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Near-infrared spectroscopy measured cerebral oxygenation in full-term infants during transition: an observational study

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Abstract

Background: Brain is one of the most sensitive organs to hypoxia during resuscitation. NIRS-measured cerebral oxygenation is an evolving brain monitoring tool for neonatal resuscitation.

Methods: We undertook a prospective observational study for monitoring of cerebral oxygenation and peripheral preductal saturation at 1, 5, and 10 min after birth. Fractional tissue oxygen extraction was calculated as well. In addition to studying factors affecting cerebral oxygenation at those points in time. For the current cohort, cerebral oxygenation centile charts were provided at those time points. This work was registered in the cinicaltrial.gov NCT05158881.

Results: Sixty healthy term neonates were enrolled to define reference ranges and centile charts of cerebral oxygenation at 1, 5, and 10 min after birth. The strongest correlations between cerebral oxygenation metrics and peripheral preductal saturation were at 5 min after birth with *r* value = 0.628. Using logistic regression analysis to determine the most significant factors affecting NIRS-measured crSO2 in healthy full-term neonates, we found that the mode of delivery was the most significant factor with OR = 4.000 (1.367–11.703) at 5 min and 8.726 (2.517–30.25) at 10 min.

Conclusions: Normal values for NIRS may help to identify infants with cerebral oxygenation below a certain value indicating regional hypoxia at certain time points and can guide neonatal resuscitation interventions. Caesarean section is the most significant factor affecting cerebral oxygenation during the transition of healthy full-term neonates.

Keywords: crSO2, FTOE, Centile charts, Transition, NIRS, Mode of delivery

Background

Fetal to neonatal transition is a very complex physiological adaptation [1]. Any disturbances occurring during transition have potentiality for longer term harm [2]. Clinical assessment of neonates using Apgar score has high inter-observer variability [3, 4].

First 10 min ranges of SpO_2 neither provide information about oxygen tissue delivery nor reflect cerebral oxygenation [5, 6]. Monitoring of brain oxygenation may influence interventions which can affect survival, as well as, short- and long-term neurodevelopment outcomes [7, 8].

Cerebral regional oxygen saturation (crSO2) measured via near infrared spectroscopy (NIRS) represents mixed tissue saturation value, thus enabling information about the balance of cerebral oxygen delivery and oxygen consumption [7, 9].

Aim of the study was to establish normal cerebral oxygenation measures, crSO2, and FTOE in healthy full-term neonates with gestational age 38 weeks or more using centile charts. In addition, we studied different factors affecting those metrics and compared the cerebral oxygenation metrics of infants born by C-section and those born vaginally.

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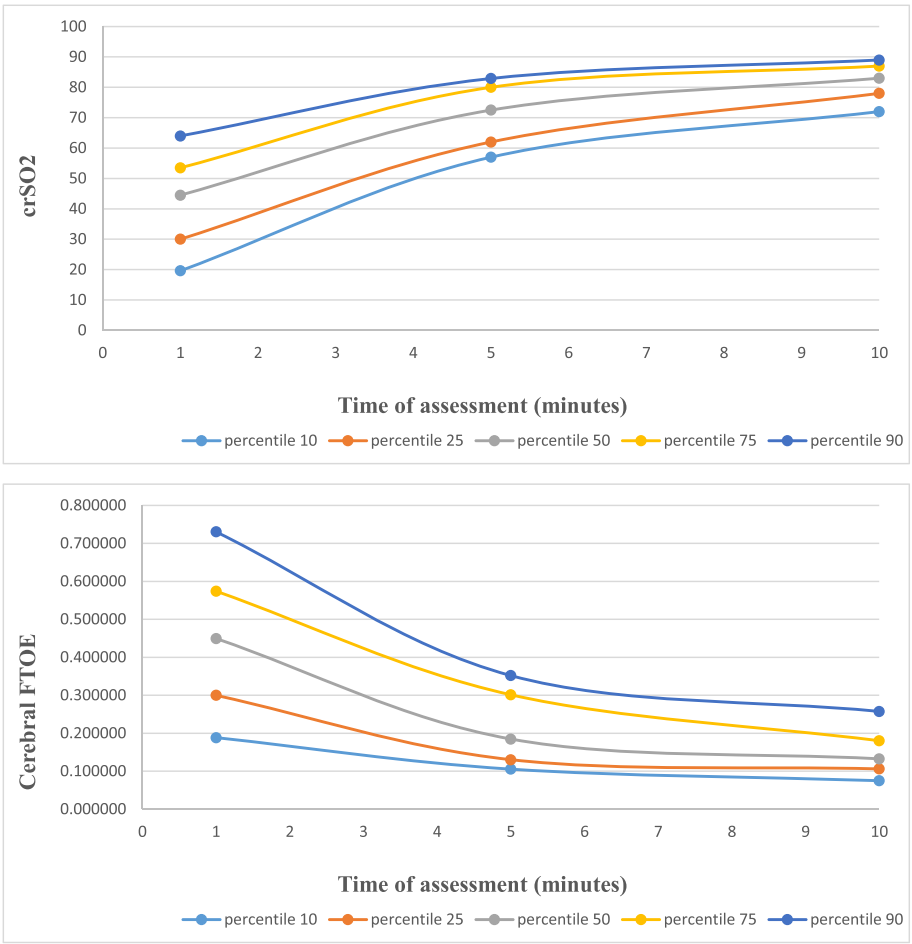

