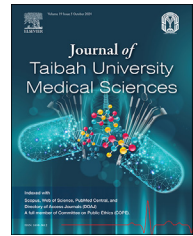




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### Original Article

## Umbilical arterial blood lactate as predictor of early neonatal outcome and evaluation of intrapartum asphyxia



Olufemi M. Badmus, FWACS, Olaide R. Adenaya, FWACS\*,  
Oluseyi A. Aderinwale, FWACS, Bernard O. Ewuoso, FWACS,  
Babatunde S. Awolaja, FWACS and Adedoyin O. Ade-Onojobi, FWACS

Department of Obstetrics and Gynaecology, Federal Medical Centre, Abeokuta, Ogun State, Nigeria

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### المخلص

**أهداف البحث:** الاختناق في الفترة المحيطة بالولادة هو السبب الرئيسي لوفيات الأطفال دون الشهر الخامسة ويمارس ضغطاً كبيراً على النظام الصحي. تعتبر المراقبة الكافية للجنين أثناء المخاض أمراً بالغ الأهمية في الكشف المبكر عن ضائقة الجنين من أجل منع الاختناق في الفترة المحيطة بالولادة. يتم استخدام عدة طرق لمراقبة الجنين بفاعلية متفاوتة. هدفت هذه الدراسة إلى التحقق من مدى فعالية مقايسة اللاكتات الشريانية السرية في التنبؤ بالنتائج الضارة في الفترة المحيطة بالولادة.

**طريقة البحث:** كانت دراسة طولية مستقبلية شملت 160 امرأة حامل في المرحلة النشطة من المخاض عند الأوان والذين استوفوا معايير الاشتمال. تم استقطابهم باستخدام تقنية أخذ العينات المتتالية وتم إجراء تخطيط القلب لهم. ثم تم تصنيفهم إلى مجموعات تخطيط القلب الطبيعية وغير الطبيعية. عند الولادة، تم جمع الدم الشرياني السري لجميع الأطفال ومعايرته من أجل اللاكتات في الدم وتم ربط المستويات بنتيجة الفترة المحيطة بالولادة. تم قياس النتائج في الفترة المحيطة بالولادة بواسطة درجات أيجار، والقبول في وحدة حديثي الولادة واعتلال الدماغ الإقفاري بنقص التأكسج. تم إجراء التحليل لتحديد حساسية ونوعية اللاكتات الشرياني السري في التنبؤ باختناق الولادة واعتلال الدماغ الإقفاري بنقص التأكسج وقبول وحدة حديثي الولادة.

**النتائج:** كان متوسط العمر  $\pm$  الانحراف المعياري بين مجموعتي تخطيط القلب، طبيعي (5.59  $\pm$  30.55) سنة وغير طبيعي (5.51  $\pm$  29.86) سنة، متشابهاً. تنبأ تركيز اللاكتات الشرياني السري الحرج الذي يزيد عن 9.1 ملليمول/لتر بدرجات أيجار  $< 7$  عند 5 دقائق مع حساسية ونوعية 76.47% (فترة الثقة

93,2-50,1) و91.55% (فترة الثقة 95,6-85,9) على التوالي. أيضاً، تم التنبؤ بالحاجة إلى قبول وحدة حديثي الولادة عند نقطة فاصلة  $> 9.1$  ملليمول/لتر مع حساسية 61.90% (فترة الثقة 81,9-38,4) ونوعية 91.30% (فترة الثقة 95,4-85,3). تنبأت مستويات لاكتات الشريان السري  $> 11.2$  ملليمول/لتر بتطور اعتلال الدماغ الإقفاري بنقص التأكسج عند الولدان بحساسية 100% (فترة الثقة 100-39,8) ونوعية 88.39% (فترة الثقة 93,0-82,3).

**الاستنتاجات:** يرتبط لاكتات الشريان السري بنتائج الحمل الضارة وهو أداة ممتازة للتنبؤ بالنتائج الضارة لحديثي الولادة.

**الكلمات المفتاحية:** نتائج أيجار؛ اعتلال الدماغ الإقفاري بنقص التأكسج؛ نتائج الفترة المحيطة بالولادة؛ الرصد أثناء الولادة؛ لاكتات الدم الشرياني السري

### Abstract

**Background:** Perinatal asphyxia is a leading cause of under-5 mortality and exerts great pressure on the health system. Adequate foetal monitoring in labour is paramount in the early detection of foetal distress to prevent perinatal asphyxia. Several methods of foetal monitoring are in use with varying efficacy. This study investigated the efficacy of umbilical arterial (UA) lactate assay in predicting adverse perinatal outcomes.

