemodynamically stable condition; 535 pairs of ABG and EtCO<sub>2</sub> were obtained for analysis.

### Statistical Methods

Data were analyzed using IBM SPSS statistics 24. Frequency distributions of variables were computed using the frequency procedure (categorical variable) and descriptive statistics

**Table 1** Baseline characteristics of ventilated children in PICU (n = 160)

Variable		Value
Sex	Male	95 (59.4%)
	Female	65 (40.6%)
Age (mo)	≤ 1 y	85 (53.1%)
	>1 y	75 (46.9%)
Weight for age (Z-score)	< -2	76 (47.5%)
	-2 to 2	83 (51.9%)
	>2	1 (0.6%)
Duration of ventilation <sup>a</sup> (d)		4.33 (4.89)
Duration of ICU stay <sup>a</sup> (d)		7.02 (9.18)
Indication of ICU admission	Respiratory distress	89 (55.6%)
	Respiratory failure	3 (1.9%)
	Low GCS	60 (37.5%)
	Others	8 (5%)
Etiology	Pneumonia	36 (22.5%)
	Meningoencephalitis	32 (20%)
	Sepsis	19 (11.9%)
	Severe malaria	12 (7.5%)
	CAHD and	24 (15.0%)
	pneumonia	37 (23.1%)
	Others	

Abbreviations: CAHD, congenital acyanotic heart disease; GCS, Glasgow coma scale; ICU, intensive care unit; PICU, pediatric intensive care unit.  
<sup>a</sup>Mean (SD).

(scale variable). Their association with normal (2–5 mm of Hg) and high gradient (> 5 mm of Hg) was computed using Chi-square test of independence (categorical variable), independent sample “t”-test (scale variable), and Mann Whitney test (when standard deviation [SD] > mean for scale variables). Pearson’s bivariate correlation between PaCO<sub>2</sub> and EtCO<sub>2</sub> was computed to study the linear correlation. Coefficient of determination was computed applying the linear regression procedure with PaCO<sub>2</sub> as the dependent and EtCO<sub>2</sub> as the independent variable. The cut-off *p*-value for the test of significance was taken as <0.05.

## Results

Out of a total of 646 patients admitted to PICU during the study period, 223 required mechanical ventilation. Three patients with congenital cyanotic heart disease were excluded. A total of 535 recordings of ABG and EtCO<sub>2</sub> were obtained from 160 critically ill ventilated patients during the hemodynamically stable condition, with a maximum of five recordings per individual patient.

Out of 160 patients, 85 (53.1%) were infants below 12 months with a male: female ratio of 1.46:1. The mean

**Table 2** End-tidal carbon dioxide recording of ventilated children in PICU (n = 535)

Variable		Value
Mode of ventilation	SIMV (PC + PS)	327 (61.1)
	SIMV (VC + PS)	193 (36.1)
	Others	15 (2.8)
Humidification	Heated wire (Active)	357 (66.7)
	HME	84 (15.7)
	None	94 (17.6)
End-tidal CO <sub>2</sub> <sup>a</sup> (mm Hg)		46.17 (13.87)
End-tidal CO <sub>2</sub> <sup>b</sup> (mm Hg)		44 (36,54)
EtCO <sub>2</sub> > PaCO <sub>2</sub> (n = 482)	Patient with pneumonia	100 (78.8%)
	Patient without pneumonia	382 (93.6%)
EtCO <sub>2</sub> –PaCO <sub>2</sub> difference (mm Hg)	Normal (2–5)	393 (73.5)
	High (>5 mm)	142 (26.5)
EtCO <sub>2</sub> –PaCO <sub>2</sub> difference <sup>a</sup> (mm Hg)		6.71 (10.14)
EtCO <sub>2</sub> –PaCO <sub>2</sub> difference <sup>b</sup> (mm Hg)		4 (2,6)

Abbreviations: HME, heat moisture exchanger; IQR, interquartile range; PC, pressure control; PICU, PICU, pediatric intensive care unit; PS, pressure support; SD, standard deviation; SIMV, synchronized intermittent mandatory ventilation; VC, volume control.