Fig. 1 Centile charts for cRsO2 and FTEO at 1, 5, and 10 min after birth in healthy full-term neonates

Methods

The present study was conducted in the delivery rooms of the Alexandria University Maternity Hospital (AUMH) from December 2020 till August 2021. Sixty-nine healthy full-term neonates with gestational age (GA) ≥ 38 weeks and normal pregnancy were included in this study. Healthy neonates had no maternal history or risk factors that would have affected their transition like severe pregnancy-induced hypertension (PIH), antepartum hemorrhage, and cord prolapse. They received only routine care or initial steps in resuscitation. They did not have respiratory distress after resuscitation. Patients with mothers with risk factors such as vaginitis, urinary tract infection (UTI), and premature rupture of membranes (PROM) should have at least 2 negative C-reactive protein (CRP), 12 h apart. Patients had no obvious anomalies antenatally or postnatally diagnosed.

Thirty patients were born through cesarean section and the other 30 were born vaginally. Nine cases were excluded in the first 10 min; four required oxygen, three needed respiratory support after resuscitation, and two required positive airway pressure during resuscitation (Fig. 1).

This study excluded patients who had perinatal asphyxia, intrauterine growth restriction, birth complications (e.g., vacuum extraction or forceps application), suspected or known brain and/or cardiac malformations, or required respiratory support or oxygen therapy within the first 10 min of birth. Measurements of crSO2 were recorded using NIRS (INVOS™ 5100C Cerebral/Somatic Oximeter Monitor; Covidien Troy, MI, USA) by placing a neonatal brain sensor on the left fronto-parietal area of the newborn's head for 10 min and crSO2 values were obtained at the end of 1, 5, and 10 min after birth.

The FTOE were calculated during the first 10 min of life with the following formula: FTOE = (SpO2-crSO2)/SpO2. At the same time, SpO2 were measured using Nellcor N-395 pulse oximeter (Tyco/Nellcor, Pleasanton, CA USA) or Masimo Set Radical 8 pulse-oximeter (Masimo Corp., Irvine, CA, USA) by applying a preductal

pulse oximetry sensor to the right wrist. Venus blood gas samples were obtained from umbilical cord blood of all neonates and clinical status was assessed by Apgar score at 1 and 5 min of life. Informed parental consents were obtained for all enrolled newborns and the criteria for the ethical committee of the faculty of medicine at Alexandria University were strictly applied.

Data were fed to the computer and analyzed with IBM SPSS software package version 20.0. The Kolmogorov–Smirnov test was conducted to verify the normality of distribution. Qualitative data were described using numbers and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, interquartile range (IQR), and percentiles. The centiles (10th, 25th, 50th, 75th, and 90th) for the crSO2 and FTOE were calculated by the least mean square (LMS) method proposed by Cole and Green. For categorical variables, chi-squared and Fisher's exact tests were conducted to compare between different groups. Student's *t* test and Mann–Whitney test were applied to both normally and abnormally distributed quantitative variables, respectively. Univariate and multivariate binary logistic regression analyses were constructed to identify independent risk factors (predictors) for low and high crSO2 norms (below and above 50th centile values). Pearson and Spearman correlation coefficients were used to correlate normally and abnormally distributed quantitative variables, respectively. Significance of the obtained results was judged at the 5% level [10].

Results

Table 1 shows descriptive analysis of the studied cases according to demographic data (sex, GA, and weight) mode of delivery, resuscitation needs, APGAR score, venous cord blood gases and clinical parameters (heart rate at 10 min, capillary refill time (CRT), preductal oxygen saturation at 1, 5, and 10 min).

There are significant positive correlations between cerebral tissue oxygenation and preductal oxygen saturation (pulse oximeter) at 1, 5, and 10 min with $r=0.532$, $r=0.73$, and $r=0.34$, respectively, as shown in Fig. 2. Whereas, there are significant negative correlations between FTOE and preductal SPO2 at 1, 5, and 10 min with $r=0.532$, $r=0.73$, and $r=0.34$, respectively.

Table 2 and Fig. 1 show centile (5th, 25th, 50th, 75th, 90th) charts for crSO2 and FTOE at 1, 5, and 10 min after birth in healthy full-term neonates. Fiftieth centile was used to classify patients into low norms and high norms.

