ORIGINAL RESEARCH ARTICLE

Comparison of Umbilical Arterial and Venous Lactate and Base Excess Values and Its Neonatal Outcome in High-risk Pregnancies

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Abstract

Aim and objective: The aim and objective of the study was to compare the paired umbilical arterial and umbilical venous blood gas analysis and its neonatal outcome in high-risk pregnancies at a risk of perinatal asphyxia.

Materials and methods: A 10–20 cm segment of umbilical cord was doubly clamped above the previous clamp immediately after delivery. Both the samples were sent for analysis immediately not exceeding 15 minutes. Blood gas analysis was done by ABG analyzer. Results were collected and compared. APGAR at 1 and 5 minutes of the neonate was noted.

Results: Sensitivity for APGAR at 5 minutes obtained for a mean value of 4.5 mmol/L for arterial lactate was 94% and the specificity was 32%. For a base excess mean value of −10 mmol/L in the arterial sample, sensitivity was 81% and specificity was 32% observed for APGAR. When lactate was compared to arterial base excess, the area under the receiver operating characteristic (ROC) curve was higher for base excess.

Conclusion: Comparison of paired cord blood gas analysis of pH, lactate, and base excess is a valuable adjunct to guide the management of newborns in high-risk pregnancies. In our study, umbilical arterial sample was superior to venous sample in predicting neonatal outcome.

Clinical significance: Paired umbilical gas analysis is an effective method of practice for predicting neonatal acidemia in high-risk pregnancies. Both lactate and base excess had a high negative predictive value for predicting birth asphyxia that will work as an obstetric quality measure as well as an audit tool.

Keywords: Adverse perinatal outcome, Amniotic fluid index, APGAR score, Fetal outcome, High-risk pregnancy, Maternal and perinatal outcomes, Nonstress test, Perinatal mortality, Perinatal outcome.

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Introduction

Birth asphyxia is a major cause of perinatal morbidity and mortality. Umbilical cord blood gas sampling is the most objective determinant of fetal metabolic condition at the time of birth. Both ACOG and RCOG recommend cord blood sampling for high-risk pregnancies. Umbilical cord blood gas analysis provides important information about the past, present, and possibly the future condition of the infant.

Analysis of paired umbilical arterial and venous cord blood gas provides insight into the aetiology of asphyxia or acidosis in the neonate.

In accordance with the Society of Obstetricians and Gynaecologists of Canada (SOGC) "Attendance at Labour and Delivery guidelines," arterial and venous cord blood gas analysis is recommended routinely for all births, as they may help in providing appropriate care to the newborns at birth and in planning subsequent management.[1] This reliable acid–base analysis may be used as an obstetric quality measure, as well as being an audit tool. Medicolegal considerations also necessitate reliable results.[2] This is because umbilical arterial blood primarily reflects fetal metabolism while venous blood primarily reflects placental functions.[3] When adequate fetal oxygenation is impaired, metabolism turns to anaerobic pathway leading to the production of lactic acid and ketoacids. Lactate is a direct end product of anaerobic metabolism and is a predictor of short-term neonatal morbidity.[4] Oxygen and nutrients diffuse across the placental membrane from maternal arterial blood and are transported to the fetus via a single large umbilical vein. After utilizing oxygen and nutrients, fetal blood returns to the placenta via two small umbilical arteries that contain products from fetal metabolism. Hence, venous cord blood reflects the combined effect of maternal acid–base status and placental function, whereas arterial cord blood reflects neonatal acid–base status.

Several studies have linked umbilical arterial acidemia with perinatal morbidity and long-term adverse outcomes.[5] Many studies are limited by their study design, small sample size, and involvement in selection bias. We conducted this study to compare the arterial and venous cord blood gas analysis (lactate and base excess) in pregnancies where the fetus is at a risk of

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perinatal asphyxia and to correlate the umbilical cord blood gas analysis with the neonatal outcome.

Materials and Methods

This was a cross-sectional study of consecutive deliveries at Sri Ramachandra University from 2017 to 2019. This study was approved by the Institutional Research Ethics Committee of Sri Ramachandra Medical College and Research Institute. Women included in this study (antenatal mothers whose fetuses are at a risk of perinatal asphyxia) have fetal distress, meconium stained liquor, severe anemia, pregnancy induced hypertension (PIH), preeclampsia, eclampsia, gestational diabetes mellitus (GDM), intrauterine growth restriction (IUGR), IUGR with Doppler changes, abruptio placenta, assisted vaginal delivery, intrapartum fever, oligohydramnios amniotic fluid index (AFI <5 cm). We excluded preterm babies, appropriately grown babies with clear liquor.