<sup>a</sup>Mean (SD).

<sup>b</sup>Median (IQR).

(SD) age of the study population was 31.15 ± 40.46 months. Weight for age (Z-score) was < -2 in 76 (47.5%) children. Pneumonia and meningoencephalitis were leading causes for admission constituting 36 (22.5%) and 32 (20%) children, respectively. Respiratory distress and neurological conditions were the leading causes of ventilation in 89 (55.6%) and 60 (37.5%) children, respectively. Median (IQR [interquartile range]) duration of ventilation was 3 (2,5) days (→ **Table 1**).

→ **Table 2** shows the EtCO<sub>2</sub> recording of ventilated children in PICU. SIMV (PC or pressure control + PS or pressure support) was the most common mode of ventilation during 327 (61.1%) recordings, and servo-controlled heated wire humidification was used during 357 (66.7%) recordings. EtCO<sub>2</sub> and PaCO<sub>2</sub> differences were normal (2–5 mm of Hg) in 393 (73.4%) pairs in the present study with a mean difference of 6.71 ± 10.14 mm of Hg. EtCO<sub>2</sub> was higher than PaCO<sub>2</sub> in 100 (78.8%) patients with pneumonia.

→ **Table 3** shows the factors affecting high PaCO<sub>2</sub>–EtCO<sub>2</sub> gradient (>5 mm of Hg). Critically ill children with lower mean weight, prolonged ventilation, pneumonia, high PaCO<sub>2</sub>, and high VI have a higher likelihood of having a high gradient. No significant difference was found with age, sex, humidification types, pH, and OI.

**Table 3** Factors affecting arterial end-tidal carbon dioxide gradient in ventilated children in PICU

Variables		Normal gradient n = 393	High gradient n = 142	p-Value
Sex	M:F	1.23:1	1.54:1	0.270
Age <sup>b</sup> (mo)		11 (4,42)	8.5 (4,27)	0.162 <sup>c</sup>
Duration of ventilation <sup>a</sup> (d)		5.07 ± 4.84	6.26 ± 5.80	<b>0.018</b>
Duration of ICU stay <sup>a</sup> (d)		7.82 ± 9.34	10.09 ± 11.32	<b>0.020</b>
Disease condition	Meningoencephalitis	73 (18.6)	20 (14.1)	<b>0.000</b>
	Pneumonia	73 (18.6)	54 (38)	
	CAHD with pneumonia	62 (15.8)	14 (9.9)	
	Sepsis	47 (12.0)	20 (14.1)	
	Severe malaria	8 (2.0)	1 (0.7)	
	Others	130 (33.1)	33 (23.2)	
Mode of ventilation	SIMV (PC + PS)	228 (58.0)	99 (69.7)	<b>0.003</b>
	SIMV (VC + PS)	157 (39.9)	36 (25.4)	
	Others	8 (2.0)	7 (4.9)	
Humidification types	Active	264 (67.2)	93 (65.5)	0.127
	HME	55 (14.0)	29 (20.4)	
	None	74 (18.8)	20 (14.1)	
Acid base status	pH <sup>a</sup>	7.40 ± 0.09	7.38 ± 0.18	0.386
	HCO <sub>3</sub> <sup>-</sup> (meq/L) <sup>a</sup>	24.63 ± 5.64	27.64 ± 8.93	<b>0.000</b>
	TCO <sub>2</sub> <sup>a</sup>	27.00 ± 20.83	27.39 ± 18.45	0.844
Oxygenation parameters	PaO <sub>2</sub> <sup>a</sup> (mm of Hg)	152.90 ± 77.46	146.36 ± 89.51	0.409
	FiO <sub>2</sub> <sup>a</sup> (%)	82.02 ± 19.79	77.01 ± 22.30	0.013
	SpO <sub>2</sub> <sup>a</sup> (%)	97.22 ± 2.51	97.77 ± 2.29	0.020
	AaDO <sub>2</sub> <sup>a</sup> (mm of Hg)	256.44 ± 157.31	248.7 ± 167.38	0.622
	OI <sup>a</sup>	46.60 ± 28.37	45.48 ± 33.84	0.703
	PF ratio <sup>a</sup>	201.85 ± 133.73	212.10 ± 148.37	0.448
Ventilatory parameters	PaCO <sub>2</sub> (mm of Hg) <sup>a</sup>	41.46 ± 10.87	48.57 ± 26.88	<b>0.000</b>
	FiCO <sub>2</sub> <sup>a</sup> (%)	3.61 ± 0.73	3.99 ± 1.42	<b>0.000</b>
	Respiratory rate <sup>a</sup>	26.35 ± 5.48	29.79 ± 5.01	<b>0.000</b>
	PIP (n = 235, normal, 104 high) <sup>a</sup>	17.48 ± 3.00	16.86 ± 3.77	0.104
	Tv (n = 158 Normal, 38 high) <sup>a</sup>	8.16 ± 1.36	8.38 ± 1.42	0.374
	PEEP	5.48 ± 0.92	5.25 ± 1.16	<b>0.016</b>
	VI (n = 235 normal, 104 high) <sup>a</sup>	15.95 ± 6.32	19.42 ± 15.14	<b>0.003</b>