Univariate logistic regression analysis for the predictors of low normal and high normal cerebral tissue oxygenation at 1, 5, and 10 min, as shown in Tables 3, 4, and 5. The most significant factor affecting cerebral oxygenation at 5 and 10 min is the mode of delivery. Infants born

Table 1 Descriptive analysis of the studied cases according to demographic, resuscitation, venous cord blood gases and clinical parameters

	Studied cases ($n=60$)	Percent
Gender		
Male	31	51.7%
Female	29	48.3%
Mode of delivery		
CS	30	50%
NVD	30	50%
GA		
Min.–max	38.0–41.0	
Median (IQR)	39.0 (38.0–39.0)	
BWT		
Min.–max	2.70–3.80	
Mean ± SD	3.18 ± 0.28	
Resuscitation		
Routine care	39	65.0%
Initial steps	21	35.0%
Apgar at 1 min		
Min.–max	6–8	
Median (IQR)	7 (7–7)	
Apgar at 5 min		
Min.–max	8–10	
Median (IQR)	9 (9–10)	
Venous cord blood gases		
PH		
Min.–max	7.11–7.45	
Mean ± SD	7.30 ± 0.08	
PCO2 mmhg		
Min. – max	20.10–74.20	
Mean ± SD	48.81 ± 10.61	
HCO3 mmol/L		
Min.–max	11.20–29.30	
Median (IQR)	24 (22–25.9)	
BE		
Min.–max	− 18.30–4.00	
Median (IQR)	− 2.10 (− 4.55 to − 0.05)	
HR b/min		
Min.–max	110.0–160.0	
Mean ± SD	137.3 ± 12.3	
CRT second		
Min.–max	2.0–4.0	
Median (IQR)	2.0 (2.0–3.0)	
Oxygen saturation %		
SpO2 at 1 min		
Min.–max	65–89	
Mean ± SD	75 ± 6	
SpO2 at 5 min		
Min.–max	83–99	
Median (IQR)	89 (86–92)	
SpO2 at 10 min		
Min.–max	91–100	
Median (IQR)	96 (94–98)	

GA: gestational age, BWT: birth weight, CRT: capillary refill time, HR: heart rate, crSO2: cerebral regional oxygen saturation, FTOE:Fractional tissue oxygen extraction

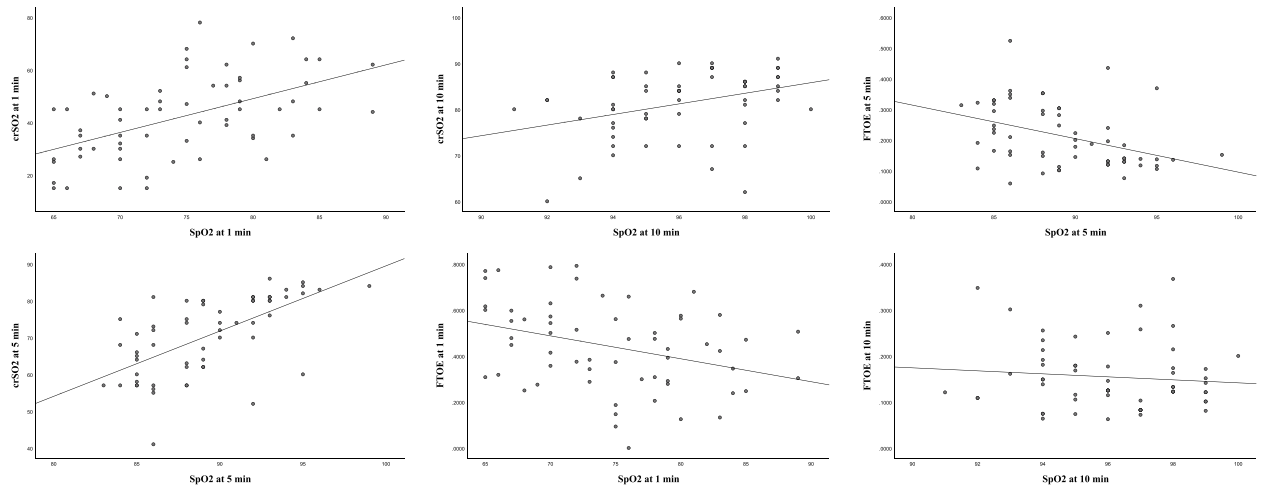

Fig. 2 Correlations between SPO2, and 1 min crSO2 ($r=0.532$, $p \leq 0.001^{*)}$, 5 min crSO2 (r 0.673*, $P<0.001$*), 10 min crSO2 r (0.390*, $p=0.002$*), 1 min FTOE ($r=-0.342$*, $p=0.008$*), 5 min FTOE ($r=-0.433$*, $p=0.001$*), and 10 min FTOE ($r=-0.076$, $p=0.563$), respectively

