OBSTETRICS

A comparison of criteria for defining metabolic acidemia in live-born neonates and its effect on predicting serious adverse neonatal outcomes

Alexandria C. Kraus, MD; Alexander M. Saucedo, MD; John J. Byrne, MD; Lina F. Chalak, MD; Jessica E. Pruszynski, PhD; Catherine Y. Spong, MD

BACKGROUND: Metabolic acidemia is a known risk factor for serious adverse neonatal outcomes in both preterm and term infants.

OBJECTIVE: This study aimed to evaluate the clinical significance of delivery umbilical cord gas measurements with regard to serious adverse neonatal outcomes, and to determine if distinct thresholds for defining metabolic acidemia differ in their ability to predict such adverse neonatal complications.

STUDY DESIGN: This is a retrospective cohort study of singleton live-born deliveries between January 2011 and December 2019. Stratification according to gestational age at birth (≥35 and <35 weeks of gestation) was performed, and comparisons of maternal characteristics, obstetrical complications, intrapartum events, and adverse neonatal outcomes were made between neonates with metabolic acidemia and those without. Metabolic acidemia (based on delivery umbilical cord gas analyses) was defined using both American College of Obstetricians and Gynecologists and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria. The primary outcome of interest was hypoxic-ischemic encephalopathy requiring whole-body hypothermia.

RESULTS: A total of 91,694 neonates born at ≥35 weeks of gestation met the inclusion criteria. By American College of Obstetricians and Gynecologists criteria, 2659 (2.9%) infants had metabolic acidemia. Neonates with metabolic acidemia were at markedly increased risk for neonatal intensive care unit admission, seizures, need for respiratory support, sepsis, and neonatal death. Metabolic acidemia by American College of Obstetricians and Gynecologists criteria was associated with an almost 100-fold increased risk of hypoxic-ischemic encephalopathy requiring whole-body hypothermia (relative risk, 92.69; 95% confidence interval, 64.42—133.35) in neonates born at ≥35 weeks of gestation. Diabetes mellitus, hypertensive disorders of pregnancy, postterm deliveries, prolonged second stages, chorioamnionitis, operative vaginal deliveries, placental abruption and cesarean deliveries were associated with metabolic acidemia in neonates born ≥ 35 weeks of gestation. The highest relative risk was in those diagnosed with placental abruption (relative risk, 9.07; 95% confidence interval, 7.25—11.36). The neonatal cohort born <35 weeks of gestation had similar findings. When comparing those infants born ≥ 35 weeks of gestation with metabolic acidemia by American College of Obstetricians and Gynecologists criteria vs *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria identified more neonates at risk for serious adverse neonatal outcomes. In particular, 4.9% more neonates were diagnosed with metabolic acidemia, and 16 more term neonates were identified as requiring whole-body hypothermia. Mean 1-minute and 5-minute Apgar scores were similar and reassuring among neonates born at ≥35 weeks of gestation with and without metabolic acidemia as defined by both American College of Obstetricians and Gynecologists and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria (8 vs 8 and 9 vs 9, respectively; $P<.001$). Sensitivity and specificity were 86.7% and 92.2%, respectively, with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria, and 74.2% and 97.2% with the American College of Obstetricians and Gynecologists criteria.

CONCLUSION: Infants with metabolic acidemia identified on cord gas collection at delivery are at considerably greater risk of serious adverse neonatal outcomes, including an almost 100-fold increased risk of hypoxic-ischemic encephalopathy requiring whole-body hypothermia. Use of the more sensitive *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria for defining metabolic acidemia identifies more neonates born at ≥35 weeks of gestation at risk for adverse neonatal outcomes, including hypoxic-ischemic encephalopathy requiring whole-body hypothermia.

Key words: adverse neonatal outcomes, hypoxic-ischemic encephalopathy, metabolic acidemia, umbilical cord gas, whole-body hypothermia

Introduction

Fetal oxygenation and pH commonly decline throughout the progression of labor.[1] Blood drawn from umbilical vessels is typically used for acid—base studies and to aid in the assessment of the metabolic status of the neonate.[2] Fetuses may develop metabolic acidemia when oxygen deprivation is extensive enough to require anaerobic metabolism to meet cellular energy requirements. Metabolic acidemia, due to intrapartum hypoxic-ischemic insults, has been shown to have a stepwise progression from moderate-severe neonatal encephalopathy to cerebral palsy[3]—the most common developmental and motor disability affecting childhood in the United States.[4,5]

Most fetuses will tolerate intrapartum acidemia with a pH as low as 7.0 without incurring neurologic impairments.[6,7] The American College of Obstetricians and Gynecologists (ACOG)[8] considers intrapartum hypoxia a potential contributor to neonatal neurologic injury if diagnosed in the setting of an umbilical arterial pH <7.0 and a base deficit ≥12 mmol/L.[9—11] The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

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AJOG at a Glance

Why was this study conducted?