**Methodology:** This was a prospective longitudinal study involving 160 pregnant women in the active phase of labour at term who met the inclusion criteria. They were recruited using a consecutive sampling technique and underwent a cardiotocography. Then they were classified into normal and abnormal cardiotocographic groups. At delivery, the UA blood of all of the babies was collected and assayed for serum lactate, and the levels were correlated with the perinatal outcome. The perinatal outcomes were measured by Apgar scores, admission into the neonatal unit, and hypoxic ischaemic

\* Corresponding address: Department of Obstetrics and Gynaecology, Oba Ademola II Maternity Hospital, Ijemo, Abeokuta, Ogun State, Nigeria.

E-mail: [adenayaolaide@yahoo.com](mailto:adenayaolaide@yahoo.com) (O.R. Adenaya)  
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encephalopathy. Analysis was done to determine the sensitivity and specificity of UA lactate in predicting birth asphyxia, hypoxic ischaemic encephalopathy, and neonatal unit admission.

**Results:** The mean age  $\pm$  standard deviation (SD) between the two cardiotocography (CTG) groups, normal years ( $30.55 \pm 5.59$ ) and abnormal years ( $29.86 \pm 5.51$ ), were similar. A critical UA lactate concentration  $> 9.1$  mmol/L predicted Apgar scores  $< 7$  at 5 min with a sensitivity and specificity of 76.47% (CI: 50.1–93.2) and 91.55% (CI: 85.7–95.6%), respectively. Also, the need for neonatal unit admission was predicted at a cut-off point  $> 9.1$  mmol/L with a sensitivity of 61.90% (CI: 38.4–81.9) and specificity of 91.30% (CI: 85.3–95.4). Umbilical artery lactate levels  $> 11.2$  mmol/L predicted the development of hypoxic ischaemic encephalopathy in neonates with a sensitivity of 100% (CI: 39.8–100.0) and specificity of 88.39% (CI: 82.3–93.0).

**Conclusion:** Umbilical artery lactate correlates with adverse pregnancy outcomes and is an excellent tool for predicting adverse neonatal outcome.

**Keywords:** Apgar scores; Hypoxic ischaemic encephalopathy; Intrapartum monitoring; Perinatal outcome; Umbilical arterial blood lactate

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## Introduction

Severe perinatal asphyxia is the fifth largest cause of under-5 mortality and exerts great pressure on the health system.<sup>1</sup> Asphyxia remains a common cause of intrapartum foetal death. Existing data reveal that approximately 4 million foetal deaths occur yearly, and 98% of them occur in developing countries.<sup>1–3</sup> Neonatal Mortality Rate (NMR) has been quoted as 39 per 1000 live births.<sup>4</sup> Fawole et al.<sup>5</sup> in a study in Ibadan, Southwest Nigeria, quoted an NMR of 49 per 1000 live births. In a study conducted by Onyearugha et al.<sup>6</sup> in a tertiary institution in the Niger Delta area of Nigeria, a prevalence of perinatal asphyxia of 45 per 1000 live births was declared with associated attendant severe neurological impairment.

Foetal monitoring in labour remains an integral part of intrapartum care instituted for prompt recognition and intervention for foetus(es) adapting poorly to labour and for the purpose of delivering a healthy baby. This monitoring includes intermittent auscultation, intrapartum cardiotocography, and foetal scalp sampling. Each of these methods has its own limitations. Although foetal scalp sampling is considered the gold standard for the diagnosis of metabolic acidosis in foetuses, it is considered expensive and requires a higher volume of blood (30–90  $\mu$ L) compared to the umbilical arterial (UA) lactate assay (0.3  $\mu$ L). A sampling failure rate of 11–20% has been reported.<sup>7,8</sup> It also requires

sufficient cervical dilation, has a transient nature that may result in the need for repeat sampling and physical inconvenience of the maternal positioning are other challenges.

Foetal electrocardiography for ST wave analysis, foetal pulse oximetry, and umbilical cord blood sampling are presently being employed to diagnose intrapartum foetal asphyxia. However, foetal electrocardiography and pulse oximetry are expensive and not available in low resource settings.

Umbilical blood sampling is innocuous to the newborn and relatively inexpensive. Point-of-care handheld lactate devices have been developed and provide easy and rapid measurement using an electrochemical strip test device, which needs smaller amount of foetal blood (0.3  $\mu$ L) with result available within 15 s.<sup>9–11</sup> This advantage favours umbilical artery lactate as an indicator of intrapartum foetal oxygenation. This is especially important in medical litigations in high-risk cases, with newborns having signs of encephalopathy to exclude intrapartum asphyxia as a leading cause for neurological morbidity. Also, the simplicity of the method makes it applicable in perinatal medicine and low resource setting.

This study determined the reliability of umbilical artery serum lactate level in the detection of foetal asphyxia.