Table 2 Descriptive analysis of the studied cases according to cerebral regional oxygenation (crSO2) and fractional tissue extraction (FTOE)

		crSO2 1 min	crSO2 5 min	crSO2 10 min	FTOE 1 min	FTOE 5 min	FTOE 10 min
Mean		42	71	81	0.44	0.21	0.15
Median		45	73	83	0.45	0.18	0.13
Minimum		15	41	60	0.00	0.06	0.06
Maximum		78	86	91	0.79	0.52	0.37
Percentiles	10th	20	57	72	0.19	0.11	0.08
	25th	30	62	78	0.30	0.13	0.11
	50th	45	73	83	0.45	0.18	0.13
	75th	54	80	87	0.57	0.30	0.18
	90th	64	83	89	0.73	0.35	0.26

by C-section have significantly higher SPO2 and crSO2, and significantly lower FTOE at 5 and 10 min after birth. In addition to mode of delivery, PROM was significantly related to crSO2 at 5 min. Despite no significant difference in cerebral oxygenation metrics and spO2 between infants born by C-section or vaginally in the first 1 min after birth, the rate of rise from 1st to 5th minutes was significantly higher in infants born vaginally (Table 6).

Discussion

The NIRS technology has been around for about 45 years and is increasingly being used in newborns' first minutes [2, 11]. It is possible to prevent hypoxic and hyperoxic brain injury [12, 13].

Here in our work, we introduce new charts for cerebral oxygenation metrics in the first 10 min of life. As far as our knowledge is concerned, they are the only charts from Africa and lower middle-income countries (LMICs) where birth asphyxia is relatively common, thus regional charts are essential [10, 14]. There may be differences in regional perfusion, skin color, and clinical practice between high-income country (HIC), LMICs, and African populations; more caesarean deliveries, different practices in maternal anesthesia [15]. Racial differences in regional perfusion of the brain might have gene determinants or environmental factors. Pulse oximeter readings as well as the regional oxygenation metrics might have racial differences [16, 17]. The concept of normality might be different according to the region.

Cerebral regional oxygen saturation measures were obtained within the first minute of life, and they gradually increased through the first 10 min. During this period cerebral oxygenation metrics should be kept between 10

Table 3 Univariate logistic regression analysis for the parameters affecting cerebral regional oxygenation (crSO2) at 1 min

	crSO2 at 1 min		Univariate	
	Below 50th centile ($n=30$)	Above 50th centile ($n=30$)	*p*	OR (95%C.I)
Cord blood gases				
PH				
Min.–max	7.11–7.45	7.19–7.44	0.962	0.985 (0.532–1.826)
Median (IQR)	7.33 (7.25–7.37)	7.31 (7.24–7.35)		
PCO2				
Min.–max	32.70–74.20	20.10–66.60	0.587	1.014 (0.966–1.064)
Mean ± SD	48.07 ± 10.45	49.54 ± 10.88		
HCO3				
Min.–max	11.20–29.30	13.40–28.80	0.811	1.017 (0.887–1.165)
Median (IQR)	23.95 (21.50–25.60)	24.10 (23.00–26.00)		
BE				
Min.–max	− 18.30–4.00	− 14.00–3.00	0.729	1.022 (0.905–1.153)
Median (IQR)	− 2.10 (− 5.50–1.00)	− 2.15 (− 3.50 to − 0.40)		
Mode of delivery				
C-section	14 (46.7%)	16 (53.3%)	0.606	1.000
NVD	16 (53.3%)	14 (46.7%)		0.766 (0.278–2.111)
Maternal history				
Anemia	16 (53.3%)	20 (66.7%)	0.294	1.750 (0.616–4.973)
PIH	4 (13.3%)	4 (13.3%)	0.999	1.000 (0.226–4.431)
UTI	12 (40.0%)	7 (23.3%)	0.169	0.457 (0.149–1.396)
Vaginitis	14 (46.7%)	16 (53.3%)	0.606	1.306 (0.474–3.602)
PROM	10 (33.3%)	6 (20%)	0.247	0.5 (0.155–1.616)

IQR interquartile range, *SD* standard deviation, *OR* odd's ratio, *C.I* confidence interval, *LL* lower limit, *UL* upper limit, *p p* value for odd's ratio for comparing between the studied groups

* Statistically significant at $p \leq 0.05$

All variables with $p < 0.05$ in Univariate was included in the multivariate

NVD normal vaginal delivery, *UTI* urinary tract infection, *PIH* pregnancy-induced hypertension, *PROM* premature rupture of membranes

and 90th centile and the use of medical support should aim at keeping the patient in these zones.

In contrast to cerebral fractional oxygen extraction readings, they gradually declined during the first 10 min after birth. Median readings (10th–90th centiles) for $crSO_2$ are 44.5% (19.6–64) at 1 min, 72.5% (57–82.9) at 5 min, and 83% (72–89) at 10 min. While median values (10th–90th centiles) for FTOE measurements are 0.44(0.18–0.73) at 1 min, at 5 min 0.18(0.1–0.35), and at 10 min 0.13(0.07–0.25).

