

# Reference range evaluation for cord blood gas parameters

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In conjunction with Apgar scores and other parameters, umbilical-cord blood gas values are used to assess newborn respiratory status.

Paired umbilical-cord gas venous and arterial samples were collected from 200 patients to establish reference ranges for blood gas/hemoximetry parameters. Umbilical-cord samples were collected by double clamping a segment of umbilical cord before the delivery of the placenta.

Samples were analyzed in duplicate immediately upon arrival in the laboratory. An Apgar score of 7 at 5 minutes was used as the limiting criteria for an infant with normal respiratory status for inclusion of data in reference range analysis.

## Introduction

Blood gas values obtained immediately after delivery from the umbilical-cord blood have been noted as a

valuable means to assess the respiratory and metabolic status of the neonate.

It is important to establish the correct etiologic diagnosis for any observed respiratory symptoms. "Not every cyanotic, rapidly breathing infant has respiratory distress syndrome or even respiratory disease.

Hypovolemia, hyperviscosity (polycythemia), anemia, hypoglycemia, congenital heart disease, hypothermia, metabolic acidosis of any etiology, or even the effects of drugs or drug withdrawal may all mimic primary respiratory disorders" [1].

Evaluation of the status of the newborn is best accomplished by assessing multiple criteria. Because the Apgar scoring system is considered subjective, it is not always accurate in the prediction of asphyxia.

Umbilical-cord acid-base balance is a more effective means of identifying hypoxia and acidemia (typically

defined as an umbilical arterial pH of less than 7.20 [2]. Gilstrap *et al* [3] have suggested that the newborn is not considered high risk resulting from asphyxia until the umbilical arterial pH is < 7.00 with an Apgar score of < 3 at both 1 minute and at 5 minutes.

Apgar scores are defined by rating the following parameters with a score of 0, 1, 2, respectively for each parameter based on the following criteria:

**Heart Rate:**

0, <100 bpm, >100 bpm.

**Respiratory Effort:**

None, Irregular, Regular

**Tone:**

Limp, Moving, Vigorous

**Reflex Irritability:**

None, Responsive/Grimacing, Regular Spontaneous Crying

**Color:**

Blue/Cyanotic, Peripheral Cyanosis, Pink

There is a lack of consensus as to when umbilical-cord blood gases should be performed. Some institutions perform them on all deliveries. Recommendations were suggested based upon a study performed by Johnson and Riley in 1993 [4].

It suggests that blood be sampled from an umbilical artery in the following situations: 1) all premature newborns, 2) the presence of meconium-stained amniotic fluid, 3) operative vaginal or abdominal deliveries for non-reassuring fetal heart-rate pattern, and 4) term newborns who are depressed at birth or who have a 5-minute Apgar score below 7 [2].

## Methods and materials

Umbilical-cord venous and arterial samples were collected before delivery of the placenta by double clamping of a 20 cm section of the umbilical cord. A

minimum of 1.5 mL blood was collected into heparinized syringes for each venous and arterial cord sample. Samples were iced and immediately transported to the laboratory.

200 paired (arterial and venous) cord samples were collected and analyzed in duplicate for standard blood gas and hemoximetry parameters on the Radiometer Medical A/S ABL505/OSM3 immediately after arrival in the laboratory. All samples were analyzed within 30 minutes of collection and within 5 minutes of arrival in the laboratory.

A minimum 5-minute Apgar score of 7 obtained by the delivery team was used as the limiting criteria for indication of an active, vigorous infant with normal respiratory status. 198 paired samples were included in the statistical analysis, omitting 2 paired samples from infants with Apgar scores below 7.

Data was then differentiated as to the type of delivery, spontaneous vaginal delivery (SVD), n=143 or cesarean section (CS), n= 55. A mean and SD were calculated for each parameter for both arterial and venous samples.

Data were then analyzed by Kruskal-Wallis analysis of variance and the F-test to determine if there were statistical differences between values obtained for vaginal deliveries versus cesarean sections.

## Results

**Table I** indicates the reference intervals that were established for our population of patients at Duke University Hospital.

Previous studies performed by Helwig *et al* [5] established the following data based on 15,073 deliveries (data from spontaneous vaginal deliveries, operative vaginal deliveries, and cesarean sections).