## Materials and Methods

This prospective longitudinal study was carried out in a tertiary institution in Abeokuta between August 2019 and February 2020. Abeokuta is the capital city of Ogun State in Southwest Nigeria. It has a population of about 500,000 people based on a 2018 population estimate.

The study was carried out in the labour ward of the Department of Obstetrics and Gynaecology and the neonatal unit of the Paediatrics department of the facility. The average delivery rate in the facility as of 2018 was 1300 live births per annum. The study was carried out among pregnant women who presented at the hospital in the first stage of labour over a period of 6 months. The inclusion criteria included consenting women in the first stage of labour with singleton live foetus in cephalic presentation at gestational age between 37 and 41 completed weeks. The exclusion criteria included intrapartum or antepartum haemorrhage, abnormal lie, gross congenital anomaly, intrauterine foetal death, medical disorders of pregnancy; hypertension, diabetes mellitus, preeclampsia, eclampsia, obesity, anaemia, haemoglobinopathy; and intrauterine growth restriction and failure to give consent. The ideal minimal sample size for the study was determined using the following formulae.<sup>12</sup>

$$n = \frac{Z^2 pq}{d^2}$$

where  $n$  is the minimum sample size,  $Z$  is the standard normal deviation set at 1.96 for the 95% confidence interval (CI), and  $p$  is the prevalence of abnormal cardiotocography (CTG) according to a previous study (11.3%)<sup>13</sup>

$q = 1 - p$

$d$  – Desired level of precision (0.05)

$$n = \frac{(1.96)^2 \times 0.113 \times 0.89}{(0.05)^2}$$

$$N = 155$$

With a total population less than 10,000

$$NF = \frac{n}{(1 + n/N)}$$

where N is the total number of deliveries per year at FMC Abeokuta = 1300/year

$$NF = \frac{155}{(1 + 155/1300)}$$

$$= \frac{155}{1.119}$$

$$= 138$$

With a 10% attrition rate sample size = 152.

The total number of parturients recruited into this study according to the calculated sample size was rounded up to 160.

The participants were recruited using a consecutive sampling technique until the sample size was complete. On admission, the women's history, including age, parity, antenatal care, menstrual and obstetric history, were documented in a data sheet. A general physical examination was done. Abdominal and vaginal examinations were performed to determine the stage of labour. Each participant was subjected to admission cardiotocography for at least 20 min with the woman in the left lateral position. The foetal heart rate (FHR) traces obtained were categorized as reactive (normal), equivocal (suspicious), or ominous (pathological) according to the classification proposed by NICE.<sup>14</sup>

The admission CTG recording of FHR and uterine contractions was done using the Huntleigh Healthcare BD4000XS (Cardiff, Wales) foetal monitor, which has a twin trace paper chamber. It also has an intuitive user interaction display, event marker, and two transducers, one for measuring foetal heart rate and the other for measuring uterine contraction.

Following the admission cardiotocogram, patients with reactive trace were monitored intermittently by auscultation for 1 min every 30 min in the first stage of labour and every 5 min in the second stage of labour post-contraction using a handheld Doppler. Readings were transferred to their partograph provided FHR patterns remained normal. Cases with suspicious or pathological trace had intrauterine resuscitation done and then underwent continuous CTG monitoring. Labour was allowed to continue among the parturients whose CTG tracing became reactive after intrauterine resuscitation. However, the CTG tracing that remained suspicious or pathological had operative intervention (operative vaginal delivery or emergency caesarean section) performed to expedite delivery depending on the stage of labour. In addition to other maternal and foetal assessment, the cardiotocogram used for further analyses for

parturients with suspicious or pathological FHR patterns was the one used for deciding operative intervention.

Following delivery of the baby, two pairs of artery clamps were applied to the umbilical cord and divided in between clamps, and the baby was handed over to the attending paediatrician. Two more pairs of artery clamps were applied toward the maternal end of the umbilical stump and also divided in between the two clamps to allow uninterrupted conduct of the third stage of labour. The result was a segment of cord, about 10–15 cm long, isolated between two pairs of artery clamps. The isolated cord segment was ensured to be full of blood for easy sampling of the umbilical cord artery by drawing the cord blood towards one clamped end, before applying a second clamp.

UA blood samples were drawn from the double-clamped segment of the umbilical cord into 2-mL plastic syringes, and lactate concentration was measured immediately with a single-use strip method.<sup>11</sup> The system consists of an enzyme-coated electrode and a small meter – the 'Lactate Pro™-2' manufactured by Arkray Inc. (Nagasaki, Japan). Lactate analyses were within 5 min of birth.