Abbreviations: AaDO<sub>2</sub>, alveolar arterial oxygen gradient; CAHD, congenital acyanotic heart disease; HME, heat and moisture exchanger; IQR, interquartile range; OI, OI, oxygenation index; PC, pressure control; PEEP, positive end expiratory pressure; PF, PaO<sub>2</sub>/FiO<sub>2</sub>; PICU, pediatric intensive care unit; PIP, peak inspiratory pressure; PS, pressure support; SD, standard deviation; SIMV, synchronized intermittent mandatory ventilation; Tv, tidal volume; SD, standard deviation; VC, volume control; VI, ventilation index.

<sup>a</sup>Mean (SD).

<sup>b</sup>Median (IQR).

<sup>c</sup>Mann-Whitney test.

Note: Bold values represent significant data.

► **Table 4** and ► **Fig. 1** compare the correlation of EtCO<sub>2</sub> with PaCO<sub>2</sub>. EtCO<sub>2</sub> had a strong positive correlation with PaCO<sub>2</sub> ( $r = 0.723$ , 95%CI [confidence interval] = 0.68–0.76). A subgroup analysis was done with different oxygenation parameters and ventilation parameters to find out any variations in the correlation between EtCO<sub>2</sub> and PaCO<sub>2</sub>. Correlation is minimally affected by oxygenation parameters, i.e., PF ratio or OI. At

PF ratio <200 and OI >25 we found a strong correlation between EtCO<sub>2</sub> and PaCO<sub>2</sub> ( $r = 0.697$ , 95% CI = 0.63–0.74 and  $r = 0.721$ , 95% CI = 0.67–0.77, respectively). However, presence of pneumonia and high ventilation index (VI >20) adversely affected the relationship with poor correlation coefficient ( $r = 0.449$ , 95% CI = 0.30, 0.58 and  $r = 0.227$ , 95% CI = 0.03, 0.41, respectively) (► **Table 4**; ► **Figs. 2** and **3**).

