Correlation of Cord Blood pH, Base Excess, and Lactate Concentration Measured With a Portable Device for Identifying Fetal Acidosis

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Abstract

Objective: To determine the effectiveness of portable lactate analyzers in identifying fetal acidosis by correlating arterial and venous lactate values from umbilical cord blood with lactate, pH, and base excess measurements from central laboratory analyzers.

Methods: We performed a prospective study using arterial and venous cord blood from 52 women with a singleton fetus delivered at term. We evaluated the correlation between the cord blood lactate concentration measured using two of the same portable devices (Lactate Plus, Nova Biomedical) with the result from a central laboratory analyzer. Analyses of the correlation between arterial lactate concentration measured on the portable device with arterial pH and base excess were then performed.

Results: We observed a median arterial pH of 7.24 (range 7.05 to 7.35) and a median arterial lactate concentration of 3.7 mmol/L (range 1.7 to 8.8 mmol/L). An excellent correlation was observed between lactate concentrations measured by the two portable devices (arterial R^2 = 0.98 and venous R^2 = 0.98), and between the portable device and the central laboratory analyzer (arterial R^2 = 0.94 and venous R^2 = 0.95). In our population, the optimal cut-offs to predict a pH < 7.20 or a base excess > −8.0 mmol/L were a lactate concentration of 4.9 mmol/L and 5.3 mmol/L, respectively, according to receiver operator characteristic analysis. With a lactate concentration > 4.9 mmol/L, the portable device had a sensitivity of 82% and a specificity of 90% to identify samples with an arterial pH < 7.20.

Conclusion: Cord blood lactate concentration measured with a portable device is a good predictor of cord blood base excess and pH. Future studies should be designed to correlate scalp blood lactate measurements with clinical outcomes.

Key Words: Lactate, fetal scalp, portable device, point-of-care testing

Competing Interests: None declared.

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Résumé

Objectif : Déterminer l'efficacité des analyseurs de lactate portatifs, pour ce qui est de l'identification de l'acidose fœtale, en mettant en corrélation les valeurs artérielle et veineuse du lactate constatées dans le sang de cordon ombilical et les mesures du lactate, du pH et de l'excès de bases révélées par les analyseurs du laboratoire central.

Méthodes : Nous avons mené une étude prospective en utilisant le sang de cordon artériel et veineux prélevé chez 52 femmes qui ont connu une grossesse monofœtale s'étant soldée en un accouchement à terme. Nous avons évalué la corrélation entre la concentration en lactate du sang de cordon mesurée au moyen de deux exemplaires du même appareil portatif (Lactate Plus, Nova Biomedical) et le résultat obtenu au moyen d'un analyseur du laboratoire central. Nous avons par la suite procédé à des analyses de la corrélation entre la concentration artérielle en lactate mesurée au moyen de l'appareil portatif et les valeurs artérielles du pH et de l'excès de bases.

Résultats : Nous avons constaté un pH artériel médian de 7,24 (plage : 7,05 - 7,35) et une concentration artérielle en lactate médiane de 3,7 mmol/l (plage : 1,7 - 8,8 mmol/l). Une excellente corrélation a été constatée entre les concentrations en lactate mesurées par les deux appareils portatifs (R^2 artériel = 0,98 et R^2 veineux = 0,98) et entre les concentrations mesurées par l'appareil portatif et par l'analyseur du laboratoire central (R^2 artériel = 0,94 et R^2 veineux = 0,95). Au sein de notre population, les seuils optimaux permettant de prédire un pH < 7,20 ou un excès de bases > −8,0 mmol/l ont été des concentrations en lactate de 4,9 mmol/l et de 5,3 mmol/l, respectivement, selon l'analyse de la fonction d'efficacité du récepteur. En présence d'une concentration en lactate > 4,9 mmol/l, l'appareil portatif comptait une sensibilité de 82 % et une spécificité de 90 % pour ce qui est de l'identification des prélèvements présentant un pH artériel < 7,20.