The Apgar scores were taken at 1 min and 5 min by the attending paediatrician by scoring the newborn from the Apgar scoring chart in the labour ward. Also, the central nervous system was examined by checking for the presence or depression of primitive reflexes including Moro grasp, sucking, plantar grasp, and grasp reflexes. The fontanelle was examined for any evidence of raised intracranial pressure.

Pulse oximetry was done using the Ohmeda Tuffsat oximeter (GE Healthcare, Chicago, IL, USA). The neonates admitted to the neonatal unit were managed by the neonatologist and paediatric residents in the neonatology unit. They were observed and monitored for neonatal seizures for up to 48 h, while those being nursed by the mother's side were observed and monitored in the postnatal ward.

At the beginning of the study, to ensure quality control, blood was taken from either of the arteries and the vein, and the results were checked to ensure that separate vessels have been sampled, as sometimes it may be difficult to obtain blood from the small arteries and a venous or a mixed arterio-venous sample may be obtained by mistake. This was repeated after every 20th sample for quality control. It is important to note that in their study, Tuuli et al.<sup>15</sup> found that venous lactate strongly predicts arterial lactic acidemia and is comparable with arterial lactate for predicting neonatal morbidity at term.

Information obtained from the participants were coded and fed into the computer. The data were analysed using SPSS version 20 (IBM, Armonk, NY, USA). Data are presented as the frequency and analysis was done using the appropriate statistical tests. The Spearman correlation was used to evaluate continuous variables while chi square was used for categorical variables. Also, confidence intervals were determined. The level of statistical significance was taken as  $p < 0.05$ .

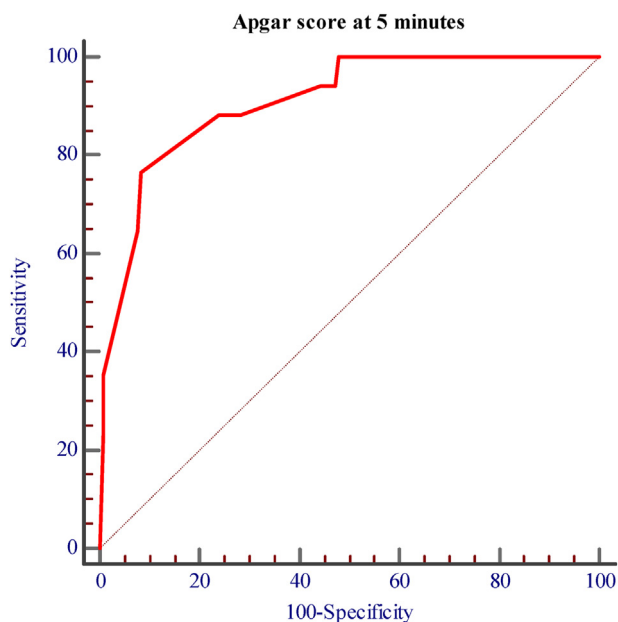
Every woman found eligible for the study was given detailed information about the study and written informed consent was obtained after detailed explanation about the nature of the study. The participants were also given the right to withdraw from the study at any time.

Quality assurance was ensured by test running the CTG on a weekly basis with a pregnant woman not in labour. The same point-of-care handheld lactate meter and recommended strips were used throughout the study.

## Results

A total of 427 parturients were seen within the study period. Of these, 245 patients were excluded according to the exclusion criteria, and 22 parturients did not give consent for the study. The consecutive and consenting 160 parturients who fulfilled the criteria for inclusion were recruited. The mean age  $\pm$  SD between the two CTG groups, normal years ( $30.55 \pm 5.59$ ) and abnormal years ( $29.86 \pm 5.51$ ), were similar. Two-thirds of the parturients had a tertiary level of education and one-third worked as civil servants. The majority of parturients were experiencing their second to fourth pregnancy. Almost all pregnant women recruited for this study were scheduled, with only 10% of study participants being unscheduled. There was no statistically significant difference in the demographic parameters of the participants in the study based on the CTG categories (i.e., the two CTG groups were well matched). According to Figure 1, the receiver operating characteristic (ROC) curve of serum lactate concentration in predicting Apgar score  $<7$  at 5 min, the area under curve (AUC) (95% confidence interval [CI]: 0.908 [0.852–0.948]) was obtained. The associated criterion from the Youden index (0.680) was  $>9.1$ , and the sensitivity and specificity at 95% CI were 76.47 (50.1–93.2) and 91.55 (85.7–95.6), respectively (Table 1).

