Re-Evaluation of Cord Blood Arterial and Venous Reference Ranges for pH, pO₂, pCO₂, According to Spontaneous or Cesarean Delivery

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Umbilical cord blood gas analysis (pO₂ and pCO₂) is now recommended in all high-risk baby deliveries and in some centers it is performed routinely following all deliveries. The aim of this study was to re-evaluate cord blood arterial and venous reference ranges for pH, pO₂, pCO₂ in newborns, delivered by spontaneous vaginal delivery (SVD) and by cesarean section (CS) performed in Faculty Hospital Motol. Two groups of subjects were selected for the study. Group I consisted of 303 newborns with SVD. Group II consisted of 189 newborns delivered by cesarean section. Cord blood samples were analyzed for standard blood gas and pH, using the analytical device Rapid Lab 845 and Rapid Lab 865. We obtained reference values

expressed as range (lower and upper reference value expressed as 2.5 and 97.5 percentiles) for cord blood in newborns with SVD: arterial cord blood: pH = 7.01–7.39; pCO₂ = 4.12–11.45 kPa; pO₂ = 1.49–5.06 kPa; venous cord blood: pH = 7.06–7.44; pCO₂ = 3.33–9.85 kPa; pO₂ = 1.80–6.29 kPa. We also obtained reference values for cord blood in newborns delivered by CS: arterial cord blood: pH = 7.05–7.39; pCO₂ = 5.01–10.60 kPa; pO₂ = 1.17–5.94 kPa; venous cord blood: pH = 7.10–7.42; pCO₂ = 3.88–9.36 kPa; pO₂ = 1.98–7.23 kPa. Re-evaluated reference ranges play essential role in monitoring conditions of newborns with spontaneous and caesarean delivery. J. Clin. Lab. Anal. 24:300–304, 2010.

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Key words: umbilical cord blood; blood gas; pH

INTRODUCTION

Umbilical cord blood gas analysis is now recommended in all high-risk deliveries and in some centers it is performed routinely following all deliveries. For optimal interpretation, paired umbilical arterial and venous samples should be collected soon after birth from a segment of cord that has been doubly clamped to be isolated from the placenta. Umbilical cord blood gas analysis is a fast and simple method to evaluate the condition of the newborn (1).

The pH value in the umbilical artery is the best investigation to evaluate the presence and intensity of the fetal acidosis, as they reflect the acid-base status of the fetal tissue. The value in the umbilical vein reflects the blood that returns to the fetus as a result of the exchange of CO₂ and O₂ through the placenta (2).

High-risk delivery is associated with possible hypoxic stress and consequent risk of brain damage. Although the exact cord blood pH value that defines significant fetal acidemia is unknown, an umbilical artery pH less than 7.0 has been associated with a greater need for resuscitation and higher incidence of respiratory, gastrointestinal, cardiovascular, and neurological complications. However, when a low pH is detected, many newborn infants will still stay neurologically normal.

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TABLE 1. Medians and Reference Values (2.5 and 97.5%) for Arterial and Venous Cord Blood in Newborns With Spontaneous Vaginal Delivery and Cesarean Section

	Newborns with SVD (<i>n</i> = 303)		Newborns with CS (<i>n</i> = 189)	
	Arterial cord blood	Venous cord blood	Arterial cord blood	Venous cord blood
pH	7.257 7.01–7.39	7.307 7.06–7.44	7.301 7.05–7.39	7.341 7.10–7.42
pCO ₂ (kPa)	6.86 4.12–11.45	5.44 3.33–9.85	7.15 5.01–10.60	5.84 3.88–9.36
pO ₂ (kPa)	2.84 1.49–5.06	3.64 1.80–6.29	2.59 1.17–5.94	4.07 1.98–7.23

CS, cesarean section; SVD, spontaneous vaginal delivery. Lower and upper reference ranges are expressed as 2.5 and 97.5 percentiles.

Many babies with acidemia at birth have no clinical problems during the neonatal period (3).

The umbilical cord blood acid-base determination is clearly indicated in newborns who are severely depressed (persistent Apgar score of 0–3 for 5 min or longer and an umbilical artery blood pH of less than 7.00). These are at risk of manifesting hypoxic ischemic encephalopathy and subsequent neurologic dysfunction. Umbilical cord blood pH and acid-base balance is most useful in association with the delivery of an infant with a low Apgar score. There is little doubt that the most significant role of umbilical cord blood acid-base analysis is in the evaluation of the very premature infants with a low Apgar score. Apgar score of those otherwise uncomplicated preterm infant are typically lower than those of term infants. Many such infants could be classified incorrectly as asphyxiated based solely on the Apgar score. Premature infants are at higher risk for intracranial hemorrhage and subsequent neurological dysfunction, such as cerebral palsy. Without umbilical cord blood gas analysis, these neurological complications could be incorrectly attributed to intrapartum or birth asphyxia, especially if the latter is solely based on Apgar scores. Normal umbilical cord blood values in the premature infant virtually eliminate the diagnosis of significant intrapartum hypoxia or birth asphyxia (3). Umbilical cord blood pH and acid-base analysis to assess newborn acid-base balance can be useful also in pregnancies complicated by meconium staining of the amniotic fluid. Tracheal visualization, intubation, or suctioning could lead to low Apgar score that might be incorrectly attributed to newborn asphyxia. In situations such as post term birth or delivery complications identification and documentation of a normal pH value excludes birth asphyxia as a cause of subsequently detected neonatal abnormality (3). Blood from the umbilical vein reflects the placenta function. The umbilical vein pO₂ is considerably lower than the maternal arterial pO₂ and even slightly lower than the maternal placental venous pO₂, because complete

O₂ diffusion equilibrium across the placenta is not achieved, whereas CO₂ equilibrium is complete. Placental dysfunction cause lower umbilical vein pO₂ and can also cause elevation of the umbilical vein pO₂ (1).