Sampling Technique

Umbilical cord blood analysis is done from a clamped segment of a cord, as if it remains in continuity with placenta, it will demonstrate progressive change in acid–base status due to ongoing placental metabolism and gas exchange. Small changes in umbilical pH occur within 60 seconds of delivery,[6] and over 60 minutes, cord arterial or venous pH can fall by more than 0.2 pH units.[7]

These changes are not observed if the cord is doubly clamped at birth, isolating a segment of cord blood from both the placenta and the environment. The pH of the blood then remains relatively constant at room temperature for an hour.[8,9]

A 10–20 cm segment of the umbilical cord is doubly clamped as shown in Figure 1, immediately after delivery as delaying can alter the cord blood gas values due to diffusion and continuing metabolism.[10] Blood is taken from both umbilical artery and vein separately into a 1–2-mL preheparinized syringe. In normal labor, the base excess changes by around 1 mmol/L per hour in the second stage. In contrast, base excess varies by around 1 mmol/L per 30 minutes, while there is a recurrent fetal heart rate deceleration.[11] Lactic acid is a principal metabolic acid responsible for the fall in cord blood pH and base excess associated with cord blood acidosis and birth asphyxia. Wiberg et al. argued that lactate may be superior to base excess because it is a direct measure of metabolic acidosis, whereas base excess is an indirect value measured from pH and pCO_2. While umbilical arterial lactate is a direct measure of fetal lactate and cord venous lactate may reflect placental lactate, the fetus has been identified as the main source of umbilical cord lactate concentration in labor with little influence by maternal and uteroplacental production. Thus, cord venous lactate after leaving the placenta remains predictive of arterial lactate.

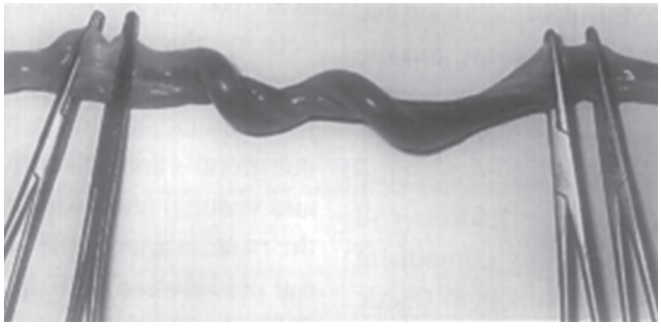

Fig. 1: Segment of umbilical cord doubly clamped immediately after delivery

Heparinized Syringe Preparation

The dilution effect of heparin may cause a fall in pCO_2 and bicarbonate concentration, and since the heparin is acidic, the use of concentrated heparin may result in an increase in pCO_2 and a reduction in pH.[12,13] Hence, flushing of the syringe with appropriate dilution is mandatory. We had diluted 1 mL of heparin (1000 IU/mL) in 9 mL of distilled water and finally took 1 mL of heparin (diluted) to flush the syringe. Two milliliters of blood is collected which resulted in a final heparin concentration of 50 IU/mL of blood. Hence, ensuring that syringes only contain sufficient heparin to wet the wall of the syringe and fill the dead space occupied by the syringe hub. This dead-space volume is around 0.1 mL for a standard 2.0-mL syringe. Plunger was moved up and down and residual heparin was removed.

Following delivery, cord was clamped cut and baby handed over to the pediatrician. A 10–20 cm segment of umbilical cord was doubly clamped above the previous clamp immediately after delivery as delay in clamping affects pH and gas values due to gaseous diffusion and continuing metabolism in the placenta. Delayed cord clamping (60 seconds) was allowed only for vigorous babies but when the babies were depressed at birth cord was immediately clamped. Blood sampling was done first from umbilical artery followed by vein. A small, narrow vessel was identified as umbilical artery. About 1.5–2 mL of sample was drawn from the same. Similarly, larger and thinner vessels were identified as umbilical vein and 1.5–2 mL sample was withdrawn. Both the samples were sent for analysis immediately not exceeding 15 minutes.

Blood gas analysis was done by ABG analyzer (ABL90 FLEX) which was in neonatal intensive care unit (NICU) close to labor room. Results were collected and compared. APGAR at 1 and 5 minutes of the neonate was noted. Lactate and base excess were compared between the arterial and venous samples. Fifth, mean, 95th percentile of arterial and venous samples were analyzed. The values of paired samples (lactate and base excess) were compared with the 5 minutes of APGAR. The course of the neonate was followed up from the requirement of immediate resuscitation measures as per the neonatal resuscitation protocols to complications encountered such as hypoxic ischemic encephalopathy (HIE), meconium aspiration syndrome, transient tachypnea of newborns, and respiratory distress syndrome.