The ROC curve of serum lactate levels in predicting neonatal admission in Figure 2 has AUC (95% CI: 0.908 [0.852–0.948]). At  $>9.1$ , the associated criterion of the

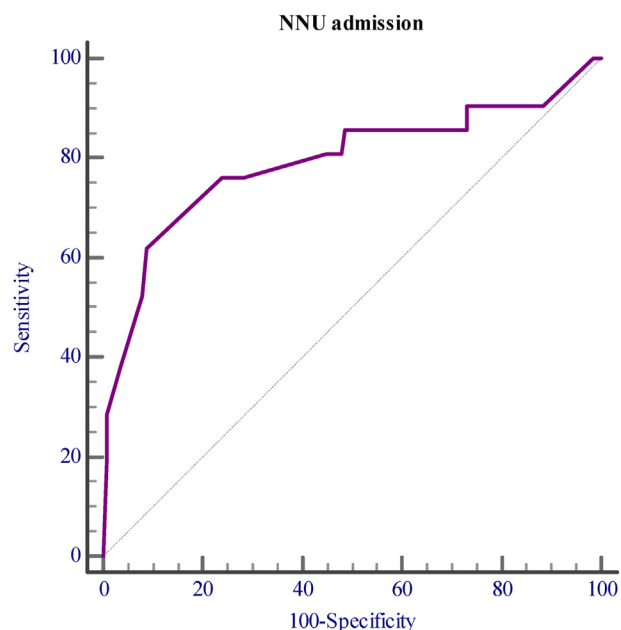


**Figure 1:** ROC curve of serum lactate level in predicting APGAR score  $<7$  at 5 min. AUC: 0.908; 95% CI: 0.852–0.948;  $p < 0.001$ .

**Table 1:** Sensitivity and specificity of serum lactate level at different cut-off values of serum lactate in predicting Apgar Scores  $<7$  at 5 min (criterion values and coordinates of the ROC curve).

Criterion	Sensitivity	95% CI	Specificity	95% CI
$>7.7$	94.12	71.3–99.9	55.63	47.1–64.0
$>8.3$	88.24	63.6–98.5	71.83	63.7–79.1
$>8.9$	88.24	63.6–98.5	76.06	68.2–82.8
<b><math>&gt;9.1</math></b>	<b>76.47</b>	<b>50.1–93.2</b>	<b>91.55</b>	<b>85.7–95.6</b>
$>11.2$	64.71	38.3–85.8	92.25	86.6–96.1
$>12$	47.06	23.0–72.2	96.48	92.0–98.8
$>12.5$	35.29	14.2–61.7	99.30	96.1–100.0

Youden index (J): 0.680; Associated criterion:  $>9.1$ . Bold signifies the values which predict the measured outcomes based on sensitivity and specificity.



**Figure 2:** ROC curve of serum lactate level in predicting neonatal admission. AUC: 0.908; 95% CI: 0.852–0.948;  $p < 0.001$ .

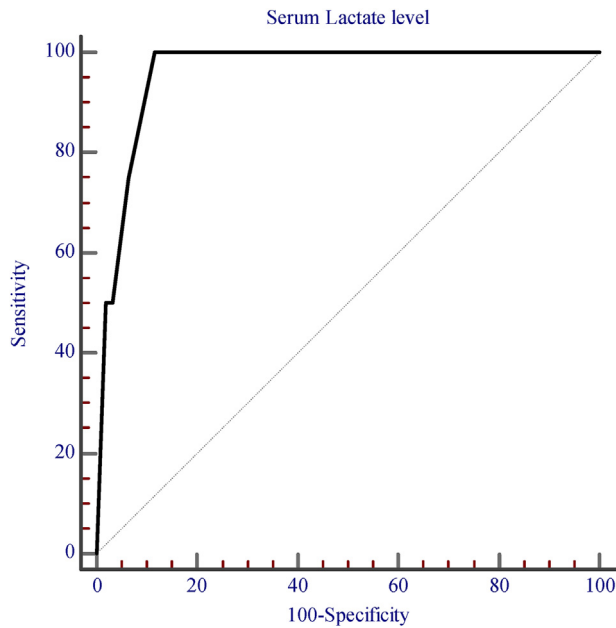
Youden index was 0.532, and the sensitivity and specificity at 95% CI were 61.90 (38.4–81.9) and 91.30 (85.3–95.4), respectively (Table 2).

**Table 2:** Sensitivity and specificity of serum lactate level at different cut-off values for neonatal admission (criterion values and coordinates of the ROC curve).

Criterion	Sensitivity	95% CI	Specificity	95% CI
$>7.7$	80.95	58.1–94.6	55.07	46.4–63.5
$>8.3$	76.19	52.8–91.8	71.74	63.5–79.1
$>8.9$	76.19	52.8–91.8	76.09	68.1–82.9
<b><math>&gt;9.1</math></b>	<b>61.90</b>	<b>38.4–81.9</b>	<b>91.30</b>	<b>85.3–95.4</b>
$>11.2$	52.38	29.8–74.3	92.03	86.2–96.0
$>12$	38.10	18.1–61.6	96.38	91.7–98.8
$>12.5$	28.57	11.3–52.2	99.28	96.0–100.0

Youden index (J): 0.532; Associated criterion:  $>9.1$ . Bold signifies the values which predict the measured outcomes based on sensitivity and specificity.