Conclusion : La concentration en lactate du sang de cordon qui est mesurée au moyen d'un appareil portatif constitue un bon facteur prédictif pour ce qui est du pH et de l'excès de bases du sang de cordon. De futures études devraient être conçues de façon à pouvoir mettre en corrélation les concentrations en lactate dans le sang prélevé sur le cuir chevelu et les résultats cliniques.

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INTRODUCTION

Fetal monitoring was introduced in the 1960s. The primary goal of its use was to screen for fetal hypoxia leading to acidemia and other important consequences including encephalopathy and death. Fetal monitoring used in this way was soon found to be disappointing, because although it was sensitive it lacked specificity.[1] The consequence of its widespread use was a large increase in obstetrical interventions including Caesarean section performed for possible fetal distress (indicated by abnormal or atypical monitor tracings). However, since its introduction fetal monitoring has not improved neonatal morbidity or mortality rates.[2]

In the early 1960s, Saling introduced a technique to sample fetal scalp blood to assess pH when an abnormal or atypical fetal heart rate tracing occurred, and this significantly slowed the rising Caesarean section rate.[3,4]

Pathologic fetal acidemia is defined by a pH < 7.00, while a base concentration > −12 mmol/L suggests metabolic acidosis that is associated with an increased risk of neonatal morbidity.[5] Most clinicians intervene (by Caesarean section or assisted delivery) when the fetal scalp blood pH is less than 7.20. However, the use of fetal scalp blood sampling to analyze pH has reduced in frequency, because of the high failure rate related to the large blood volume required (30 to 90 μL), frequent contamination of the blood with air and other biological liquids, and a lack of available analyzers in delivery rooms.[6]

The presence of lactate in the newborn's blood is another marker of fetal hypoxia. Lactic acid is preferentially produced anaerobically in the Kreb's cycle. Some researchers believe that lactate levels may theoretically permit differentiation between metabolic and respiratory acidosis (the latter being more dangerous for the newborn).[7] It has been found that lactate levels also increase when fetal and maternal blood sugar levels are elevated, and in the second stage of labour during maternal pushing.[7,8]

The alternative to fetal scalp blood sampling for pH determination used in many European and Australian centres is fetal scalp blood lactate microassay using a portable reader.[9–11] This technique requires less than 5 μL of fetal blood from only one scalp incision (compared with 2 incisions for traditional scalp blood assays), allows faster analysis (120 seconds compared to 230), and, most importantly, has a lower failure rate (1% to 2% compared with 14% to 39%).[1,6]

Many studies have demonstrated a strong correlation between fetal scalp blood or umbilical cord arterial lactate concentrations and umbilical cord pH or base excess concentrations.[9,12–14] Other studies have shown that scalp and umbilical cord blood lactate levels are comparable to pH assessment in predicting Apgar scores.[6,11,14,15]

The aims of this study were:

1. to validate the performance of a new portable device to analyze blood lactate levels compared with standard laboratory biochemical analysis (the current standard),
2. to evaluate the correlation between lactate levels measured with a portable device and pH/base excess values from umbilical cord blood as analyzed with currently accepted laboratory equipment, and
3. to define the specificity and sensitivity of this method in diagnosing neonatal acidosis.

MATERIALS AND METHODS

We collected whole blood specimens (arterial and venous) from umbilical cords from 52 successive deliveries of singleton pregnancies immediately after delivery, using sodium heparin syringes. Specimen syringes were capped immediately to prevent atmospheric contamination, placed on ice, and sent to a central laboratory.

Lactate concentration was measured from each sample using two of the same portable devices (Lactate Plus, Nova Biomedical Corp., Mississauga ON) and the central laboratory analyzer (pHOx + L, Nova Biomedical Corp., Mississauga ON). Base excess and pH values were obtained on the Bayer Rapid Lab 850 (Siemens AG, Munich, Germany).

Each whole blood specimen was mixed and placed on a lactate reagent strip, and the lactate concentration was measured on the two Lactate Plus meters. The remainder of the whole blood specimen was then analyzed on the central laboratory analyzers. All cord whole blood specimens were analyzed within five minutes of collection to minimize variability.