**Table 4** Correlation between EtCO<sub>2</sub> and PaCO<sub>2</sub> in the study population

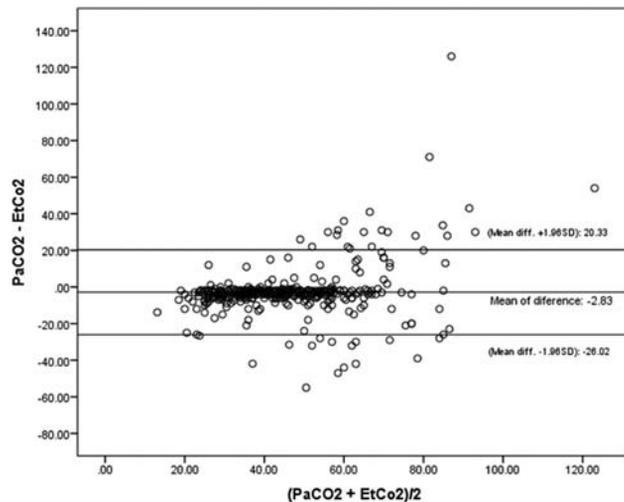
No. of pairs	PaCO <sub>2</sub> <sup>a</sup>	EtCO <sub>2</sub> <sup>a</sup>	Correlation coefficient	95% CI	Coefficient of determination
Total no of Pairs (n = 535)	43.35 (16.95)	46.17 (13.87)	0.723 <sup>c</sup>	0.68–0.76	0.522
Children with pneumonia (n = 127)	49.43 (21.78)	50.99 (16.01)	0.449 <sup>c</sup>	0.30–0.58	0.202
Children without pneumonia (n = 408)	41.5 (14.7)	44.7 (12.8)	0.867 <sup>c</sup>	0.84–0.89	0.867
PF ratio >200 (n = 214)	41.09 (14.81)	44.75 (12.85)	0.770 <sup>c</sup>	0.71–0.82	0.593
PF ratio ≤ 200 (n = 321)	44.85 (18.10)	47.12 (14.44)	0.697 <sup>c</sup>	0.63–0.74	0.486
OI >25 (n = 405)	44.16 (17.20)	46.58 (13.89)	0.721 <sup>c</sup>	0.67–0.77	0.519
OI ≤ 25 (n = 130)	40.83 (15.92)	44.92 (13.80)	0.728 <sup>c</sup>	0.63–0.80	0.529
VI >20 (n = 95)	62.61 (17.62)	60.31 (13.90)	0.227 <sup>b</sup>	0.03–0.41	0.051
VI ≤ 20 (n = 244)	37.35 (11.28)	42.88 (12.19)	0.742 <sup>c</sup>	0.68–0.80	0.550

Abbreviations: CI, confidence interval; OI, oxygenation index; PF, PaO<sub>2</sub>/FiO<sub>2</sub>; SD, standard deviation; VI, ventilation index.

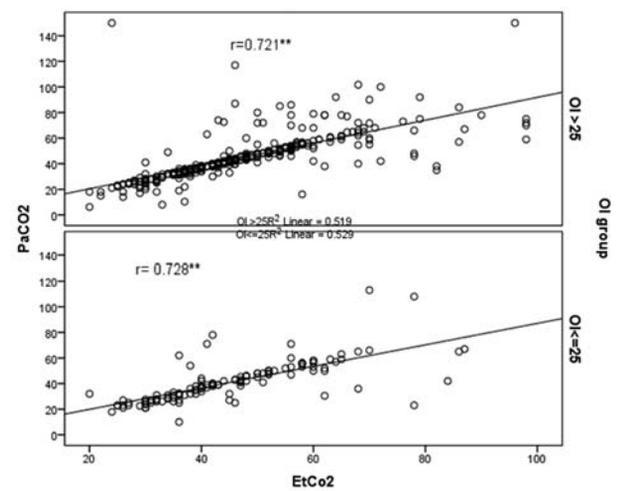
<sup>a</sup>Mean (SD).

<sup>b</sup>Significant at 0.05 level.

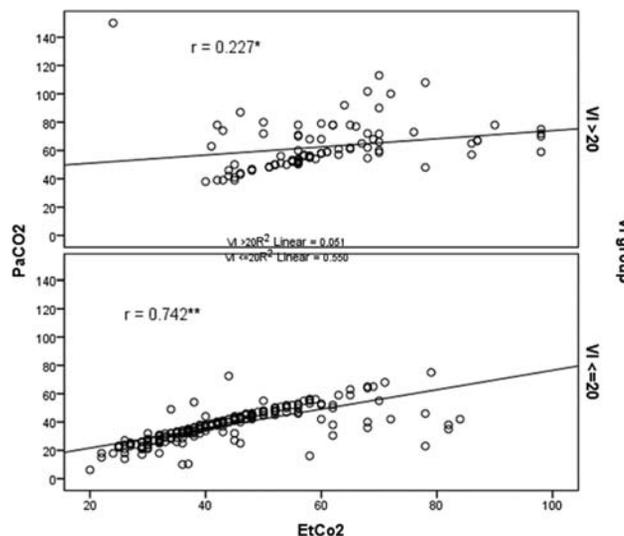
<sup>c</sup>Significant at 0.01 level.