The aim of this study was to re-evaluate and compare reference values in arterial and venous samples of newborns with spontaneous vaginal delivery (SVD) and cesarean section (CS). Many different pH reference values were published. Most published data set the mean values range between 7.20 and 7.29 (4). Published mean, median, and ranges for pH, pCO₂, and pO₂ vary owing to differences in the number of subjects, population, sampling frequency and sampling technique used in the studies.

MATERIALS AND METHODS

Two groups of subjects were selected for the study. Group I consisted of 303 newborns with SVD and Group II consisted of 189 newborns delivered by CS.

The material for the study was arterial and venous cord blood. Umbilical cord blood samples were obtained immediately after delivery. Samples of arterial and venous cord blood were collected before delivery of placenta into heparinized plastic syringes for each. The samples were collected on ice and transported to the laboratory, where they were immediately analyzed. Sample of cord blood were mixed gently before analysis. Cord blood samples were analyzed for standard blood gas by analytical device Rapid Lab 845 or Rapid Lab 865 (Siemens Medical Diagnostics, Bayer, Tarrytown, NY).

D'Agostino and Pearson omnibus test for normality was used to determine the distribution of data in both groups. If the distribution was not normal, logarithmic transformation of the data was performed. Outlying values were eliminated. If the logarithmically transformed data were not normally distributed, nonparametric bootstrap procedure based on equation $0.025 \cdot (n+1)$ and $0.975 \cdot (n+1)$ (*n* is the number of samples) was used to calculate the upper and lower reference ranges.

TABLE 2. Studies Reporting Umbilical Cord Values for Term and Preterm Newborn

Study characterization	Umbilical artery (mean $\pm$ SD)				Umbilical venous (mean $\pm$ SD)				References
	pH	pCO ₂ (kPa)	pO ₂ (kPa)		pH	pCO ₂ (kPa)	pO ₂ (kPa)	Number	
Our study (SVD)	7.24 $\pm$ 0.10	7.02 $\pm$ 1.75	2.98 $\pm$ 1.14		7.29 $\pm$ 0.10	5.70 $\pm$ 1.60	3.74 $\pm$ 1.39	303	
Our study (CD)	7.28 $\pm$ 0.08	7.30 $\pm$ 1.29	2.82 $\pm$ 1.27		7.28 $\pm$ 0.08	7.30 $\pm$ 1.29	2.82 $\pm$ 1.27	189	
All types of gestations, Apgar score > 7	7.26 $\pm$ 0.07	7.05 $\pm$ 1.33	2.26 $\pm$ 0.80		7.34 $\pm$ 0.06	5.45 $\pm$ 0.93	3.86 $\pm$ 0.93	15 073	Helwig et al. (6)
Four term, Nulliparous, all delivery types	7.24 $\pm$ 0.07	7.49 $\pm$ 1.14	2.38 $\pm$ 0.92		7.32 $\pm$ 0.06	5.83 $\pm$ 0.89	3.82 $\pm$ 0.97	1694a 1820v	Thorp et al. (7)
Term singleton infants, vaginal delivery	7.27 $\pm$ 0.07	6.60 $\pm$ 1.48	2.45 $\pm$ 1.09		7.34 $\pm$ 0.06	5.41 $\pm$ 1.05	3.79 $\pm$ 1.02	3522	Riley and Johnson (8)
Preterm infants 24–36 weeks, normal cardiotocogram	7.26 $\pm$ 0.08	7.05 $\pm$ 1.33	2.53 $\pm$ 1.05		7.33 $\pm$ 0.07	5.77 $\pm$ 1.10	3.88 $\pm$ 1.29	1393a 1526v	Dickinson et al. (9)
Uncomplicated vaginal deliveries	7.28 $\pm$ 0.05	6.54 $\pm$ 1.11 (49.2 $\pm$ 8.4) ^a	2.39 $\pm$ 0.82 (18.0 $\pm$ 6.2) ^a		7.35 $\pm$ 0.05	5.08 $\pm$ 0.74 (38.2 $\pm$ 5.60) ^a	3.88 $\pm$ 0.78 (29.2 $\pm$ 5.90) ^a	146	Yeomans et al. (10)
Cord blood gas reference values	7.28 $\pm$ 0.07	7.44 $\pm$ 1.47 (56.0 $\pm$ 11.1) ^a	2.79 $\pm$ 1.2 (21.0 $\pm$ 9.0) ^a		7.33 $\pm$ 0.06	6.25 $\pm$ 1.10 (47 $\pm$ 8.3) ^a	3.72 $\pm$ 1.02 (28 $\pm$ 7.7) ^a	198	Fouse (5)
Umbilical blood values	7.15 $\pm$ 0.04	6.4 $\pm$ 1.30	3.40 $\pm$ 1.05		7.30 $\pm$ 0.07	5.35 $\pm$ 1.08	3.85 $\pm$ 1.08	4667	Huch et al. (11)
Umbilical cord artery blood at the time 5, 65, and 125 min after birth	7.27 $\pm$ 0.07 ^a 7.28 $\pm$ 0.06 ^b 7.28 $\pm$ 0.06 ^c	7.21 $\pm$ 1.35 ^a 5.83 $\pm$ 1.14 ^b 4.99 $\pm$ 1.01 ^c	1.66 $\pm$ 0.70 ^a 1.97 $\pm$ 0.60 ^b 2.25 $\pm$ 0.80 ^c		–	–	–	52	Valenzuela et al. (2)