In Tables 3, 4, and 5, FTOE centiles are highest in the first minute, reflecting oxygen consumption of the brain. They then decrease to their third or half values by 5 min and remain relatively constant from 5 to 10 min. For example, the 50th centile value of FTOE is 0.45 at 1 min and then drops sharply to 0.18 and 0.13 at 5 and 10 min, respectively. This means that cerebral oxygen consumption is higher at 1 min than at 5 and 10 min.

In short, the discrepancy between crSO2 and SPO2 values, as well as the high FTOE, may also be caused by changes in cerebral autoregulation at 1 min relative to 5 and 10 min. Day1-FTOE is the earliest and most sensitive predictor for both clinical seizures and abnormal MRI [18].

Table 7 shows cerebral oxygenation centiles in the two NIRS devices at different time points that included full-term neonates in their studies. Current work, Nastase et al. and Pichler et al. used INVOS 5100, and Baik et al. used NIRO200NX device [7, 11, 19]. Current work and Nastase et al. recorded cerebral oxygenation at 1 min, while Baik et al. and Pichler et al. recorded cerebral oxygenation starting from 2 min after birth.

NIRO200NX device shows lower 90th centile values of cerebral oxygenation measures than INVOS 5100 at 5 and 10 min. It also displays the lowest 10th, 50th, and 90th centile values at 10 min [19]. The current work shows higher centile values of cerebral oxygenation at different time points in comparison to other studies.

Table 4 Univariate logistic regression analysis for the parameters affecting cerebral regional oxygenation (crSO2) at 5 min

	crSO2 at 5 min		Univariate	
	Below 50th centile ($n=30$)	Above 50th centile ($n=30$)	*p*	OR (95%C.I)
Cord blood gases				
PH				
Min.–max	7.11–7.45	7.16–7.45	0.626	1.167 (0.627–2.169)
Mean ± SD	7.30 ± 0.10	7.31 ± 0.07		
PCO2				
Min.–max	31.60–74.20	20.10–65.00	0.853	1.005 (0.957–1.054)
Mean ± SD	48.55 ± 10.82	49.06 ± 10.56		
HCO3				
Min.–max	11.20–29.30	13.40–28.80	0.587	1.039 (0.905–1.192)
Median (IQR)	23.55 (20.90–25.60)	24.30 (23.40–26.70)		
BE				
Min.–max	− 18.30–4.00	− 14.00–3.70	0.567	1.036 (0.917–1.171)
Median (IQR)	− 2.40 (− 4.80 to − 0.40)	− 2.00 (− 3.40–0.30)		
Mode of delivery				
C-section	20 (66.7%)	10 (33.3%)	0.011*	1.000
NVD	10 (33.3%)	20 (66.7%)		4.000 (1.367–11.703)
Maternal history				
Anemia	16 (53.3%)	20 (66.7%)	0.294	1.750 (0.616–4.973)
PIH	4 (13.3%)	4 (13.3%)	0.999	1.000 (0.226–4.431)
UTI	10 (33.3%)	9 (30.0%)	0.781	0.857 (0.288–2.547)
Vaginitis	14 (46.7%)	16 (53.3%)	0.606	1.306 (0.474–3.602)
PROM	4 (13.3%)	12 (40%)	0.025*	4.33 (1.203–15.605)

IQR interquartile range, *SD* standard deviation, *OR* odd's ratio, *C.I* confidence interval, *LL* lower limit, *UL* upper limit, *p p* value for odd's ratio for comparing between the studied groups, *NVD* normal vaginal delivery, *UTI* urinary tract infection, *PIH* pregnancy-induced hypertension, *PROM* premature rupture of membranes

* Statistically significant at $p \leq 0.05$

All variables with $p < 0.05$ in Univariate was included in the multivariate

Pichler et al. (excluded infants with oxygen support, device; IVNOS5100) and Fuchs et al. (infants receiving oxygen support and/or respiratory support, device; FORE-SIGHT) had centile charts for preterm infants in their cohorts. Their cerebral oxygenation measures were similar at 5 min, despite they were measured by different devices and oxygen supplements were different in both studies [7, 20]. At 10 min, the metrics were lower in Fuchs et al. chart, nevertheless, they used oxygen in resuscitation.

In Pichler et al.'s study, the centile values were higher in preterm infants in comparison to full-term infants in the same study whether born by C-section or NVD at 10 min. At 5 min preterm centiles were similar to those of term infants born by NVD and higher than infants delivered by C-section. The ineffective cerebral autoregulation of preterm infants is expected to result in higher cerebral oxygenation values.

Based on Table 7, the current study's higher crSO2 values were closer to those of Pichler et al., who used common charts for both preterm (with relatively higher crSO2) and full-term infants.