**Figure 3:** ROC curve of serum lactate level in predicting HIE. AUC: 0.960; 95% CI: 0.917–0.984;  $p < 0.001$ .

**Table 3: Sensitivity and specificity of serum lactate level at different cut-off values of serum lactate for predicting HIE (criterion values and coordinates of the ROC curve).**

Criterion	Sensitivity	95% CI	Specificity	95% CI
<b>&gt;11.2</b>	<b>100.00</b>	<b>39.8–100.0</b>	<b>88.39</b>	<b>82.3–93.0</b>
>12	75.00	19.4–99.4	93.55	88.5–96.9
>12.5	50.00	6.8–93.2	96.77	92.6–98.9
>15.9	50.00	6.8–93.2	98.06	94.4–99.6
>16.8	0.00	0.0–60.2	100.00	97.6–100.0

Youden index (J): 0.884; Associated criterion: >11.2. Bold signifies the values which predict the measured outcomes based on sensitivity and specificity.

Figure 3 shows the ROC curve serum lactate level in predicting HIE. The AUC (95% CI) of the ROC curve was 0.960 (0.917–0.984). The associated criterion of the Youden index (0.884) was >11.2 and the sensitivity and

**Table 5: Evaluation of performance of lactate level cut-off values derived from ROC curve in predicting 5-min Apgar score <7, NNU admission, and development of HIE.**

Evaluation	5-min Apgar score	Neonatal admission	HIE
Sensitivity	76.5%	61.9%	100.0%
Specificity	91.6%	91.3%	88.5%
Positive predictive value	52.0%	52.0%	18.2%
Negative predictive value	97.0%	94.1%	100.0%
False positive	8.4%	8.6%	11.5%
False negative	23.5%	38.1%	0.0%
Accuracy	90.0%	87.5%	88.8%

NB: cut-off values of lactate were set at >9.1 for 5-min Apgar score and neonatal, while >11.2 was used for HIE.

specificity at 95% CI were 100 (39.8–100.0) and 88.39 (82.3–93.0) respectively (Table 3).

The UA lactate level of 9.1 mmol/l (from associated criterion from the ROC curve) was applied to determine the threshold for Apgar scores of <7 at 5 min and the need for neonatal admission, while at >11.2 mmol/l, it was applied to determine hypoxic-ischaemic encephalopathy (HIE) (Table 4). Of the 17 newborns that had Apgar scores <7 at 5 min, 13 (76.5%) newborns actually had UA lactate values > 9.1 mmol/l. There was a statistically significant difference between UA lactate level and Apgar scores at 5 min (Kappa = 0.564,  $p < 0.001$ ). For the neonates that required neonatal unit admission, 13 (61.9%) of the 21 neonates had lactate levels greater than 9.1 mmol/l. There was also statistically significant association between serum lactate level and admission into the neonatal unit (Kappa = 0.493,  $p < 0.001$ ). At UA lactate cut-off level >11.2 mmol/l, all of the newborns had HIE. The relationship between UA lactate at this cut-off point and development of HIE was statistically significant (Kappa = 0.227,  $p < 0.001$ ).

With the use of ROC curve, cut-off points >9.1 mmol/L of arterial lactate and >11.2 mmol/L of lactate were found to predict adverse neonatal outcomes. Table 5 illustrates the performance of arterial lactate as a standard of care in predicting adverse neonatal outcomes. Arterial lactate level at a cut-off point >9.1 mmol/L has a similar high specificity and negative predictive value for 5-min Apgar scores

**Table 4: Arterial cord blood lactate at 9.1 mmol/l and adverse neonatal outcome (5 min Apgar and NNU admission).**

	Arterial cord blood lactate levels			K	p value
	>9.1	≤9.1	Total		
Variable	n (%)	n (%)	N (%)		
<b>5-min Apgar score</b>					
<7	13 (76.5)	4 (23.5)	17 (100.0)	0.564	<b>&lt;0.001*</b>
≥7	12 (8.4)	131 (91.6)	143 (100.0)		
<b>Neonatal admission</b>					
Yes	13 (61.9)	8 (38.1)	21 (100.0)	0.493	<b>&lt;0.001*</b>
No	12 (8.6)	127 (91.4)	139 (100.0)		
	<b>&gt;11.2</b>	<b>≤11.2</b>			
<b>HIE</b>					
Yes	4 (100)	0 (0)	4 (100)	0.227	<b>&lt;0.001*</b>
No	18 (11.5)	138 (88.5)	156 (100)		

K: Kappa (Measure of Agreement); \* $p < 0.05$ . Bold signifies the values which predict the measured outcomes based on sensitivity and specificity.

and need for NNU admission. They also have a similar degree of accuracy at this ROC cut-off point for UA lactate concentration. Arterial lactate at a cut-off point of 11.2 mmol/L will predict that all neonates will develop HIE and has a sensitivity of 100%. There will be no false-negative result. It will predict the development of HIE in a newborn with an accuracy of 88.8%.

