Reference Values for Umbilical Cord Blood Gases of Newborns Delivered by Elective Cesarean Section

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Background: *Umbilical cord blood gas values are better indicators of perinatal asphyxia than Apgar scores. Many studies have reported normal ranges of umbilical cord blood gases, which vary greatly due to many factors. This study aimed to establish the reference values of umbilical cord blood gases of normal cesarean newborns in a university hospital setting.*
Material and Method: *Blood samples from the umbilical artery and vein were collected from 160 newborns delivered by elective cesarean section. The indications for caesarean section were not due to fetal distress, intrauterine growth retardation, or non-reassuring fetal heart rate. The blood samples were collected immediately after birth in the operating room and then sent for blood-gas analysis. The blood-gas values were statistically analyzed and reported.*
Results: *The cord blood collected from 160 newborns was analyzed in this study. Seventy-eight percent (115) of the parturients were hypotensive before delivery. All Apgar scores at one and five minutes after delivery were at least 7. The calculated reference range of the umbilical arterial pH was 7.18-7.42, of pO_2 was 6.43-29.43 mmHg, of pCO_2 was 33.44-66.56 mmHg, and of HCO_3 was 15.60-30.70 mEq/L. The reference range obtained for the umbilical venous pH was 7.28-7.44, for pO_2 was 13.97-37.13 mmHg, for pCO_2 was 30.70-57.0 mmHg, and for HCO_3 was 18.50-29.90 mEq/L.*
Conclusion: *The study determined normal reference values as a result of umbilical cord blood gas analyses.*

Keywords: *Umbilical cord blood gas analysis, Fetal asphyxia, Cord blood reference*

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An Apgar score is used to evaluate all newborns in delivery rooms as a standard practice. This score provides a rapid and convenient way of evaluating the physical condition of newborn infants, especially the five-minute score, which is a significant predictor of neonatal mortality in both preterm and term infants[1,2]. However, an umbilical cord blood gas analysis provides more objective information of the neonatal metabolic condition, and this can be used as part of the overall assessment of the neonatal condition. Umbilical cord blood gas values may also assist obstetricians and pediatricians in their retrospective evaluations of an infant and indicate the occurrence of an acute, intrapartum hypoxic event[3-5]. In addition, a stressed newborn usually has a catecholamine surge to activate the body's defense mechanisms; this may affect most components of the Apgar score[6]. As a result, there may not always be a correlation between a high Apgar score and normal umbilical cord blood gas values. In our practice at Siriraj Hospital, an umbilical cord blood gas analysis was not being routinely performed on all newborns. Instead, an umbilical cord blood gas analysis was generally only conducted in high risk deliveries, as recommended by both the 1994 American College of Obstetrics and Gynecology Committee Opinion on Obstetric Practice and the 1993 Royal College of Obstetrics and Gynecology Study Group on Intrapartum Fetal Surveillance[2,7].

Many studies have previously reported the normal ranges of the umbilical cord blood gases[8-11]. However, the definition of "normal" and the studied population utilized in those studies varied widely. This raises concerns about the different techniques utilized in collecting the blood samples, any ethnicity

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differences, and variations in the labor ward practices. The presented study aimed to establish reference values for umbilical cord blood gases in newborn infants delivered by elective cesarean section at Siriraj Hospital.

Material and Method

The study protocol was approved by the Institutional Review Board of the Faculty of Medicine, Siriraj Hospital. Cord blood gases were obtained from parturients with term singleton pregnancy who were undergoing elective cesarean section under spinal anesthesia; prior informed consent was obtained from all. Parturients were excluded if they had any one of the following conditions: preoperative hypoxemia or hypoxemia before delivery (oxygen saturation $\leq$94%), diabetes mellitus, hypertension, heart disease, obesity, placenta previa, premature rupture of membranes, and intrauterine growth retardation[12].