In the Nastase L's study (2017), the same NIRS device (INVOS 5100) was used with the same criteria, resulting in median crSO2 readings of 35% (15–58.2) at 1 min, 64% (46.2–85) at 5 min, and 76% (67.6–87.4) at 10 min. The higher 1 min crSO2 readings in our study might have been attributed to maternal exposure to 40% oxygen through a face mask during cesarean section, an anaesthiologist's practice, which was not mentioned in Nastase L. [11].

A high risk for brain injury is still present in infants who suffer mild encephalopathy within the first 6 h of life [18, 21–23]. According to a recent systematic review published in 2018, a significant proportion of infants with mild (subclinical) hypoxic ischemic encephalopathy (HIE) have abnormal outcomes at follow-up [24]. This finding contrasts with historical observations that infants with mild encephalopathy had normal neurodevelopmental outcomes [25]. The cerebral oxygenation metrics during transition not only provide guidance during

Table 5 Univariate logistic regression analysis for the parameters affecting cerebral regional oxygenation (crSO2) at 10 min

	crSO2 at 10 min		Univariate	
	Below 50th centile ($n=30$)	Above 50th centile ($n=30$)	*p*	OR (95%C.I)
Cord blood gases				
PH				
Min.–max	7.11–7.45	7.14–7.45	0.310	0.721 (0.383–1.356)
Median (IQR)	7.33 (7.27–7.38)	7.30 (7.24–7.35)		
PCO2				
Min.–max	31.60–74.20	20.10–65.00	0.309	1.026 (0.977–1.078)
Median (IQR)	46.85 (37.30–52.00)	51.75 (42.10–57.00)		
HCO3				
Min.–max	11.20–29.30	13.40–28.80	0.737	1.024 (0.893–1.174)
Median (IQR)	24.00 (22.30–25.50)	24.20 (22.00–26.80)		
BE				
Min.–max	− 18.30–4.00	− 14.00–3.70	0.949	1.004 (0.890–1.133)
Median (IQR)	− 2.05 (− 4.40 to − 0.40)	− 2.30 (− 4.70–0.30)		
Mode of delivery				
C-section	23 (76.7%)	7 (23.3%)	< 0.001*	1.000
NVD	7 (23.3%)	23 (76.7%)		10.796 (3.263–35.718)
Maternal history				
Anemia	17 (56.7%)	19 (63.3%)	0.598	1.321 (0.469–3.721)
PIH	3 (10.0%)	5 (16.7%)	0.452	1.800 (0.398–8.323)
UTI	10 (33.3%)	9 (30.0%)	0.781	0.857 (0.288–2.547)
Vaginitis	13 (43.3%)	17 (56.7%)	0.303	1.710 (0.616–4.748)
PROM	5 (16.7%)	11 (36.7%)	0.086	2.895 (0.86–9.745)
HR (b/min) at 10 min				
Min.–max	110–160	115–160	0.167	1.031 (0.987–1.076)
Mean ± SD	135.1 ± 12.67	139.5 ± 11.72		

IQR interquartile range, *SD* standard deviation, *OR* odd's ratio, *C.I* confidence interval, *LL* lower limit, *UL* upper limit, *p p* value for Odd`s ratio for comparing between the studied groups, *NVD* normal vaginal delivery, *UTI* urinary tract infection, *PIH* pregnancy-induced hypertension, *HR* heart rate at 10 min, *PROM* premature rupture of membranes

* Statistically significant at $p \leq 0.05$

resuscitation, but also might be an early indicator of mild HIE, where there are no obvious encephalopathy signs.

Neonatal encephalopathy progresses differently depending on the time of the insult. Despite the fact that the timing of the insult is predominantly perinatal, it is not always evident and can occur prenatally, acutely, and chronically. Infants who had a severe antenatal event may recover by the time of birth at which time the stage of encephalopathy is perceived as mild. In contrast, an infant with a more acute insult can have only mild abnormalities on neurological examination in the first 6 h of age. These abnormalities can then evolve to moderate or severe abnormalities after the first day of life. Furthermore, confounding variables such as maternal sedation, anesthesia, or tocolytics (e.g., magnesium sulfate) may affect the accuracy of determining the stage of HIE during a neurological examination immediately following birth [26].

A tool capable of guiding the clinician to early detection of perfusion disturbances is therefore urgently needed. Clinical diagnosis of mild encephalopathy might be improved by using NIRS for measuring cerebral oxygenation [8, 19]. Furthermore, there is strong correlation between cerebral oxygenation measures and initial Thompson score, and cerebral oxygenation measures are early predictors of HIE grades [18].