Umbilical Artery (UA) ranges were established based upon the following achieved UA means and SDs: pH = 7.26 ± 0.07, pCO<sub>2</sub> = 53 mmHg ± 10, pO<sub>2</sub> = 17 mmHg ± 6, base excess (BE) = -4 mEq/L ± 3. Umbilical Vein

Analyte	Arterial UCBG Mean $\pm$ SD	Arterial Reference Interval	Venous UCBG Mean $\pm$ SD	Venous Reference Interval
pH	7.281 $\pm$ 0.070	7.14 - 7.42	7.331 $\pm$ 0.056	7.22 - 7.44
pCO <sub>2</sub> mmHg	56 $\pm$ 11.1	34 - 78	47 $\pm$ 8.3	30 - 63
pO <sub>2</sub> mmHg	21 $\pm$ 9.0	3 - 40	28 $\pm$ 7.7	12 - 43
cHCO <sub>3</sub> <sup>-</sup> mmol/L	25 $\pm$ 2.2	21 - 29	24 $\pm$ 2.0	20 - 28
ctCO <sub>2</sub> mmol/L	27 $\pm$ 2.4	22 - 32	25 $\pm$ 2.2	21 - 29
ABE mmol/L	-2.4 $\pm$ 2.4	-7 to +2	-2.1 $\pm$ 2.1	-6 to +2
ctHb g/dL	15.2 $\pm$ 1.8	11.6 - 18.8	15.2 $\pm$ 1.9	11.4 - 19.0
FO <sub>2</sub> Hb %	38.2 $\pm$ 21.0	0 - 80	58.4 $\pm$ 17.8	23 - 94
FCOHb %	3.1 $\pm$ 1.2	0.7 - 5.5	3.8 $\pm$ 1.8	0.2 - 7.3
FMetHb %	0.94 $\pm$ 0.2	0.5 - 1.4	0.93 $\pm$ 0.2	0.5 - 1.4
ctO <sub>2</sub> %	8.1 $\pm$ 4.5	0 - 17	12.3 $\pm$ 3.9	5 - 20

TABLE I: Reference Intervals for Arterial and Venous Umbilical Cord Blood Gases (UCBG). Mean and SD values for all arterial and venous blood gas parameters. Reference Intervals based on  $\pm$  2SD limits. Apgar scores > 7 at 5 minutes.

Analyte	Mean (CS)	Mean (SVD)	Kruskal-Wallis	F-Test Probability
pH	7.263	7.288	p = 0.0077 **	p = 0.0245*
pCO <sub>2</sub> mmHg	60.38	53.69	p = 0.0000 ***	p = 0.0001***
pO <sub>2</sub> mmHg	17.46	22.22	p = 0.0000 ***	p = 0.0007 ***
ctHb g/dL	15.09	15.25	Not Significant	Not Significant
FO <sub>2</sub> Hb %	28.05	42.15	p = 0.0000 ***	p = 0.0000 ***
FCOHb %	2.98	3.12	Not Significant	Not Significant
FMetHb %	0.961	0.938	Not Significant	Not Significant
ctO <sub>2</sub> %	5.87	8.93	p = 0.0000 ***	p = 0.0000 ***

TABLE II: Statistical Comparison for CS vs. SVD Delivery – Arterial Blood. Means of sample population for Cesarean Section (CS) and Spontaneous Vaginal Delivery (SVD) for arterial umbilical cord samples and the probability of significant differences in all measured blood gas and hemoximetry analytes. Compiled data evaluated with Kruskal-Wallis Analysis of Variance and F - Test Statistical Tests.

\* indicates p < 0.05  
 \*\* indicates p < 0.01.  
 \*\*\*indicates p < 0.001

(UV) achieved means and SDs were: pH = 7.34  $\pm$  0.06, pCO<sub>2</sub> = 41 mmHg  $\pm$  7, pO<sub>2</sub> = 29 mmHg  $\pm$  7, and BE = -3 mEq/L  $\pm$  3.

**Table II** depicts the differences observed for all measured parameters for both CS and SVD deliveries on UA blood samples. Statistical differences were observed for all parameters except ctHb (concentration of total hemoglobin) in g/dL, fraction of carboxyhemoglobin

(FCOHb), and fraction of methemoglobin (FMetHb) using the Kruskal-Wallis Analysis of Variance and F-Test.

**Table III** depicts the differences observed for all measured parameters for both CS and SVD deliveries on UV blood samples. Again, statistical differences were observed for all parameters except ctHb, FCOHb, and FMetHb using the Kruskal-Wallis Analysis of Variance and F-Test.

Analyte	Mean (CS)	Mean (SVD)	Kruskal-Wallis	F-Test Probability
pH	7.310	7.339	p = 0.0038 **	p = 0.0014**
pCO <sub>2</sub> mmHg	50.97	44.86	p = 0.0000 ***	p = 0.0000***
pO <sub>2</sub> mmHg	24.06	28.97	p = 0.0002 ***	p = 0.0000 ***
ctHb g/dL	15.03	15.28	Not Significant	Not Significant
FO <sub>2</sub> Hb %	49.88	61.61	p = 0.0003 ***	p = 0.0000 ***
FCOHb %	3.90	3.73	Not Significant	Not Significant
FMetHb %	0.957	0.916	Not Significant	Not Significant
ctO <sub>2</sub> %	10.23	13.11	p = 0.0000 ***	p = 0.0000 ***

TABLE III: Statistical Comparison for CS vs. SVD Delivery – Venous Blood. Means of sample population for Cesarean Section (CS) and Spontaneous Vaginal Delivery (SVD) for venous umbilical cord samples and the probability of significant differences in all measured blood gas and hemoximetry analytes. Compiled data evaluated with Kruskal-Wallis Analysis of Variance and F - Test Statistical Tests.