On arrival in the operating theatre, 300-500 mL of isotonic solution was given to parturients before the spinal anesthesia, which used 0.5% hyperbaric bupivacaine and 0.2 mg morphine. With the parturients in a lateral position, the anesthesia was administered using aseptic precautions. The parturients were subsequently positioned supine, with a 15-degree, left lateral tilt. Loss-of-cold sensation at the fourth thoracic dermatome was considered adequate for surgery. Patient monitoring included non-invasive blood pressure measurements, electrocardiography, and pulse oximetry. The non-invasive blood pressure monitor was recorded one minute after the spinal injection, and the automatic cycling time was set to one minute until delivery. Subsequent to that, the blood pressure was recorded at five-minute intervals until the end of all procedures. A Doppler Fetus Detector (FD-390) was also applied to detect the fetal heart beat before and after administration of the spinal anesthesia. Supplemental oxygen was not administered before delivery. Any incidences of hypotension (defined as a systolic blood pressure less than 80% of baseline) were recorded and treated with incremental doses of intravenous ephedrine or norepinephrine to maintain a systolic arterial pressure of greater than 90 mmHg or 20% of the baseline values. Desaturation was defined as a reduction of oxygen saturation (SpO_2) below 94% for more than 30 seconds, verified by the signal quality and the probe attachment.

Apgar scores were assessed one and five minutes after delivery. Samples of the umbilical arterial (UA) and umbilical venous (UV) blood from a double-clamped segment of the umbilical cord were collected into heparinized, plastic syringes. The samples were mixed and checked to ensure there was no air in the syringes. If air bubbles were found, they were expelled from the syringe, and a small quantity of blood in the distal end of the needle was discarded in order to avoid its equilibration with environmental air. The samples were capped using a rubber stopper, and the syringes were labeled with an identity number, the site (artery or vein), and the date and time of delivery before being placed in ice and taken to the laboratory as soon as possible. Each sample's oxygen partial pressure (pO_2), carbon dioxide partial pressure (pCO_2), oxygen saturation, and pH were measured using a blood gas analyzer (Stat Profile pHOx, Nova Biomedical Corporation, Waltham, MA, USA).

Statistical analysis

The objective of this study was to establish the reference values of umbilical cord blood gases. The sample size calculation was based on the standard deviation of pH of arterial umbilical cord blood gas, which was taken as 0.06[13,14], with a 95% confidence interval (CI) and a margin of error of 0.01. At least 139 samples of cord blood gases were needed. Descriptive statistics were used to describe the characteristics of parturients and newborns as well as the values of the cord blood gases taken from the artery and the vein. Data were presented as number (percent), mean $\pm$ standard deviation (SD), or median (min, max), as appropriate. According to reference ranges of umbilical cord gases, the Kolmogorov-Smirnov test was used to determine the normal distribution of the data. The normal ranges of the umbilical cord blood gas analyses were reported as mean $\pm$ 2SD for normal distributed data. Meanwhile, for non-normal distributed data, the lower and upper limit values derived from the rank-based method were reported[15]. The statistical analysis was conducted using the software program, SPSS (version 18, SPSS Inc., Chicago, Illinois, USA).

Results

One hundred and sixty term newborns were assessed in this study. Five parturients were excluded from the study because they were desaturated and had to receive supplemental oxygen before delivery. Results from two cord-gas samples with a time longer than 90 minutes between their collection and analysis were also omitted, as was the data from six other cases that were considered to be outliers. Data from the remaining 147 new borns were then analyzed.

The three most common indications for a

cesarean delivery in this study were previous cesarean section (63.94%), elective cesarean section (19.73%), and breech presentation (6.12%). Of the 147 parturients whose outcomes are described in this study, 78.2% (115) were hypotensive before delivery. All of those hypotensive episodes were transient and easily managed with fluid resuscitation and vasopressor drugs. Ephedrine was utilized more often than norepinephrine as the first line vasopressor drug treatment for the maternal hypotension cases. The amount of preload and total fluid, the total dose of 0.5% heavy marcaine used, the time from the uterine incision to delivery, the surgical time, and the blood loss consumption are at Table 1.

The fetal heart rates did not differ in the period before and after the spinal block. The Apgar scores at one minute after delivery ranged from 7 to 10, with a median of 9, while the Apgar scores at five minutes after delivery ranged from 9 to 10, with a median of 10. The birth weight ranged from 2,380 to 4,070 grams, with a mean of 3,197 grams. No neonatal postoperative complications were reported in the first 24 hours. The newborn characteristics are at Table 2.