**Fig. 1** Bland Altman plot in infants and children (EtCO<sub>2</sub> PaCO<sub>2</sub> pairs 535).



**Fig. 3** Correlation of EtCO<sub>2</sub> and PaCO<sub>2</sub> in relation to OI. OI, oxygenation index.



**Fig. 2** Correlation of EtCO<sub>2</sub> and PaCO<sub>2</sub> in relation to VI. VI, ventilation index.

## Discussion

In the present study, we have evaluated the relationship of EtCO<sub>2</sub> with PaCO<sub>2</sub> in critically sick ventilated infants and children. We found the EtCO<sub>2</sub> had a strong positive correlation with PaCO<sub>2</sub>, and it provides a clinically relevant and valid estimation of ventilation in critically sick ventilated children. In patients with high ventilation index (VI > 20) and pneumonia, it showed a correlation coefficient of 0.227 and 0.449, respectively, and R<sup>2</sup> is suggestive of only 5 to 20% variation in PaCO<sub>2</sub> that could be explained by EtCO<sub>2</sub>.

Bohr equation states that physiological dead space ventilation (VD) is equal to Tv multiplied by PaCO<sub>2</sub> minus partial pressure of expired carbon dioxide (PeCO<sub>2</sub>) divided by PaCO<sub>2</sub>.<sup>9</sup> As the VD is directly related to the gradient, the weak correlation of EtCO<sub>2</sub> and PaCO<sub>2</sub> in the present study may be explained by the increase in the physiological dead space in critically sick children with a different lung condition which might be driving the gradient between EtCO<sub>2</sub> and PaCO<sub>2</sub>.

In a prospective study in children with traumatic brain injury, Yang et al analyzed agreement between arterial carbon dioxide levels with EtCO<sub>2</sub> levels (the agreement was defined as PaCO<sub>2</sub>-EtCO<sub>2</sub> gradient between 0 and 5 mm Hg). There was 42% agreement, and on average, PaCO<sub>2</sub> was 2.7 mm Hg (95% limits of agreement, -11.3 to 16.7) higher than EtCO<sub>2</sub>. Low PaCO<sub>2</sub>-EtCO<sub>2</sub> agreement was seen in patients with acute respiratory distress syndrome (ARDS). However, in the present study, the PaCO<sub>2</sub>-EtCO<sub>2</sub> gradient was reported to be normal in 73.4% of children. We found poor correlation coefficient ( $r = 0.449$ , 95% CI = 0.30, 0.58) in the children with pneumonia in agreement with the study by Yang et al.<sup>10</sup>

Mehta et al studied the predictive capability of EtCO<sub>2</sub> in sick ventilated infant and children and found PaCO<sub>2</sub> having an excellent correlation with EtCO<sub>2</sub> ( $n = 96$ ,  $r = 0.914$ ), similar to our study. They found the PF ratio < 200 adversely affected relationship with a correlation coefficient of 0.83 similar to our result. However, Mehta et al found a good correlation at high VI in contrary to our findings, which might be due to small sample size in their study compared with our study (15 vs. 95 pairs).<sup>11</sup>

Meredith and Monaco and McDonald et al also found a strong positive correlation ( $n = 1,708$ ,  $r = 0.716$ ), and ( $n = 132$ ,  $r = 0.79$ ) and a negative impact of severe lung disease, similar to our study. However, both the studies had drawn an average of 17 and eight pairs per patient, respectively, whereas we drew up to five pairs per patient to maintain better validity of coefficient of correlation.<sup>12,13</sup> Previous studies by Hopper et al and McDonald et al also found the influence of VI and PF ratio on the PaCO<sub>2</sub>-EtCO<sub>2</sub> relationship similar to our study.<sup>13,14</sup> Similarly, McDonald et al reported the PaCO<sub>2</sub>-EtCO<sub>2</sub> gradient to be higher with increasing duration of mechanical ventilation. However, in contrary to our findings, their study found more percentage of the high gradient (> 10 mm of Hg) in children with PF ratio of < 200 compared with that of > 200 (35 vs. 10%). We found an insignificant difference in PF ratio in both normal and high gradient group.<sup>13</sup>