There are several factors that influence crSO2 ranges, including the NIRS device used, gestational age, and the need for respiratory support. Different NIRS devices calculate cerebral oxygenation values using different algorithms, so the calculated values vary between vendors. According to Lucia Gabriella (2009), preterm infants have higher brain oxygenation metrics due to impaired brain autoregulation as well as a reduced ability of brain tissue to extract oxygen [27]. Schwaberger B (2014) found that neonates who require respiratory support have lower

Table 6 Comparison between the two studied groups (C-section and NVD) according to HR, CRT, cerebral oxygenation parameters (crSO2 and FTOE), and oxygen saturation (SPO2)

	Mode of delivery		Test of Sig	*p*
	C-section	NVD		
HR (B/min) at 10 min				
Min.–max	110–155	119–160	$t = -1.266$	0.211
Mean ± SD	135 ± 13	139 ± 12		
CRT (seconds) at 10 min				
Min.–max	2–4	2–3	$U = 401$	0.370
Median (IQR)	2 (2–3)	2 (2–3)		
SpO2 at 1 min				
Min.–max	65–89	65–89	$U = 352$	0.146
Median (IQR)	73 (68–78)	75 (72–81)		
SpO2 at 5 min				
Min.–max	83–95	84–99	$U = 230^*$	0.001*
Median (IQR)	88 (85–90)	92 (89–93)		
SpO2 at 10 min				
Min.–max	91–100	94–99	$\underline{U} = 306^*$	0.031*
Median (IQR)	95 (94–98)	97 (95–98)		
$crSO_2$ 1 min				
Min.–max	15–70	15–78	$t = 1.260$	0.213
Mean ± SD	45 ± 14	40 ± 17		
$crSO_2$ 5 min				
Min.–max	41–86	52–85	$U = 229.5^*$	0.001*
Median (IQR)	67 (57–74)	80 (67–81)		
$crSO_2$ 10 min				
Min.–max	60–89	67–91	$U = 219.5^*$	0.001*
Median (IQR)	80 (74–82)	86 (84–88)		
Rate of rise in crSO2 from 1 to 5 min				
Min.–max	6–44	2–62	$t = -3.989^*$	< 0.001*
Median (IQR)	22 (17–27)	36 (20–46)		
FTOE 1 min				
Min.–max	0.09–0.77	0.00–0.79	$t = -1.845$	0.070
Mean ± SD	0.40 ± 0.16	0.49 ± 0.21		
FTOE 5 min				
Min.–max	.08–.52	0.06–0.43	$U = 259.5^*$	0.005*
Median (IQR)	0.22 (0.16–0.33)	0.14 (0.12–0.24)		
FTOE 10 min				
Min.–max	0.07–0.37	0.06–0.31	$U = 254.5^*$	0.004*
Median (IQR)	0.17 (0.12–0.21)	0.12 (0.08–0.14)		

U Mann–Whitney test, *t* Student's *t* test, *p p* value for comparing between the two studied groups, *CRT* capillary refill time, *HR* heart rate

* Statistically significant at $p \leq 0.05$

arterial oxygen saturation levels and limited perfusion than those without disturbed transition [28].

In the current study, those factors will not affect readings since only healthy full-term neonates were monitored using the same device. We divided patients into high and low norms based on their 50th centile values in order to discover other factors that might influence cerebral oxygenation. In order to determine which predictors were significant for low and high norms, we constructed logistic regression models. The only significant factor that affected cerebral oxygenation at 5 and 10 min was the mode of delivery. Therefore, we divided the patients into C-section and NVD groups and compared them as regards different clinical and oxygenation parameters.

Preductal SpO_2 measures were compared at 1, 5, and 10 min of life in patients delivered vaginally or by C-section as presented in Table 7. Oxygen saturation at the first minute showed no statistically significant difference between the 2 studied groups ($p = 0.146$). This might be attributed to maternal oxygen administration through a face mask with FIO_2 (fraction of inspired oxygen) 40% which was reported in all cases during cesarean delivery. Additionally, the normal vaginal and C-section groups showed statistically significant differences in SpO2 at 5 and 10 min ($p = 0.001$ and $p = 0.031$, respectively). The reason for this might be a delayed clearance of fetal lung fluid after cesarean delivery [29].

NIRS measurements of crSO2 at 1, 5, and 10 min of life were compared between CS and NVD patients in Table 7. In a number of studies, crSO2 was affected differently by delivery mode. As opposed to Nastase L et al. (2017) study, there was no statistically significant difference ($p = 0.213$) between patients born vaginally and those born by C-section regarding crSO2 at the first minute. As a result of maternal oxygen administration through face masks during C-section, fetal oxygen saturation at birth may consequently be elevated. $crSO_2$ measures at 5 and 10 min showed significant difference between the patients delivered vaginally or by C-section. The normal vaginal group averaged 74.67% crSO2 at 5 min compared with 66.37% in the cesarean group ($p = 0.001$), while the NVD group averaged 84.13% crSO2 at 10 min compared to 78.37% in the CS group ($p = 0.001$). Nastase L et al. (2017) found the same result, in contrast with Gerhard Pichler et al. (2013) and Berndt Urlesberge et al. (2011) [11, 29]. The rate of rise from 1 to 5 min of life was statistically significantly higher among the vaginal group (36%) than the cesarean group (22%) with $p < 0.001$.