This study aimed to compare adverse neonatal outcomes when using differing thresholds for defining metabolic acidemia by umbilical cord gas measurements.

Key findings

Metabolic acidemia as defined by American College of Obstetricians and Gynecologists (ACOG) criteria was associated with 100-fold increased risk of hypoxic-ischemic encephalopathy requiring whole-body hypothermia in neonates born at ≥35 weeks of gestation. The more sensitive criteria of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) identified 4.9% more neonates born at ≥35 weeks of gestation with metabolic acidemia, and 16 more neonates requiring whole-body hypothermia when compared with the ACOG criteria.

What does this add to what is known?

Universal umbilical cord gas measurement and use of NICHD criteria for defining metabolic acidemia should be considered as predictive tools for level of pediatric support and intervention following delivery.

(NICHD) Neonatal Research Network recognized newborns with metabolic acidemia with similar standards. These criteria included an umbilical artery pH ≤7.0 or a base deficit ≥16 mmol/L; an infant with a history of an acute perinatal event and either no blood gas available, a pH from 7.01 to 7.15, or a base deficit from 10 to 15.9 mmol/L with a 10-minute Apgar score ≤5; or assisted ventilation initiated at birth.[12] These criteria are also used to screen infants who may benefit from whole-body hypothermia to reduce the risk of neonatal encephalopathy.

In recent times, there has been no comprehensive examination of the relationship between universal umbilical artery blood sampling and the risk of serious adverse neonatal outcomes, and specifically, hypoxic-ischemic encephalopathy (HIE) requiring whole-body hypothermia. Furthermore, there has been no recent study comparing how well the ACOG and NICHD standards of metabolic acidemia identify at-risk neonates. Thus, the purpose of this study is 2-fold: (1) to evaluate the clinical significance of umbilical cord gas measurements collected upon delivery and serious adverse neonatal outcomes, and (2) to determine if distinct thresholds for defining metabolic acidemia differ in their ability to predict such serious adverse neonatal complications.

Materials and Methods

This is a single-center, retrospective cohort study performed at Parkland Hospital, a safety-net hospital that is operated by the Dallas County Hospital District. Obstetrical and neonatal outcomes for all women who give birth at Parkland Hospital are stored into a computerized database. Universal umbilical cord gas collection is done at all deliveries immediately following birth. Apgar scores are assigned by pediatric nurses or physicians at each delivery in standard fashion. Research nurses then assess the data for accuracy and completeness before entering the information into an obstetrical database. Infant outcomes are extracted from discharge records. Parkland Hospital has a level III neonatal intensive care unit (NICU) adjacent to the labor and delivery (L&D) unit.[13] The Obstetrics and Neonatology services are staffed by resident house physicians and faculty of the University of Texas Southwestern Medical School.

The obstetrical database was queried for all live-born singleton deliveries between January 1, 2011 and December 31, 2019. All deliveries that had umbilical cord gas sampling obtained at delivery were included in the study. A complete cord gas profile included pH, base deficit, pCO_2, and bicarbonate. Parkland Hospital's protocol for collection and transport of umbilical cord blood samples is as follows. Umbilical cord blood samples are obtained from a doubly clamped segment of umbilical cord into a heparinized 3-mL plastic syringe. These samples are then placed in ice for transport to the laboratory for analysis. Deliveries with missing or incomplete cord gas profiles (due to either insufficient sample or clotting of the umbilical artery vessels before collection) were excluded from analysis. Stillbirths, multiple gestations, and neonates with congenital anomalies were also excluded.