All data were recorded in Microsoft Excel (Microsoft Corp., Redmond WA), and this was also used for linear regression and calculation of median, sensitivity, specificity, and positive and negative predictive values. The relationship between lactate concentration and pH or base excess was tested using the linear correlation coefficient of Pearson, performed using R statistical software. MedCalc (Medcalc Software, Ostend, Belgium) was used for receiver operator characteristic analysis to determine the lactate concentration cut-off that was the most predictive for acidosis. A value of $P < 0.05$ was considered statistically significant.

Table 1. Distribution of lactate, pH, and base excess data (n = 52)

	Arterial lactate			Arterial pH	
	Device 1	Device 2	pHOx +L	Rapid Lab 850	Base excess
Minimum	1.4	1.5	1.7	7.05	−9.5
Maximum	11.5	11.4	8.8	7.35	−0.1
Median	3.7	3.7	3.7	7.24	−4.8
Interquartile range	(2.6 to 4.9)	(2.6 to 5.2)	(2.8 to 4.8)	(7.21 to 7.28)	
	Venous lactate			Venous pH	
	Device 1	Device 2	pHOx +L	Rapid Lab 850	
Minimum	1.4	1.4	1.7	7.10	
Maximum	8.8	9,0	8.0	7.45	
Median	2.9	3.0	3.0	7.30	
Interquartile range	(2.1 to 4.3)	(2.0 to 4.3)	(2.4 to 4.3)	(7.27 to 7.33)	

The hospital's Research Ethics Board stated that ethics approval for the study was not required.

RESULTS

Lactate concentrations and pH levels measured on the devices are presented in Table 1. We observed a median arterial pH of 7.24 (range 7.05 to 7.35) and a median arterial lactate concentration of 3.7 mmol/L (range 1.7 to 8.8 mmol/L).

Lactate concentration was measured on two Lactate Plus portable devices (Nova Biomedical Corp., Mississauga ON) to assess the reproducibility of the measurement. Excellent correlations were observed for arterial and venous samples, and for the combination (Figure 1, arterial $R^2 = 0.98$, venous $R^2 = 0.98$ and combined $R^2 = 0.98$). These results support the conclusion that values obtained could be consider equivalent, even though multiple devices are used in the department.

Excellent correlations were also observed between lactate concentrations measured with the portable devices and with the central laboratory analyzer (Figure 2, arterial $R^2 = 0.94$ and venous $R^2 = 0.95$), with most of the values using the portable device matching those of the central laboratory ± 20%. For two arterial samples, the portable device overestimated lactate values by more than 20% compared with the central laboratory: 6.0 vs. 8.4 (bias 40%) and 8.8 vs. 11.4 (bias 30%). However, the pH of these two samples was < 7.20 (respectively 7.05 and 7.16), so this bias should not have any impact on clinical follow-up, considering that obstetrical intervention is indicated regardless.

Lactate values for arterial cord blood on the portable device were correlated with base excess (Figure 3) and pH (Figure 4) measured on the central laboratory analyzer. Pearson correlation coefficients were calculated to examine the relationship between lactate and both parameters. These analyses indicated that lactate concentration was significantly correlated with pH ($r = -0.678$, $P < 0.001$) and base excess ($r = -0.719$, $P < 0.001$), even though moderate values of R^2 were observed (respectively 0.52 and 0.46).

The area under the ROC curve for fetal acidemia defined by a base excess > −8 mmol/L was 0.952 and when defined by a pH < 7.20 it was 0.980. The lactate concentration thresholds with the highest accuracy (maximal sensitivity and specificity) were 5.3 and 4.9 mmol/L, respectively (Figure 5). The sensitivity and specificity of the test in identifying acidemia defined by a base excess > −8 mmol/L (Table 2) or a pH < 7.20 (Table 3) are shown using different cut-offs of lactate concentration that have been previously reported.[8,9,11] With a cut-off of −8 mmol/L for base excess and 5.3 mmol/L for lactate concentration, a sensitivity of 100% and a specificity of 93% were observed. With a pH < 7.20 and lactate concentration cut-offs of 4.2, 4.8, and 4.9 mmol/L, specificities of 71%, 88%, and 90% were observed, respectively, with a maximal sensitivity of 82%. At the optimal lactate concentration cut-off of 4.9 mmol/L, positive and negative predictive values of 69% and 95%, respectively, were obtained.