The 147 blood samples were analyzed for the arterial and venous blood values of pH, pO_2, pCO_2, HCO_3 and O_2 saturation. The resulting reference ranges of the arterial and venous umbilical cord blood of the newborns delivered by elective cesarean section are listed at Table 3. The reference ranges of the pH, pO_2 and pCO_2 of the arterial blood, and the reference ranges of the pH and pO_2 of the venous blood, were reported by using mean and 2 standard deviations (2SD). The upper and lower levels of the values were used to report the reference range for the rest of the umbilical cord blood variables.

Table 1. Perioperative maternal characteristics

Variables	Parturients received room air (n = 147)
Age (years)	32.11±4.20
Body mass index (kg/m^2)	27.25±3.03
Indications for surgery (%)	
Previous cesarean section	94 (63.94)
Elective cesarean section	29 (19.73)
Breech presentation	9 (6.12)
Cephalopelvic disproportion	3 (2.05)
Other	12 (8.16)
Baseline hematocrit (%)	35.60±2.80
Amount of preload fluid (ml)	471.77±192.94
Total volume of 0.5% heavy Marcaine and morphine for spinal block (ml)	2.19±0.06
Uterine incision to delivery interval (seconds)	120.60±73.20
Hypotension before delivery	115 (78.20)
First line treatment with ephedrine (cases)	92 (80.00)
Ephedrine consumption (mg)	19.00±11.00
First line treatment with Norepinephrine (cases)	23 (20.00)
Norepinephrine consumption (µg)	11.00±8.00
Surgical time (minutes)	53.34±13.20
Estimated blood loss (ml)	356.46±121.95
Total fluid administration (ml)	1,281.43±342.36

Data presented as mean ± standard deviation or number (%)

Table 2. Newborn characteristics

Variables	n = 147
Fetal heart sound (beats per minute)	
Preoperative	140.00±9.00
After spinal block	141.00±10.00
Birth weight (grams)	3,197.00±348.00
Apgar scores at 1 minute*	9 (7, 10)
Apgar scores at 5 minute*	10 (9,10)
Collect-test cord blood gas time (minutes)	21.77±10.49

Data shown as mean ± standard deviation
* Data shown as median (min, max)

Discussion

The reference ranges that we established in this study could be representative of the normal values of newborns for two reasons. First, the umbilical cord blood gas values were sourced from newborns who were delivered by healthy parturients and in uneventful elective cesarean sections. Moreover, the sample size of 147 blood samples was large enough, given that it significantly exceeded the recommended minimum of 120 samples and the calculation using the statistical estimation formula[16]. Reference ranges for the mean umbilical arterial and venous pH were therefore able to be determined from the presented study (7.3±0.12, and 7.36±0.08, expressed as mean ± 2SD, respectively). The lower limit of the reference range for arterial pH calculated in our study is lower than those in previously reported reference ranges (Table 4). However, most of the previously published reference ranges were derived from studies undertaken more than 12 years ago. The impact of new technologies and updated knowledge in healthcare needs to be recognized. In addition, these reference ranges were analyzed from infants born

Table 3. Reference range of umbilical cord blood gas analysis parameter

Variables	Umbilical artery				Variables	Umbilical vein			
	n	Mean	SD	Reference range		n	Mean	SD	Reference range
pH*	147	7.30	0.06	7.18-7.42	pH*	147	7.36	0.04	7.28-7.44
pO_2 (mmHg)*	147	17.93	5.75	6.43-29.43	pO_2 (mmHg)*	147	25.55	5.79	13.97-37.13
pCO_2 (mmHg)*	147	50.00	8.28	33.44-66.56	pCO_2 (mmHg)$^+$	147	42.94	6.63	30.70-57.00
HCO_3 (mEq/L)$^+$	147	24.96	3.78	15.60-30.70	HCO_3 (mEq/L)$^+$	147	24.89	2.97	18.50-29.90
Base excess$^+$	134	-1.34	4.36	-12.30-4.70	Base excess$^+$	133	-0.50	3.31	-7.40-4.90
O_2 saturation (%)$^+$	147	23.83	13.01	4.20-51.40	O_2 saturation (%)$^+$	147	45.52	14.42	12.00-68.60

* Reference range was reported as mean $\pm$ 2SD for normal distribution data, $^+$ Reference range was reported as lower-upper limit analysed by rank-based method for non-normal distribution data

pO_2 = partial pressure of oxygen, pCO_2 = partial pressure of carbon dioxide, HCO_3 = bicarbonate

Table 4. Mean and standard deviation (SD) of umbilical cord blood gas analysis parameters[8]