Neonates with metabolic acidemia were identified using both the ACOG and NICHD criteria. Patients were stratified according to gestational age: ≥35 and <35 weeks of gestation. This gestational age cutoff was selected on the basis of the definition of neonatal encephalopathy by the ACOG Task Force on Neonatal Encephalopathy.[8] Comparisons were then made within the strata between neonates with identified metabolic acidemia and those without. Serious adverse neonatal outcomes included a composite morbidity risk (seizure, grade 3-4 intraventricular hemorrhage [IVH], grade 3/4 periventricular leukomalacia [PVL], NICU admission, mechanical ventilation or continuous positive airway pressure [CPAP] within the first 24 hours following delivery, necrotizing enterocolitis [NEC] requiring surgery, culture-proven sepsis, HIE requiring whole-body hypothermia, and neonatal death). Strict NICHD criteria were used to determine the need for whole-body hypothermia, and the details of these criteria and their specific application at Parkland Hospital can be reviewed in the work by Nelson et al.[14] The risk of metabolic acidemia was calculated for selected obstetrical interventions and complications, including diabetes mellitus, hypertensive disorders of pregnancy, chronic hypertension, placenta previa, placental abruption, prolonged second stage of labor, chorioamnionitis,

shoulder dystocia, operative vaginal delivery, cesarean delivery, and emergent cesarean delivery. Comparisons were then made between neonates with fetal acidemia identified by ACOG criteria[8] (ie, umbilical arterial pH <7.0 and a base deficit ≥12 mmol/L[13]) and those identified by NICHD criteria[12] (ie, umbilical artery pH ≤7.0 or a base deficit ≥16 mmol/L; an infant with a history of an acute perinatal event and either no blood gas available, a pH from 7.01−7.15, or a base deficit from 10−15.9 mmol/L with a 10-minute Apgar score ≤5; or assisted ventilation initiated at birth).

This analysis was accomplished using deidentified data, and was approved by the institutional review board at the University of Texas Southwestern Medical School. Categorical variables were summarized using frequencies and percentages; normally distributed variables were summarized using means and standard deviations, and nonnormally distributed variables were reported as medians and interquartile ranges. Categorical variables were compared between the cohorts using chi square and Fisher exact tests, as appropriate for the data. Normally distributed variables were compared using the Student *t* test; nonnormally distributed variables were compared using the Kruskal−Wallis test. Effect sizes were estimated using relative risks (RRs) and 95% confidence intervals (CIs). Univariable risk for individual intrapartum events of metabolic acidemia is expressed as RR with a 95% CI. All statistical analysis was done using R, version 3.6.1 (R Core Team, Vienna, Austria). *P* values <.05 were considered statistically significant.

Results

Between January 2011 and December 2019, a total of 104,729 deliveries occurred; 101,709 were singleton, liveborn neonates, and of those, 99,802 had no major anomalies. A total of 91,694 singleton, live-born, nonanomalous neonates at ≥35 weeks of gestation, and 2898 live-born, nonanomalous neonates at <35 weeks of gestation had complete cord gas profiles collected. In the cohort born at ≥35 weeks of gestation, metabolic acidemia was identified in approximately 2659 (2.9%), whereas 89,035 (97.1%) had no metabolic acidemia according to ACOG criteria. Table 1 describes the maternal characteristics of live births with metabolic acidemia compared with those without. Neonates born at ≥35 weeks of gestation with metabolic acidemia were more likely to be born to older, nulliparous, Hispanic women with higher body mass indexes. Among the live-born neonates delivered at <35 weeks of gestation, approximately 161 (5.6%) were found to have metabolic acidemia by ACOG criteria, as opposed to 2737

TABLE 1
Maternal characteristics in women with umbilical artery blood gases analyzed at delivery by American College of Obstetricians and Gynecologists criteria

	≥35 wk			≤35 wk		
	Acidemia	No acidemia		Acidemia	No acidemia	
Characteristics	(n=2659)	(n=89,035)	*P* value	(n=161)	(n=2737)	*P* value
Age (y)	28.4 (6.7)	27.6 (6.4)	<.001	28.6 (7.6)	28.3 (6.9)	.677
Race			.002			.186
Black	434 (16)	12,102 (14)		43 (27)	583 (21)	
White	78 (3)	2595 (3)		7 (4)	127 (5)	
Hispanic	2058 (77)	71,098 (80)		105 (65)	1969 (72)	
Asian	40 (2)	1462 (2)		4 (3)	33 (1)	
Other	49 (2)	1778 (2)		2 (1)	25 (1)	
Parity	1 (0−2)	1 (0−2)	<.001	1 (0−2)	1 (0−2)	.520
Nulliparous	959 (36)	24,727 (28)	<.001	50 (31)	855 (31)	.961
BMI at first PNC visit	28.9 (25.2−33.8)	27.8 (24.2−32.1)	<.001	29.7 (24.3−35.9)	28.9 (24.7−33.9)	.173
BMI at first PNC visit			<.001			.176
<25	464 (24)	20,273 (30)		24 (22)	527 (27)	
25 to <30	645 (33)	22,899 (34)		32 (29)	572 (29)	
30 to <35	429 (22)	14,268 (21)		23 (21)	443 (23)	
35 to <40	231 (12)	6166 (9)		14 (13)	240 (12)	
>40	165 (9)	3807 (6)		17 (15)	171 (9)	