\* indicates p < 0.05  
 \*\* indicates p < 0.01.  
 \*\*\*indicates p < 0.001

Our data agree, in general, with reported values for the basic gas parameters. The hemoximetry data presented here is unique. It is worthwhile to note that the fraction of oxyhemoglobin (FO<sub>2</sub>Hb) and the oxygen content (ctO<sub>2</sub>) are significantly different for SVD versus CS in both UA and UV samples.

## Discussion

In order to apply the results of umbilical-cord blood gases to the clinical condition of the newborn fetus, it is important to understand the basics of the fetal circulation in-utero.

The placenta acts both as “lungs” and “kidneys” for the fetus by supplying oxygen and removing carbon dioxide and metabolites [2]. It provides efficient gas exchange as well as allows nutritional substances such as vitamins, glucose, free fatty acids, and electrolytes to pass between the two circulations without allowing the two circulations to mix.

The blood in the intervillous space is supplied by spiral arteries which provide a pulsatile flow of maternal blood. The blood flows through the intervillous space to be drained from the placenta by endometrial veins.

The villi are supplied with fetal blood by branches of the umbilical arteries. Blood flows through the capillaries of the villi, where the gas and nutrient exchange occurs, and is collected in the branches of the umbilical vein to be returned to the fetal circulation.

The supply of oxygen is dependent on 1) adequate maternal oxygenation, 2) blood flow to the placenta and adequate transfer across the placenta, 3) fetal oxygenation and delivery to fetal tissues. The removal of carbon dioxide depends on fetal blood flow to the placenta and transport across the placenta [2].

When the fetus is unable to remove carbon dioxide from its tissues and excrete it across the placenta, the pCO<sub>2</sub> increases resulting in respiratory acidosis. Also, when the exchange of oxygen across the placenta from the mother to baby is inadequate, anaerobic metabolism occurs resulting in lactic acid production and the development of metabolic acidosis [6].

If the oxygen supply continues to drop, the physiological compensatory mechanisms also begin to fail and this results in a reduced cardiac output [7].

Umbilical venous cord blood gas values are similar to the maternal intervillous oxygen and acid-base status

because the oxygen and carbon dioxide can equilibrate between these two compartments, whereas umbilical arterial cord blood gases represent the fetal status [8]. Umbilical venous blood has higher pH,  $pO_2$ , base excess and lower  $pCO_2$  than umbilical arterial blood [9].

Over the years, investigators have noticed differences between umbilical arterial versus venous cord blood gas values and have tried to predict outcomes based upon them.

Belai *et al* [6] noted a strong interrelationship between umbilical arterial and venous  $pCO_2$  concentrations in a cohort of infants born with severe acidemia (pH <7.0). When the difference in umbilical arteriovenous  $pCO_2$  exceeded 25 mmHg, there was a significant increase in the incidence of seizures, hypoxic-ischemic encephalopathy, cardiopulmonary and renal dysfunction.

Egan *et al* [9] noted  $\Delta$ pH discordancy (arteriovenous pH differences of >0.12) from 53 neonates. The  $\Delta$ pH discordant group not only had lower arterial pH, but also had a higher venous pH. A fetus with a discordant pH was more likely to be acidemic than one without discordancy.

Their data suggested that vaginal delivery, cord compression, and normal placental reserve were the most common factors associated with  $\Delta$ pH discordancy.

In a retrospective study, Johnson and Richards [10] noted that in abruptio placentae and in other cases of reduced maternal oxygen delivery to the placenta due to reduced maternal cardiac output, increased uterine arterial resistance, and maternal hypoxia, there was very little difference in pH and oxygen saturation between umbilical arterial versus venous cord blood gas samples.

On the other hand, large umbilical vein-umbilical artery pH and oxygen saturation differences were noted with reduced fetal perfusion of the placenta such as is found with umbilical-cord prolapse. In cord prolapse, umbilical-cord blood flow is significantly reduced, thereby reducing the rate of oxygen delivery to the fetal tissues.

## Conclusion

Umbilical-cord blood acid-base analysis provides an objective means to evaluate a newborn's condition especially with regard to hypoxia and acidemia [11].

Specimens for analysis should generally be obtained from the umbilical artery, not the umbilical vein. The umbilical artery contains blood returning from the fetus to the placenta and thus should provide the most useful information on the acid-base of the fetus [12].

Studies have demonstrated that the collection of both arterial and venous umbilical-cord samples may further help to determine the pathogenesis of marked fetal acidosis [6, 9, 10].

In accordance with good laboratory practice, it is important for each institution to establish or verify the reference ranges used for interpretation of umbilical cord gas values.

As newer instrumentation now allows the ability to measure, not only blood gas and hemoximetry parameters, but also electrolytes and metabolites on very small sample aliquots, it will be important to develop reference ranges for all parameters on cord blood samples. This then provides us with new diagnostic tools to help predict fetal outcomes.

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