## Discussion

The results of the present study showed a moderate inverse relationship between lactate levels and Apgar score. With increasing lactate levels, Apgar scores tended to be lower or poorer. This is as expected as lactic acidosis, which results from hypoxic events sustained during the intrapartum period, may be responsible for depressing the foetus' respiratory centres, thereby making it difficult for the newborn to initiate spontaneous respiration at birth. A systematic review by Allanson et al.<sup>16</sup> corroborated this finding in the review of reports by Abessolo et al.<sup>17</sup> and Linet et al.,<sup>18</sup> who correlated venous and arterial lactate, respectively, with Apgar score. Revathy also correlated high lactate levels with poor Apgar score.<sup>19</sup> Different studies have used different modalities to determine the predictive power of lactate for adverse neonatal outcome. The present study found UA lactate cut-off points for prediction of poor Apgar score/neonatal unit admission and development of HIE at >9.1 and 11.2 mmol/L, respectively. Eltaieb and Elkholy<sup>20</sup> in their study in Cairo, Egypt obtained a value of lactate >10 mmol/L for adverse neonatal outcome. Ramanah et al.<sup>21</sup> and Gjerris et al.<sup>9</sup> found the threshold for adverse neonatal outcome at lactate levels >8 mmol/L. Another study by Nordstrom et al.<sup>22</sup> obtained a cut-off point >4.8 mmol/L, which was close to a lactate level <3.9 mmol/L determined by Tuuli et al.<sup>16</sup> for adverse neonatal outcome. Early neonatal death was at a lactate level >13 mmol/L, as obtained by Chilinda et al.<sup>23</sup> in their study in Malawi. The area under the ROC curve for predicting poor Apgar score (<7 at 5 min) was 0.98. This was greater than 0.873, 0.833, and 0.635 obtained by Eltaieb and Elkholy<sup>20</sup> in Egypt, Allanson et al.<sup>24</sup> in South Africa, and Chilinda et al.<sup>23</sup> in Malawi, respectively. The AUC is an index that evaluates the overall ability of a diagnostic test; the closer the AUC is to 1, the more excellent the result for discrimination.<sup>25</sup>

For predicting neonatal unit admission, the AUC of 0.908 reported in this study was greater than 0.873 and 0.673 obtained by Eltaieb and Elkholy<sup>20</sup> and Allanson et al.<sup>24</sup> respectively. At the value of 0.908, lactate prediction of need of NNU admission was excellent.<sup>12</sup> The development of HIE was predicted by an AUC of 0.906 in the current study. Eltaieb and Elkholy<sup>20</sup> in Cairo, Egypt obtained a similar value of 0.905 in their study as well as Patil et al.<sup>26</sup> in India. This has shown that lactate is a useful tool in predicting the development of HIE in the newborn. The cut-off point of lactate was >9.1 mmol/L/Apgar scores. This was higher than the cut-off points obtained by Hamed,<sup>27</sup> Allanson et al.,<sup>24</sup> and Chilinda et al.,<sup>23</sup> which were 4.8, 5, and 5.56 mmol/L respectively. The coefficient of variation (CV) of the handheld Lactate Pro-2 meter (Arkray) used in

this study was 1.7–8.4%, which is higher than that used by Allanson et al.<sup>24</sup> (CV: 1.8–3%) and Chilinda<sup>23</sup> (CV: 5.5%). While CV is more precise at estimating the mean at lower values, the device used in the present study also used a minimal amount of blood and has a shorter result turn over time. The observed difference could also have been due to the difference in the blood compartment (plasma or whole blood) from which lactate concentration was measured.