BMI, body mass index; *PNC*, prenatal care.

Kraus. Comparison of criteria for metabolic acidemia. Am J Obstet Gynecol 2023.

(94.4%) without metabolic acidemia. Maternal characteristics were similar between the 2 groups of neonates born at <35 weeks of gestation.

When comparing neonates delivered with and without metabolic acidemia according to ACOG criteria, neonates born at ≥35 weeks of gestation experienced substantially increased risk for all adverse outcomes except PVL, IVH, NEC, and bronchopulmonary dysplasia (BPD) (Table 2). Neonates with metabolic acidemia had an increased risk of NICU admission (12% vs 1%; *P*<.001), need for mechanical ventilation or CPAP (11% vs 1%; *P*<.001), seizures (1.3% vs 0.06%; *P*<.001), and neonatal death (0.3% vs 0.01%; *P*<.001). Mean 1-minute and 5-minute Apgar scores were similar and reassuring among neonates born at ≥35 weeks' gestation with and without metabolic acidemia (8 vs 8 and 9 vs 9, respectively; *P*<.001). Most notably, neonates with metabolic acidemia had an increased risk for HIE requiring whole-body hypothermia (4% vs 0.04%; RR, 96.39; *P*<.001).

Preterm neonates born at <35 weeks of gestation also had similar increased adverse event risk profiles. Preterm neonates with metabolic acidemia had a markedly increased risk of NICU admission (78% vs 54%; *P*<.001), mechanical ventilation or CPAP (65% vs 52%; *P*=.001), seizures (4% vs 1%; *P*<.001), grade 3-4 IVH (4% vs 2%; *P*=.04), and neonatal death (5% vs 1%; *P*=.005). The mean 1-minute Apgar score was 4 in neonates with acidemia and 7 in those without (*P*<.001); however, 5-minute Apgar scores were comparable and reassuring in both groups (7 vs 9; *P*<.001). Similar to what was observed for their term counterparts, HIE occurred more frequently (2% vs 0%; *P*<.001) in preterm neonates diagnosed with metabolic acidemia than in those without.

Diabetes mellitus, hypertensive disorders of pregnancy, postterm deliveries, prolonged second stages, chorioamnionitis, operative vaginal deliveries, and cesarean deliveries were associated with neonates born at ≥35 weeks of gestation with metabolic acidemia as defined by ACOG criteria (Table 3). The highest RR

TABLE 2
Comparison of neonatal outcomes between neonates with and without metabolic acidemia at birth according to American College of Obstetricians and Gynecologists criteria

	≥35 wk				< 35 wk			
Outcomes	Acidemia (n=2659)	No acidemia (n=89,035)	*P* value	RR (95% CI)	Acidemia (n=161)	No acidemia (n=2737)	*P* value	RR (95% CI)
Composite: seizure, IVH, PVL	35 (1)	54 (0)	<.001	21.71 (14.21–33.15)	12 (7)	67 (2)	.001	3.04 (1.68–5.51)
Admission to NICU	313 (12)	1132 (1)	<.001	9.26 (8.22–10.43)	125 (78)	1490 (54)	<.001	1.43 (1.39–1.56)
Ventilator, first 24 h	87 (3)	185 (0)	<.001	15.75 (12.24–20.26)	43 (27)	346 (13)	<.001	2.11 (1.61–2.78)
CPAP	193 (7)	1049 (1)	<.001	6.16 (5.31–7.15)	61 (38)	1066 (39)	.789	0.97 (0.79–1.19)
Ventilator or CPAP, first 24 h	280 (11)	1234 (1)	<.001	7.60 (6.71–8.60)	104 (65)	1412 (52)	.001	1.25 (1.11–1.41)
Infant seizures	35 (1)	52 (0)	<.001	22.54 (14.71–34.53)	7 (4)	18 (1)	<.001	6.61 (2.80–15.60)
PVL	0 (0)	1 (0)	>.999	—	0 (0)	20 (1)	.624	—
IVH, grade 3–4	0 (0)	1 (0)	>.999	—	6 (4)	43 (2)	.039	2.37 (1.02–5.49)
Necrotizing enterocolitis, surgery	0 (0)	1 (0)	>.999	—	0 (0)	5 (0)	>.999	—
Bronchopulmonary dysplasia	0 (0)	1 (0)	>.999	—	19 (12)	248 (9)	.243	1.30 (0.84–2.02)
Culture proven sepsis	12 (0)	77 (0)	<.001	5.22 (2.84–9.58)	0 (0)	9 (0)	>.999	—
Neonatal death	7 (0)	8 (0)	<.001	29.30 (10.63–80.74)	8 (5)	41 (1)	.005	3.32 (1.58–6.96)
Cooled/HIE	95 (4)	33 (0)	<.001	96.39 (64.99–142.97)	3 (2)	0 (0)	<.001	—