DISCUSSION

This study demonstrated that arterial and venous cord blood lactate values measured on a portable device correlated significantly with those obtained on the central laboratory analyzer. An excellent correlation was also observed in values obtained with two of the portable devices, indicating good inter-device precision. This is

Figure 1. Reproducibility of lactate measured in arterial and venous cord blood by two identical portable devices

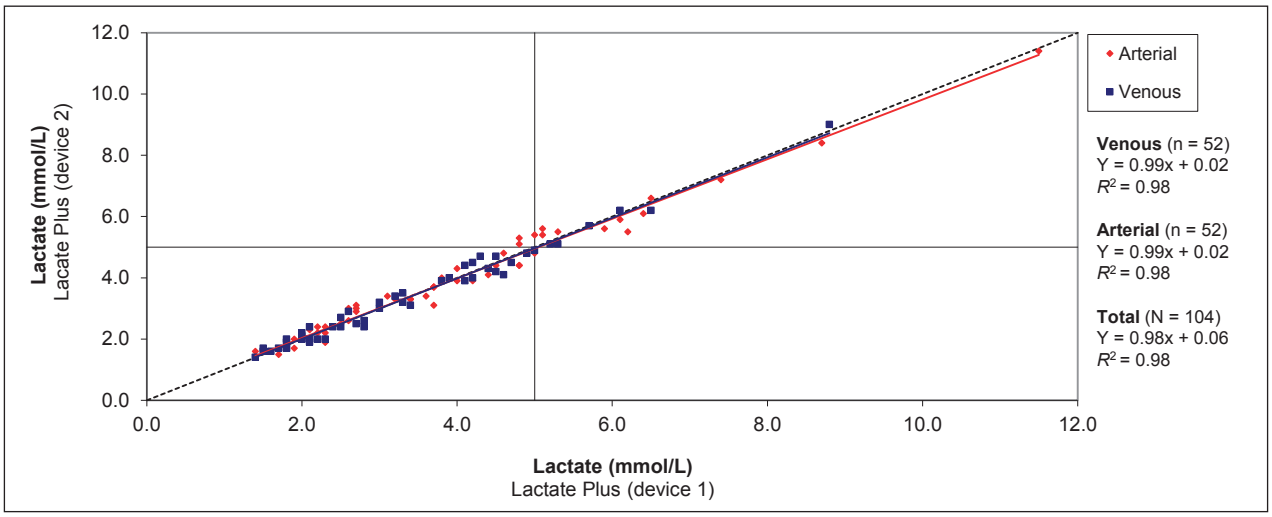


Figure 2. Correlation of lactate measured in arterial and venous cord blood with the portable device Lactate Plus and the central laboratory analyzer