The data entry was done using Microsoft Excel, and then, data analysis was made using SPSS software version 21.0. Further graphical representations were done using Microsoft Excel.

Results

One-hundred and seventy-eight samples were taken, but due to sampling error, 28 samples were excluded. A total of 150 paired samples were analyzed and validated. The samples were taken from 37 to >40 weeks of gestation, among which most (33.8%) of the samples were taken from 39 to 40 weeks. Fifty-eight percent of the samples were taken from primigravida and 42% were from multigravida. Among 150 cases, 52% of the samples were collected from lower segment caesarean section (LSCS), 43% were from normal vaginal delivery, and 5% from assisted vaginal delivery. Meconium stained liquor (32.4%), fetal distress (33.7%), and IUGR (8.6%) were contributed maximum to the study.

The ROC curve plotted for arterial lactate showed an area under the curve as 0.604 predicting that lactate had a good predictive accuracy as shown in Figure 2. The cutoff value of arterial lactate (4.5 mmol/L) had a sensitivity of 94% and specificity being 32% as shown in Table 1. ROC curve plotted for arterial base excess showed an area under the curve as 0.69 predicting a high predictive accuracy as shown in Figure 3. The cutoff value of arterial base excess (−10 mmol/L) had a sensitivity of 81% and specificity being 32% as shown in Table 2. These cutoff values examined demonstrated the best sensitivity and specificity for the neonatal morbidity. When lactate was compared to arterial base excess, the area under the ROC curve was higher for base excess, although the difference was not statistically significant.

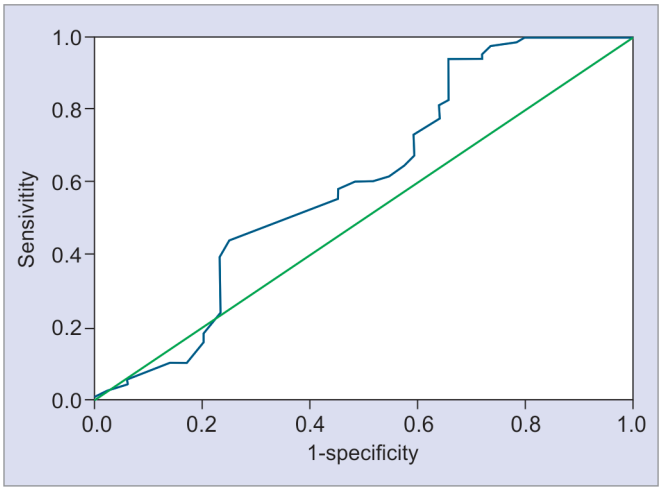

Fig. 2: Receiver operating characteristic curves of arterial lactate for predicting neonatal morbidity ($N = 150$)

Table 1: Mean umbilical arterial and venous lactate and base excess values in predicting neonatal morbidity

	APGAR		
	Normal (≥7/10)	*Abnormal (<7/10)*	*p value*
Lactate			
Arterial (mmol/L)	2.6	3.5	0.002
Venous (mmol/L)	3.1	4.1	0.007
Base excess			
Arterial (mmol/L)	−5.6	−8.4	0.000
Venous (mmol/L)	−4.6	−6.8	0.003

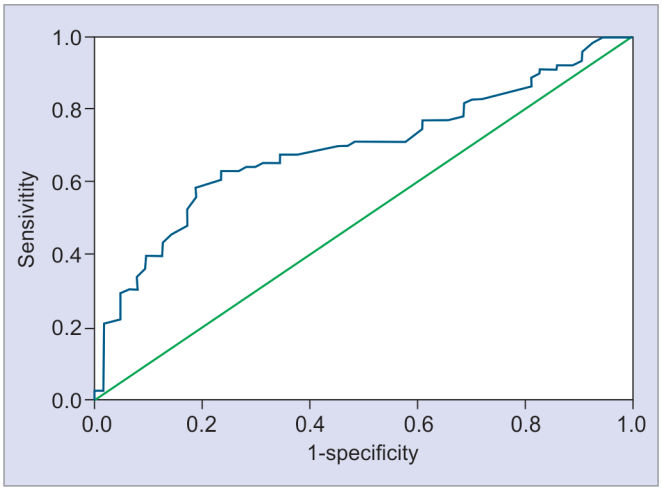

Fig. 3: Receiver operating characteristics curves of arterial base excess for predicting neonatal morbidity ($N = 150$)

Predictive characteristics of different cutoff values that showed a mean arterial lactate and base excess were significantly different in neonates with and without neonatal morbidity. Mean arterial lactate value was higher in neonates with low APGAR scores. Similarly, mean base excess value was higher in neonates with low APGAR scores as shown in Table 1.