Arterial (a) and venous (v) sample numbers are given separately. Where available, samples are collected at the time of 5 min (a), 65 min (b), and 125 min (c) after birth.

^aOriginal data presented as mmHg.

If the distribution of the logarithmically transformed data was normal, then parametric procedure was used to calculate the reference values. Kruskal–Wallis test was used to compare the differences between medians in both population groups. Value of $P < 0.05$ was considered as statistically significant. CB Stat software version 3.7 (Kristian Linnet, DK) and GraphPad Prism software version 5.0 (San Diego, CA) were used for statistical analysis. Statistical comparison of median values for arterial and venous values of SVD and CS groups of newborns was performed.

RESULTS

Median values and reference ranges for arterial and venous cord blood in newborns delivered spontaneously and by CS are listed in Table 1. It is important to emphasize that medians of measured blood gases and pH in sample populations for SVD and CS for umbilical cord blood arterial and venous are not statistically different (Kruskal–Wallis test, $P > 0.05$).

DISCUSSION

The determination of umbilical cord blood pH and gas are important in understanding the fetal circulation in utero. Although it is important to interpret laboratory data according to the relevant reference ranges, we did not prove statistically significant differences in medians for SVD and CS.

Presented results confirm the fact that newborns born by CS have results which are close to normal adult values (higher pH, pO_2). The repeated uterine contractions of SVD exert appreciable metabolic stress in fetus. Regional spinal anesthesia is associated with increased incidence of cord blood acidosis. Sympathetic blockade reduces uteroplacental perfusion and the resulting CO_2 retention leads to respiratory acidosis without clinical outcome (1).

Statistical analysis revealed mostly nonparametrical asymmetric distributions (5). Lower limit of reference ranges for pH for our study is lower than commonly reported reference ranges. Studies reporting umbilical cord values for term and preterm newborns are listed in Table 2.

Valenzuela et al. presented a study that included 50 cases. The pH, pO_2 , and pCO_2 values of umbilical cord blood were clamped immediately and then drawn 5 min (time 0), 65 min (time 60), and 125 min (time 120) after birth. No significant differences were found after 60 min in the average values for the pH in the arterial and venous paired samples, although the arterial and venous pCO_2 values declined significantly and the arterial pO_2 values increased significantly. After 120 min, no significant differences were found in the average values for

the venous pH and venous pO_2 paired samples. However, the arterial pH and pO_2 values increased significantly, whereas the arterial and venous pCO_2 values declined significantly (2).

pH values lower than 7.0 are considered with high-risk incidence of complications. The association between umbilical arterial acidosis and adverse neurological events in infants is characterized with arterial $pH < 7.20$. Neonatal death, which was much more likely, was $pH < 7.05$ and for unexplained events that became more likely was $pH < 7.00$. It was recommended that the value for defining pathological acidemia is $pH < 7.00$. It was found that hypoxic–ischemic encephalopathy occurred in 12 % of infants with $pH < 7.00$, 33 % with $pH < 6.9$, 60 % with $pH < 6.8$, and 80 % with $pH < 6.7$. In our study, we eliminated pH levels lower than 6.9. The levels above 6.9 were not associated with neonatal complications.

In mothers ventilated with 100 % O_2 during CS, the upper 95 % confidence level for umbilical arterial pO_2 was 4.9 kPa. These data indicated that cord arterial samples with pO_2 greater than 5.0 kPa are likely to have been affected by the presence of an air bubble contamination in the specimen. Because CO_2 content of air is very low, this can be accompanied by lowering the pCO_2 followed by a large rise in pH, with consequent risk of misinterpretation. Maternal hyperventilation lowers fetal pO_2 (1).

Most of the previously published reference ranges come from the studies more than 15 years old, so re-evaluation was required owing to new technologies and recent standards in healthcare.

Although the reference values of all selected studies correlate with our results, reference values presented in our study reflect the current considerations and insights in preanalytical phase (12), instrumentation, and standardization (13–15).

Analysis of blood gas and pH is a valuable tool in monitoring a newborn's condition. Ideally, cord blood would be performed on all deliveries.

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