FTOE indicates an increase in oxygen consumption due to increased cerebral metabolic rate, decreased oxygen delivery or both [14]. FTOE at 1, 5, and 10 min were calculated and compared between patients delivered

Table 7 Cerebral oxygenation centiles in the two NIRS devices at different time points. The current study shows the highest cerebral oxygenation values at 1, 5, and 10 min, followed by Pichler et al. that included preterm and full-term infants' cerebral oxygenation values in their centiles

Time point		1 min			5 min			10 min			FT/PT	Author/year
Centiles		10th	50th	90th	10th	50th	90th	10th	50th	90th		
Device	INVOS 5100	20	45	64	57	73	83	72	83	89	FT	Current study
	INVOS 5100	15	35	58	46.2	64	85	67.6	76	87.4	FT	Năstase 2017 [11]
	INVOS 5100				45.3	68.4	85.3	65.0	79.4	90.3	FT + PT	Pichler 2013 [7]
	NIRO200NX				50.9	65.6	78.2	61.8	74.5	85	FT	Baik 2015 [19]

vaginally or by C-section. Although crSO2 was not different between the 2 groups, FTOE at 1 min had a tendency to show a statistically significant difference between the 2 groups with median values (0.38) in the C-section group and 0.52 in the normal vaginal group ($p = 0.07$). FTOE decreased from 5 to 10 min and showed statistically significant differences between infants born by NVD and C-section at 5 and 10 min ($p = 0.005$ and $p = 0.004$ respectively), following the Nastase L study (2017) [11].

Higher brain oxygenation metrics and peripheral oxygen saturation were found to be significantly higher in the vaginal group. This is likely due to the raised level of carbon dioxide which is the most potent cerebral vasodilator [29]. According to Kenichi Isobe et al. (2002), vaginally delivered newborns had significantly higher catecholamine levels at birth in comparison to those born by cesarean section. Released catecholamines act to constrict peripheral blood vessels, thereby increasing cerebral blood flow. Additionally, fetal lung fluids are cleared more rapidly during vaginal delivery [5].

It is logical that SPO2 and cerebral oxygenation parameters (crSO2 and FTOE) should be correlated. At 1, 5, and 10 min, however, their relationship is not constant. At 5 min, SPO2 and cerebral oxygenation parameters (crSO2 and FTOE) showed the highest correlation ($r = 0.6$ and $r = 0.4$, respectively).

Many factors can explain the discrepancy in correlation strength at those time points. Firstly, crSO2 reaches a plateau faster than peripheral arterial saturation (SpO2), and oxygen is delivered to the brain more efficiently in the first minutes of life. Second, after 5 min, the cerebral vascular bed constricts to protect the brain from excessive oxygen exposure following the postnatal rise in blood oxygen levels. The third hypothesis proposed by Kehrer M et al. (2005) is that an increase in left ventricular output could result in a decrease in cerebral blood flow as a result of an increased left-to-right shunt through the patent ductus arteriosus [30–32].

The main limitation of this work is the small sample size, but the cost of the sensor was the main restraint.

Conclusions

The use of NIRS to measure crSO2 in conjunction with centile charts allows resuscitation teams to monitor and quantify cerebral oxygenation in a rapid and non-invasive manner during resuscitation. It might influence interventions needed during resuscitation and might be a predictor of short- and long-term outcomes. NIRS-measured crSO2 in healthy full-term neonates is significantly affected by delivery mode.

Supplementary Information

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Additional file 1: Figure 1: flow chart of patients

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Authors' contributions

Hesham Abd EL-Rahim Ghazal conceived of the presented idea. Bahaa Salah-El Din Hammad, Alaa Ibrahim and Marwa M. Farag worked out all of the technical and medical details. Alaa Ibrahim collected the data. Marwa M. Farag and Alaa Ibrahim verified the analytical methods. Alaa Ibrahim, Marwa Farag, and Bahaa Salah-El Din Hammad contributed in interpretation of results. Marwa Farag and Alaa Ibrahim wrote the first draft of the manuscript. Hesham Abd EL-Rahim Ghazal supervised the findings of this work. All authors provided critical feedback and helped shape the research, analysis, and approved the final version of the manuscript.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol has been approved by the Research Ethics Committee of Alexandria faculty of medicine. Approval no. is 0106540 in 17 September 2020 (date of approval). IRB no. is 00012098 and FWA no. is 00018699. Written informed consent was obtained from parents or authorized legal representatives of all newborns who participated in the study for publication of anonymous patients' data.

Consent for publication
Informed written consent was obtained from parents or authorized legal representatives of all newborns who participated in the study for publication of anonymous patients' data.

Competing interests
The authors declare that they have no competing interests.

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