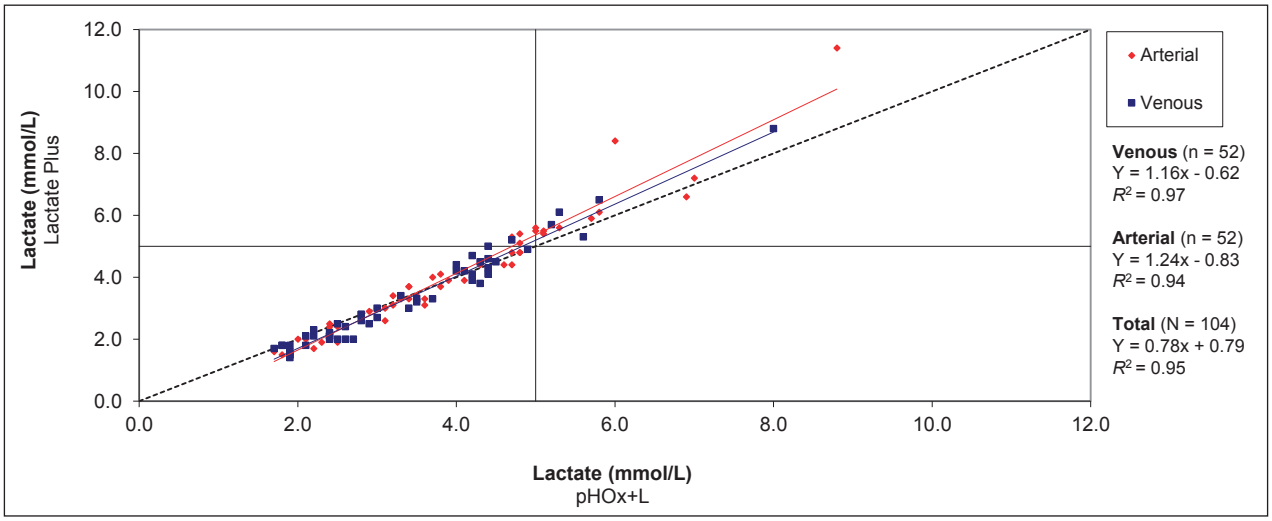


Figure 3. Correlation of base excess with lactate measured on a portable device in arterial cord blood

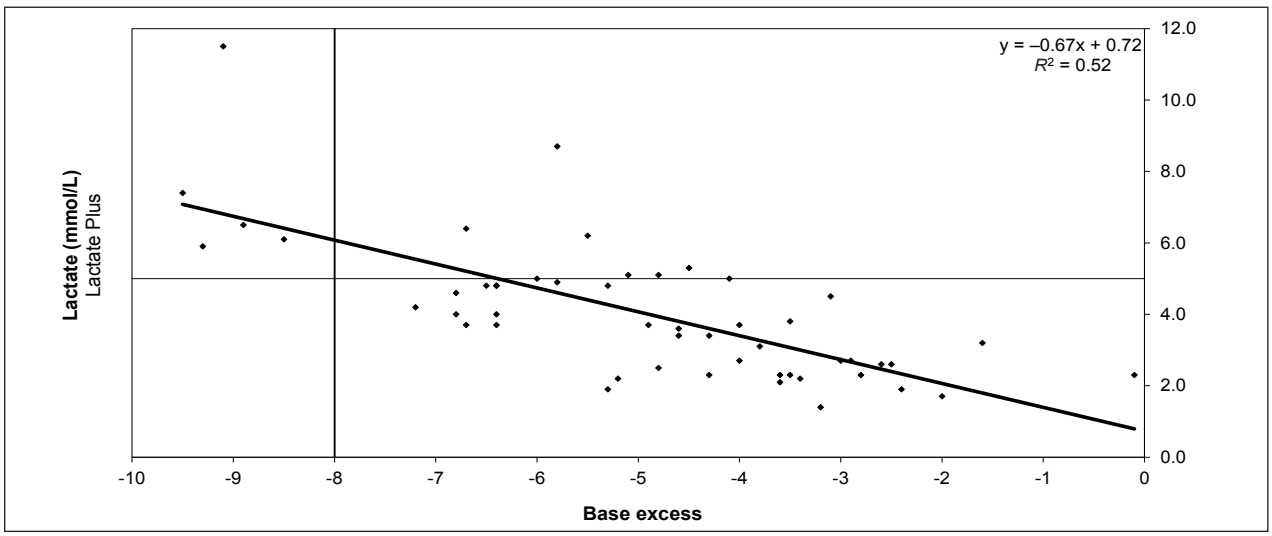


Figure 4. Correlation of lactate measured on a portable device with pH in arterial cord blood