Author	Umbilical artery				Umbilical vein			
	pH	Base excess (mmol/L)	pCO_2 (mmHg)	pO_2 (mmHg)	pH	Base excess (mmol/L)	pCO_2 (mmHg)	pO_2 (mmHg)
Victory et al 2004 (n = 20,456)	7.24 (0.07)	-5.6 (3.0)			7.33 (0.06)	-4.5 (2.4)		
Helwig et al 1996 (n = 15,073)	7.26 (0.07)	-4.0 (3.0)	52.80 (9.9)	16.90 (6.0)	7.34 (0.06)	-3.0 (3.0)	40.87 (6.9)	28.95 (6.9)
Thorp et al 1989 (n = 1,694a, 1,820v)	7.24 (0.07)	-3.6 (2.7)	56.17 (8.5)	17.85 (6.9)	7.32 (0.06)	-2.9 (2.4)	43.73 (6.7)	28.65 (7.3)
Riley et al 1993 (n = 3,522)	7.27 (0.07)	-2.7 (2.8)	50.18 (11.1)	18.38 (8.2)	7.34 (0.06)	-2.4 (2.0)	40.58 (7.8)	28.43 (7.6)
Dickinson et al 1992 (n = 1,393a, 1,526v)	7.26 (0.08)	-3.2 (2.9)	52.88 (10)	18.98 (7.9)	7.33 (0.07)	-2.6 (2.5)	43.28 (8.2)	29.10 (9.7)

Data is presented as mean (SD).

Where available, arterial (a) and venous (v) sample numbers are given separately.

from different parity, modes of delivery and ages of gestation[8].

Several factors influenced the acid-base balance in the umbilical-cord blood parameters. In the case of maternal factors, we selected healthy parturients who had no conditions during pregnancy and labor. We also selected neonates who had normal fetal growth and were delivered at term. The newborns delivered from those parturients who received oxygen before delivery were excluded from this study because an oxygen supplement to a parturient might affect the fetal oxygen partial pressure level[17].

The mode of delivery also affects umbilical blood gas parameters, as reported by Lynn A et al[4]. A newborn's arterial-cord pH and base excess values at birth after an elective caesarean section group are significantly better than the results obtained after a normal vaginal delivery. Additionally, uterine contraction during the second stage of labor may impair placental blood flow, and repeated uterine contraction may increase fetal hypoxia and acidosis[8]. Repetitive and intermittent umbilical cord occlusions, resulting from the effects of oxytocin use and hyperactive uterine contractions, are also the cause of fetal hypoxia and acidosis[8]. As well, placental perfusion impairment can be found during maternal hypotension as a result of acute blood loss, regional anesthesia, and systemic illness and impairment can also result from crisis events such as placental abruption and acute umbilical cord compression[18]. Spinal anesthesia was the preferred means for cesarean section in this study, being a safe technique for parturients compared with general anesthesia. However, its effects on neonatal outcome are controversial. Prompt treatment with appropriate vasopressor drugs is effective in maintaining maternal blood pressure. Ephedrine is associated with a lower arterial pH than phenylephrine because ephedrine crosses the placenta more readily than phenylephrine[11,19,23]. Depression of fetal pH and base excess is caused by the significant beta adrenergic receptor activity of ephedrine[11]. The umbilical blood sampling values from parturients with hypotension before delivery were not significantly different from those of the normotensive, before-delivery group in our study. Simin et al showed no difference in fetal acid-base status or clinical neonatal outcomes between the use of ephedrine and phenylephrine for the treatment of maternal hypotension during spinal anesthesia for cesarean section[21]. Ngan Kee et al compared phenylephrine with norepinephrine in maintaining blood pressure during spinal anesthesia for cesarean delivery, finding a greater UV pH and oxygen content in the norepinephrine group than in the phenylephrine group[20]. At Siriraj Hospital, we currently use norepinephrine for the treatment of hypotension, including maternal hypotension after spinal anesthesia for cesarean section.

There were many methodological confounding factors from sampling to analysis and the interpretation of the acid-base values of the umbilical cord blood. The blood samples were stored between 0°C and 4°C to retard cellular metabolism. Provided arterial blood samples are stored at a cool temperature, a period of less than 95 minutes from collecting the samples to their subsequent analysis does not change the results of the gas analyses[22]. Lynn A et al found that the arterial and venous cord blood are stable in a plastic syringe at room temperature (22.5°-24°C) within 30 minutes of delivery[4]. As the mean time from blood sampling to analysis in our study was 21.77 minutes, we concluded that our cord blood collections could be used for analysis to reflect the fetal condition during labor.