Sidestream distal EtCO<sub>2</sub> was measured by a microstream capnograph via the extra port of a double-lumen endotracheal tube by Kugelman et al in 27 ventilated neonates with 222 measurements and found a good correlation and agreement between PaCO<sub>2</sub> and mainstream proximal EtCO<sub>2</sub>. However, our study using proximal mainstream EtCO<sub>2</sub> excluded neonates. Further studies comparing neonate and older children with proximal and distal EtCO<sub>2</sub> recording are required to validate these results.<sup>15</sup>

Goonasekera et al reported EtCO<sub>2</sub> values to be higher than PaCO<sub>2</sub> in 22.7% of the observation in ventilated children. Similarly, we found EtCO<sub>2</sub> values to be higher than PaCO<sub>2</sub> in 105 (19.6%) children. The PaCO<sub>2</sub>-EtCO<sub>2</sub> difference correlated positively with the alveolar-arterial oxygen tension or pressure difference (AaDO<sub>2</sub>) difference ( $p = 0.381$   $p < 0.0001$ ). We have not studied the correlation of PaCO<sub>2</sub>-EtCO<sub>2</sub> difference with AaDO<sub>2</sub>, but we observed no statistically significant difference in AaDO<sub>2</sub> in both normal and high gradient group ( $p = 0.622$ ).<sup>16</sup>

McSwain et al monitored mechanically ventilated children using volumetric capnography and compared the

EtCO<sub>2</sub>-PaCO<sub>2</sub> correlation in different ranges of physiological dead space to tidal volume ratio ( $Vd/Vt$ ). The correlation coefficient between EtCO<sub>2</sub> and PaCO<sub>2</sub> ranges from 0.78 to 0.95. The EtCO<sub>2</sub>-PaCO<sub>2</sub> gradient increased predictably with increasing  $Vd/Vt$ . We found a correlation coefficient of 0.723 in our cohort; the low correlation in our study could be due to higher prevalence of severe lung disease (pneumonia and ARDS) with high  $Vd/Vt$ .<sup>17</sup>

There are several limitations to our study. The study was conducted at a single center in a limited resource PICU with most children admitted with pneumonia and/or respiratory failure. Studies with different etiologies in multiple centers need to be conducted to validate the results. Only mainstream capnometer was used. However, previous studies comparing both mainstream and sidestream capnometer reveal similar results and can be extrapolated to include both types. Several factors affecting the EtCO<sub>2</sub> and PaCO<sub>2</sub> gradient may be confounding to each other, and a regression analysis could give better results. All efforts have been taken to take the reading at stable hemodynamic state; however, some reading might have been taken in unstable condition confounding the results. Again, capnography, the graphical representation though very useful for an individual patient, it could not be used for analysis and deriving statistical inference.

## Conclusion

In hemodynamically stable yet critically ill ventilated children, continuous noninvasive monitoring of ventilation, i.e., EtCO<sub>2</sub> correlates strongly with the gold standard monitoring, i.e., PaCO<sub>2</sub>, obviating the need for repeated ABG in resource-poor settings. This emphasizes the practice of EtCO<sub>2</sub> use in PICU. EtCO<sub>2</sub> showed good validity to predict PaCO<sub>2</sub> and not much affected by oxygenation parameters. The correlation was greatly affected by the presence of pneumonia and high ventilation index; hence it is recommended to monitor PaCO<sub>2</sub> invasively in these patients until a good correlation is established.

### Authors' Contributions

B.K.M. conceived and designed the study, analyzed the data, revised the article, and act as the guarantor of the study. A.K. and D.D.P. collected the data and drafted the paper. A.K. and S.K.S. analyzed the data and revised the article. All the authors approved the final manuscript.

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### Conflict of Interest

None.

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