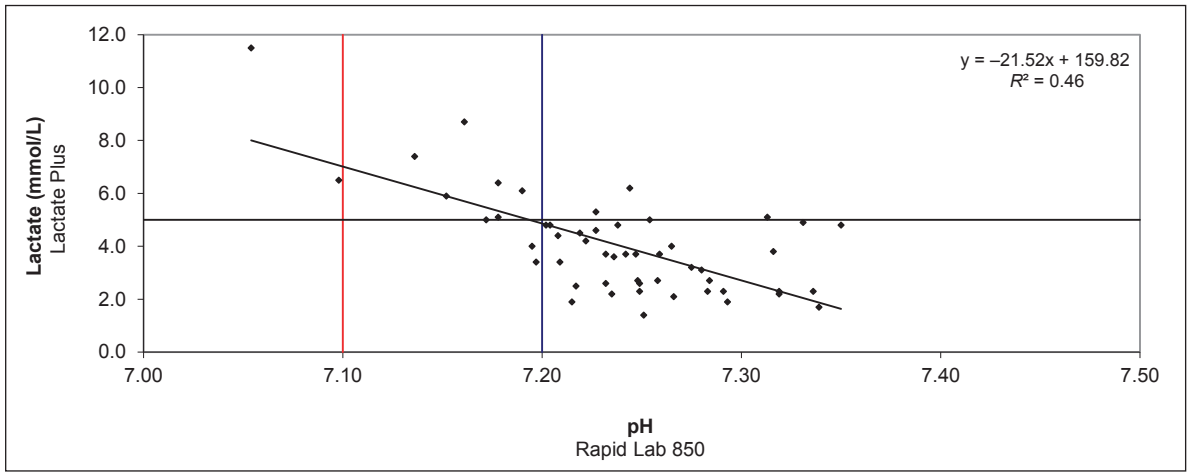
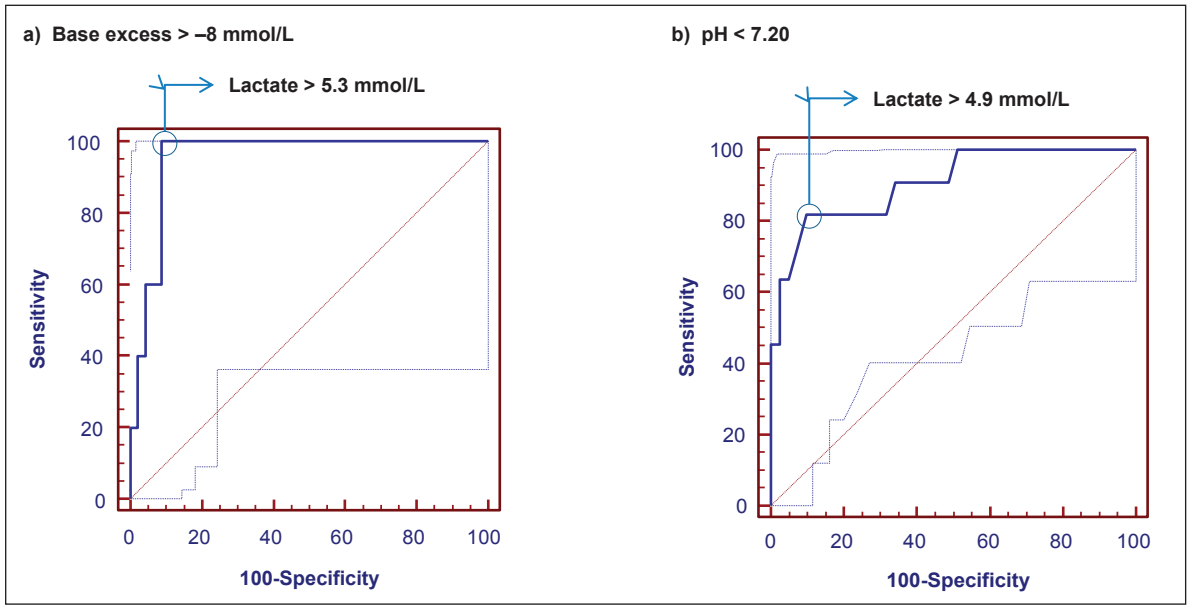


Figure 5. ROC curve for lactate to predict an arterial cord blood a) base excess > −8 mmol/L or b) pH < 7.20



important in the clinical context where a delivery unit uses more than one of the devices. Similar correlations with central laboratory analyzers were analyzed in previous studies, with R^2 values between 0.94 and 0.99.[16,17] In another study comparing the Lactate Plus device with an ABL700 analyzer (Radiometer America Inc., Westlake OH), the Lactate Plus underestimated lactate values with a consistent negative bias of 0.8 mmol/L.[17] By contrast, the Vitros LAC slide assay (Ortho Clinical Diagnostics, Markham ON) reported an overestimation of lactate values, as illustrated by a significant number of samples that were classified in an higher risk category when the Lactate Plus device values were used.[16] These studies emphasize the importance to each centre of correlating the values obtained on a new device with their laboratory standard before implementation.