The sensitivity obtained in the present study was similar to Allanson et al.<sup>24</sup> and higher than that obtained by Wiberg et al.<sup>28</sup> and Hamed<sup>27</sup> in Egypt. Hence, UA lactate at cut-off point >9.1 mmol/L will identify the majority of newborns who genuinely have a poor Apgar score. The specificity in the present study was as high as that obtained by Wiberg et al.<sup>28</sup> (97%), although that of Hamed<sup>27</sup> was marginally lower. The implication is that at the set cut-off point of >9.1 mmol/L, UA lactate was normal in the majority of neonates with good Apgar scores. The cut-off point that predicted a need for neonatal unit admission was at lactate levels >9.1 mmol/L. This was higher than the cut-off points from other studies.<sup>19,23,24</sup> The sensitivity obtained in this study is corroborated by Allanson et al.,<sup>24</sup> who had a similar sensitivity but a much lower specificity than obtained in the present study. The higher specificity of lactate in the present study revealed that lactate is able to prevent the unnecessary neonatal admission of newborns.

HIE was predicted at a lactate cut-off point of >11.2 mmol/L with a sensitivity and specificity of 100% and 88.5%, respectively. The cut-off point and sensitivity (at a similar 95% CI as in the present study) from Wiberg's study were much lower, though at a slightly higher specificity.<sup>29</sup> Eltaieb and Elkholy<sup>20</sup> in Egypt and Patil et al.<sup>26</sup> in India observed neonatal seizures within the first 24 h of life at lactate level >10 mmol/L, which was close to the cut-off point from this study. From the current study, it was apparent that lactate was an excellent diagnostic tool for predicting all cases of HIE at cut-off point >11.2 mmol/L. Severe levels of hypoxia during the intrapartum period causes the foetus to revert to anaerobic respiration with resultant build up in lactate concentration. In other words, the higher the lactate levels, the severe the level of intrapartum hypoxia/asphyxia.

There was no early neonatal death throughout the study period. Allanson et al.,<sup>24</sup> Revathy et al.,<sup>19</sup> Gurung et al.<sup>30</sup> and Patil et al.<sup>26</sup> also did not record any neonatal death during the course of their studies. By contrast, Chilinda et al.<sup>23</sup> in Malawi recorded neonatal death within the first 24 h of life at lactate levels >13 mmol/L. Lactate value beyond the cut-off point in the present study represents severe acidosis, which is often accompanied by HIE. HIE ultimately results in neonatal death and neurodevelopmental morbidity as revealed in the work of Simiyu et al.<sup>31</sup> in Tanzania in 2017, who found that neonatal mortality occurred among newborns with severe HIE. In fact, in their study, as many as 84.2% of newborns that suffered from severe HIE died compared with the 1.4% mortality among foetuses that sustained moderate HIE.

## Limitations

Due to the variations in the technology and calibration of the point-of-care handheld lactate meter, adaption of its use for the clinical setting must be ensured. As a standard of care, some of the participants had interventions such as induction of labour and augmentation of labour, which may be associated with the development of adverse neonatal outcome. The sample size may be a plausible reason for not having any case of neonatal death in this study. Subsequent study involving more participants may allow analysis of this adverse outcome.

## Conclusion

This study established a significant negative relationship between AU lactate and Apgar score. It also demonstrated the AU lactate at a cut-off point of 9.1 mmol/L will predict poor Apgar scores (<7 at 5 min) and the need for NNU admission, while lactate levels >11.2 mmol/L will predict the development of HIE. This study further indicates that UA lactate is a useful tool for the prediction of foetal asphyxia with good sensitivity and specificity.

## Recommendation

It is recommended that the measurement of UA lactate concentrations with a point-of-care handheld lactate meter is useful in evaluation of the foetal well-being at parturition.

- UA lactate should be adopted in audit cycle for quality control through which an obstetric team can evaluate the quality of intrapartum care rendered.
- The documentation of UA lactate concentration may be useful in resolving any medicolegal claims in the event that a newborn sustains brain injury, with consequent long-term neurological sequelae, from causes other than hypoxic insults sustained during the intrapartum period.

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## Conflict of interest

The authors have no conflict of interest to declare.

## Ethical approval

Ethical approval was obtained from the Hospital Research and Ethical Committee on 5th February, 2018 with an extension on 11th September, 2019 with protocol number FMCA/470/HREC /02/2018/02.

## Authors contributions

Olufemi M. BADMUS: Conceptualization, methodology, software, formal analysis, investigation, resources,

validation, writing— original drafting and writing — review and editing. Olaide R. ADENAYA: Conceptualization, methodology, software, formal analysis, investigations, resources, validation, writing — original drafting and writing — review and editing. Oluseyi A. ADERINWALE: Conceptualization, methodology, software, validation, writing — review and editing, supervision, and project administration. Bernard O. EWUOSO: conceptualization, methodology, validation, writing— original drafting and review, visualization and project administration. Babatunde S. AWOLAJA: conceptualization, methodology, formal analysis, investigations, data curation, writing-review and editing. Adedoyin O. ADE-ADEONOJOBI: conceptualization, methodology, resources, visualization, data curation and writing-review and editing. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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