All eight babies who had high lactate (>6.1 mmol/L) had low arterial pH and required varying degrees of ventilatory support. Two babies developed HIE as shown in Table 3. Among 150 patients, 7 babies had APGAR <7/10 at 1 minute (4.6%) and 4 babies had APGAR <7/10 at 5 minutes (2.6%). About 14.7% of the babies did not require admission, whereas 3.3% of the babies had a prolonged hospital stay. Eight babies had complications as shown in Table 3. Among HIE, one had stage 2 and the other had stage 3.

Among 150 babies, 8 (5.3%) babies had high lactate and 4 among them had high base excess (>−12 mmol/L) which suggested poor outcome (Table 3). Two had HIE (stage 2 and stage 3). All eight babies had low arterial pH and prolonged NICU stay (Table 4).

Discussion

Comparison of paired cord blood gas analysis was carried out to predict neonatal asphyxia and thereby metabolic acidosis in newborns in pregnant women satisfying inclusion criteria (pregnancies at a risk of perinatal asphyxia). Cord blood analysis presents both longitudinal and static measurements of acid–base conditions and might be a valuable tool in predicting the prognosis. Diagnosis of newborns at a risk of encephalopathy is mainly important because of decision-making for the early intervention. Investigating both arterial and venous samples might help in understanding the physiology and possible cause of acidosis. We found that umbilical cord arterial lactate and base excess is a more discriminating measure of neonatal morbidity at term than pH.

Lactate being a major specific end product of anaerobic metabolism was analyzed by Wiberg et al. among 17,867 newborns and found that umbilical arterial lactate to be at least as good as a base deficit for predicting 5 minutes of APGAR less than 4 or 7. In 2016, Allanson et al. analyzed lactate as a predictor of neonatal risk. Therefore, we are analyzing lactate and its effect on neonatal outcome. Westgren et al. suggested that lactate like pH and base

Table 2: Sensitivity and specificity of mean arterial and venous cutoffs

	Sensitivity	*Specificity*
Arterial lactate	94%	32%
Arterial base excess	81%	32%

Table 3: Complications observed

Complications	*Number of babies*
TTN	1
MAS	2
HIE	2
Respiratory distress	3

Table 4: High lactate and its analysis

Indication	*Lactate (mmol/L)*	*Base excess (mmol/L)*	*Arterial pH*	*Venous pH*	*APGAR (5 minutes)*	*NICU admission (days)*	*Complication*
Abruption	10.6	−17.4	6.92	6.953	5	7	2 episodes of seizure, HIE stage 3
Abruption	8.3	−21.7	6.949	6.95	5	5	HIE stage 2
MSL	8.5	−12.6	7.111	7.24	7	3	MAS, CPAP
Fetal distress	8.4	−17.4	7.123	7.152	7	2	Mild respiratory distress
MSL	6.8	−6.5	7.15	7.226	7	2	Mild MAS
AVD	9.7	−8.2	7.175	7.24	7	3	Respiratory distress, grunting
GHTN	6.4	−8.8	7.178	7.21	7	1	Observation, TTN
GHTN	6.1	−6.2	7.182	7.114	7	3	CPAP

excess predicts low APGAR scores. Chou et al.[14] found that the presence of high lactate of over 4.1 mmol/L and a high lactate/pyruvate ratio predicts neonatal encephalopathy with a 100% sensitivity and 95.4% specificity. This disparity of sensitivity was explained because of a large 4,045 sample size; therefore, we require further a more sample size to achieve the sensitivity. Further lactate/pyruvate ratio was not calculated in our study. Various studies showed various mean umbilical arterial lactate values which may be attributed to the type of blood (hemolyzed or whole blood) for analysis or differences in the mode of delivery.

Low et al.[15] determined that the threshold for fetal metabolic acidosis at delivery, which predicts newborn complications, is an umbilical artery base excess of −12 to −16 mmol/L. In our study, four babies had an umbilical artery base excess of >−14 mmol/L along with high lactate. Two neonates had HIE (HIE 3-1; HIE 2-1), and two required ventilatory support. The cutoff values obtained in this study are by estimating the optimal cutoff values based on maximal Youden Index.

Large arterial–venous base differences usually result from cord entanglement or a stasis of umbilical cord flow secondary to cardiac failure.[16] It is probable that large arterial–venous base differences reflect an acute onset of fetal metabolic acidosis. In our study, we have observed six babies who had large arterio-venous base difference; we did not observe any difference in the clinical outcome. The babies were observed for further metabolic derangement in NICU but none of them developed complications or required ventilatory support.