One limitation of our study was that the cord blood from newborns, who were delivered from parturients who had desaturation and/or received oxygen supplement, was not explored. Another limitation was that the time frame counts from after cord clamping to sample collection was not recorded. A future study may focus on the correlation between immediate pH values and the long-term, neurological outcomes. Additionally, defining the cut-off value of the pathological pH would also be interesting.

Conclusion

Our study has established the reference values of umbilical cord blood gases of normal newborns after a cesarean section at Siriraj Hospital. This is the first study in Thailand that has considered what the reference values of umbilical cord blood gases are.

What is already known on this topic?

There is not always a correlation between a high Apgar score and normal umbilical-cord blood values at birth.

What this study adds?

The reference values of umbilical cord blood gases of normal newborns after elective cesarean section.

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Potential conflicts of interest

None.

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ค่าอ้างอิงก๊าซในเลือดจากสายสะดือทารกแรกเกิดในการผ่าตัดคลอดปกติ

ขัตติยา มโนมยางกูร, อรุโณทัย ศิริอัศวกุล, อัครินทร์ นิมมานนิตย์, ทัศยุ อยู่เย็น, โสภาพรรณ เงินฉ่ำ, คณิต ริสุขุมาล

วัตถุประสงค์: *เพื่อศึกษาหาค่าอ้างอิงของก๊าซในหลอดเลือดจากสายสะดือของทารกแรกเกิดที่คลอดจากการผ่าตัดคลอดในโรงพยาบาลศิริราชโดยที่ไม่มีปัญหาแทรกซ้อนใดๆ ในช่วงฝากครรภ์และระหว่างคลอด*

วัสดุและวิธีการ: *การส่งตรวจวิเคราะห์ค่าก๊าซในหลอดเลือดแดงและดำจากสายสะดือของทารกแรกเกิดจำนวน 160 คนที่คลอดจากการผ่าตัดคลอดโดยไม่มีข้อบ่งชี้ในการผ่าตัดคลอดจากภาวะทารกในครรภ์เครียด ภาวะทารกโตช้าในครรภ์ การเต้นของหัวใจทารกในครรภ์ผิดปกติหรือก้ำกึ่ง*

ผลการศึกษา: *ทารกแรกเกิดที่นำมาศึกษามีจำนวน 147 คน มารดาที่มีความดันโลหิตต่ำก่อนคลอดมีจำนวน 115 คนคิดเป็นร้อยละ 78.2 คะแนน Apgar หลังคลอดที่เวลา 1 และ 5 นาทีได้ค่ามากกว่า 7 ค่าอ้างอิงของก๊าซในหลอดเลือดแดงจากสายสะดือมีค่า pH 7.18-7.42 ค่าความดันบางส่วนของก๊าซออกซิเจน 6.43-29.43 มิลลิเมตรปรอทค่าความดันบางส่วนของก๊าซคาร์บอนไดออกไซด์ 33.44-66.56 มิลลิเมตรปรอทและค่าไบคาร์บอเนต 15.60-30.70 มิลลิอิควิวาเลนท์ต่อลิตร สำหรับค่าอ้างอิงของก๊าซในหลอดเลือดดำจากสายสะดือมีค่า pH 7.28-7.44 ค่าความดันบางส่วนของก๊าซออกซิเจน 13.97-37.13 มิลลิเมตรปรอท ค่าความดันบางส่วนของก๊าซคาร์บอนไดออกไซด์ 30.70-57.0 มิลลิเมตรปรอท และค่าไบคาร์บอเนต 18.50-29.90 มิลลิอิควิวาเลนท์ต่อลิตร*

สรุป: *การวิเคราะห์ก๊าซในหลอดเลือดจากสายสะดือของทารกแรกคลอดจากการผ่าตัดในโรงพยาบาลศิริราชโดยที่ไม่มีปัญหาแทรกซ้อนใดๆ ในช่วงฝากครรภ์และระหว่างคลอดในการศึกษานี้น่าจะใช้เป็นค่าอ้างอิงของทารกแรกเกิดปกติได้*