This study also showed a statistically significant correlation between lactate values obtained on the Lactate Plus device and pH values measured in the central laboratory. Even though the R^2 value was moderate ($R^2 = 0.46$), it was similar to values reported in the literature (R^2 between 0.29 and 0.45).[1,9,18] Our results thus support previous studies demonstrating that lactate measurement is a good predictor of cord blood base excess and pH, and therefore the acid-base status, of the newborn[12–14]; however, these

Table 2. Sensitivity and specificity of lactate measurement on portable device, at different cut-offs, to identify a base excess > −8 mmol/L

	Base excess > −8 mmol/L			
Lactate	> 4.2 mmol/L	> 4.8 mmol/L	> 5.0 mmol/L	> 5.3 mmol/L
Sensitivity, %	100	100	100	100
95% CI	(57 to 100)	(57 to 100)	(57 to 100)	(57 to 100)
Specificity, %	65	72	83	93
95% CI	(51 to 77)	(64 to 88)	(74 to 94)	(83 to 98)

Table 3. Sensitivity and specificity of lactate measurement on portable device, at different cut-offs, to identify a pH < 7.20

	pH < 7.20			
Lactate	> 4.2 mmol/L	> 4.8 mmol/L	> 4.9 mmol/L	> 5.0 mmol/L
Sensitivity, %	82	82	82	73
95% CI	(52 to 95)	(52 to 95)	(48 to 98)	(43 to 90)
Specificity, %	71	88	90	93
95% CI	(56 to 82)	(74 to 95)	(77 to 97)	(81 to 97)
Positive predictive value, %	43	64	69	73
Negative predictive value, %	94	95	95	93

previous studies had sample sizes between 200 and 350 patients, which were larger than ours.

In our study, we have shown by ROC curve analysis that the best cut-off for prediction of a pH ≤ 7.20 is a lactate value of 4.9 mmol/L using the Lactate Plus device. This threshold is comparable to those in other studies evaluating the utility of lactate measurement in diagnosi ng acidosis that leads to neonatal asphyxia.[1,6–9,12,18] At this optimal lactate concentration cut-off of 4.9 mmol/L, we found a sensitivity of 82% and a specificity of 90%.

The principal limitation to our study is the small sample size, as this prevented us from determining lactate values that correlate with critical values commonly used (pH < 7.0 and base excess of > −12 mmol/L). Few of our patients had results in this range of values, which generally correlates with a poor fetal outcome. In addition, it would be interesting to calculate the respiratory component of acidemia and compare lactate values with corrected pH reflecting the metabolic component of the cord blood pH.[19] It would be interesting to investigate this correlation in a subsequent study.

Despite these limitations, our results are of interest because lactate analysis is not used clinically in North America despite widespread use in Europe and Australia. Since lactate concentration may be a better indicator of neonatal metabolic acidosis than the currently used pH and base deficit measures,[20] subsequent studies in analyzing umbilical blood lactate values are required and will need larger sample sizes to better define the sensitivity and specificity of this testing method for diagnosing neonatal acidosis, and to correlate these data with delivery features and neonatal clinical outcomes.

CONCLUSION

Cord blood lactate concentration measured with a portable device is a good predictor of cord blood base excess and pH. Future studies should be designed with larger sample sizes to validate and correlate lactate measurements in scalp blood with clinical outcomes. In our opinion, these validation studies are urgently required because lactate analysis is seldom, if ever, used in North America for this type of analysis. Its use could help obstetricians in the evaluation and management of atypical or abnormal monitoring during labour by allowing the use of reliable and validated devices in determining fetal hypoxia.

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