Low et al. have worked with their samples and found that neonates with metabolic acidosis and narrow arterial–venous buffer base differences had a poorer neonatal outcome than those with metabolic acidosis and large arteriovenous differences. One baby which had narrow arteriovenous base difference with a high lactate value of 8.3 mmol/L developed neonatal encephalopathy. Majority of the babies were observed for 4–5 hours in view of grunting and tachypnea. Two babies had a prolonged stay of 7 days as they had perinatal asphyxia in view of abruption. Two babies had HIE. 6 hours later blood gas analysis showed an increase in the base excess along with lactate; hence, both were given therapeutic hypothermia and were observed for a prolonged period of time in NICU. In this study, there was a significant difference between arterial and venous blood lactate, venous and arterial blood base excess, in samples from the fetus with intrapartum distress. A study conducted by Mokarami et al. showed that even after a delayed clamping in the depressed newborns, the values remain unchanged: pH was 7.01 at both times, pCO_2 changed from 11.2 to 11.8 kPa, base excess changed from −14.9 to −14.4 mmol/L, and lactate concentration was 13.3 mmol/L; hence, taking cord blood values in pregnancy with fetus at a risk of hypoxia justifies. A total of 5.3% of the babies had neonatal complications. Among 150 cases, 8 samples were sorted out with high base excess along with high lactate which suggests poorer neonatal outcome. Along with arterial base excess and lactate, pH was also analyzed which showed that most cases had less arterial pH and a low APGAR score with an increased NICU stay and complications, i.e., HIE and meconium aspiration syndrome. Two babies with high arterial base excess and high arterial lactate had poorer neonatal outcomes.

Hence, base excess also offers a more direct insight into the metabolic acidosis and is adjusted for discrepancy in pCO2. In a study by Allanson et al.,[17] the ability of umbilical arterial lactate to predict acidosis showed a sensitivity of 50–82% and a specificity of 90–92%. The ability of umbilical artery lactate (>6 mmol/L) to classify acidosis, when acidosis was defined as an umbilical artery less than−8 mmol/L, was reported in two studies, with 79 cases. Sensitivity estimates were 50–63%, and specificity estimates were 95–100%.[17] Among the eight babies with complications, umbilical arterial lactate was a better predictor for the outcome of the baby when compared to venous sample as one out of eight (12.5%) had lower lactate value in venous sample which could have been missed. High base excess was found in 17 babies, among which arterial was a better predictor as 11 babies out of 17 (64.7%) had lower base excess values in the venous sample.

Therefore, arterial base excess was a predictor for perinatal asphyxia. Therefore, umbilical cord blood pH, base excess along with lactate are best predictors of the outcome. Since lactate has difficulty in crossing the placenta when it is detected in umbilical cord blood, its origin is mainly from the fetus. Goodwin et al. documented an incidence of encephalopathy of 31% (with an umbilical artery pH <7).[18] Neonatal seizures occurred in 9% of infants with an umbilical artery pH between 6.9 and 6.99 and in 80% of infants with an umbilical artery pH between 6.61 and 6.70. (There were three stillbirths and five neonatal deaths in their study). In this study, no neonatal deaths were noted but two babies had seizures due to HIE with an arterial pH of less than 7, incidence being 1.3%.

Hence, paired umbilical gas analysis is an effective method of practice for predicting neonatal acidemia in high-risk pregnancies. Evidence-based interpretation of cord blood gas values enables the neonatologist to guide the care of newborns.

Lactate mean of 4.5 mmol/L had good sensitivity and specificity. In our study, analysis of all babies who were admitted to NICU showed lactate values above 6.2 mmol/L and were associated with low pH and high base excess and needed varying degrees

of ventilatory support. When −10 mmol/L was taken as a mean for base excess, 81% sensitivity was predicted. When −14 mmol/L that is 2 SD> mean was taken, two babies had HIE and two required respiratory support. Analyzing the neonatal outcome: eight out of 128 admissions to NICU, all babies had low pH, high lactate, and high base excess (two had HIE); required ventilatory support; and required more than 5 days of NICU admission.

Conclusion

Comparison of paired cord blood gas analysis showed umbilical arterial sample was superior to venous sample in predicting neonatal outcome. Both lactate and base excess had a high negative predictive value for predicting birth asphyxia. However, large sample-sized studies are needed to determine the cutoff values to predict an adverse neonatal outcome.

Clinical Significance

Paired umbilical arterial and umbilical venous lactate and base excess are the parameters which will determine the neonatal acid–base status in high-risk pregnancies and will act as an assessment tool in obstetric units.

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