Cooled/HIE: only neonates born at ≥35 weeks diagnosed with HIE underwent treatment with whole-body hypothermia.

CI, confidence interval; *CPAP*, continuous positive airway pressure; *HIE*, hypoxic-ischemic encephalopathy; *IVH*, intraventricular hemorrhage; *NICU*, neonatal intensive care unit; *PVL*, periventricular leukomalacia; *RR*, risk ratio.

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was noted with the obstetrical diagnosis of placental abruption (RR, 9.07; 95% CI, 7.25−11.36) and those who underwent emergent cesarean deliveries (RR, 8.65; 95% CI, 7.75−9.66). Neonates born at <35 weeks of gestation were also more likely to be born to women with hypertensive disorders of pregnancy. Similarly, the highest RR was noted in those with the obstetrical diagnosis of placental abruption (RR, 4.10; 95% CI, 2.94−5.73) and those who underwent emergent cesarean deliveries (RR, 4.28; 95% CI, 3.14−5.82).

Of the 84,522 neonates born at ≥35 weeks of gestation, 7172 (7.8%) had metabolic acidemia identified according to NICHD criteria (Table 4). Average 1-minute and 5-minute Apgar scores were comparable and reassuring among neonates born at ≥35 weeks of gestation with and without metabolic acidemia (8 vs 8 and 9 vs 9; $P<.001$). In this cohort, approximately 111 (1.5%) and 17 (0.02%), respectively, had increased risk of HIE requiring whole-body hypothermia (RR, 76.95; $P<.001$). When examining neonates born at <35 weeks of gestation, 348 (12%) neonates with metabolic acidemia and 2550 (88%) neonates without metabolic acidemia were compared. Mean 1-minute Apgar scores differed slightly (5 vs 7; $P<.001$) between those born at <35 weeks of gestation with metabolic acidemia and those without; however, 5-minute Apgar scores were similar (9 vs 9; $P<.001$). In this cohort, 3 neonates with metabolic acidemia were diagnosed with HIE vs 0 of those without metabolic acidemia ($P=.002$). Maternal characteristics and selected obstetrical outcomes for neonates with fetal acidemia identified according to NICHD criteria can also be found in the supplemental tables.

To further compare diagnostic accuracy between the ACOG and NICHD criteria in correctly assessing neonates at risk for poor outcomes related to metabolic acidemia, the sensitivity and specificity of each criterion were assessed. The NICHD criteria were more sensitive (sensitivity, 86.7%) and less specific (specificity, 92.2%) when compared with ACOG criteria, which were less sensitive (sensitivity, 74.2%) and more specific (specificity, 97.2%). This is visualized in the receiver operating characteristic curve shown in the Figure. Furthermore, the positive predictive value (PPV) of the ACOG criteria was calculated at 99.9% and the negative predictive value (NPV) at 1.5%, whereas the PPV of the NICD criteria was computed at 3.6% and the NPV at 99.9% (Table 5).

Comment

Principal findings

Using the ACOG criteria, approximately 2.9% of neonates born at ≥35 weeks of gestation were identified to have metabolic acidemia. Women diagnosed with obstetrical complications including hypertensive disorders of pregnancy, diabetes mellitus, chorioamnionitis, and postterm gestations were also more likely to have neonates with metabolic acidemia. Intrapartum events associated with increased risk included placental abruption, a prolonged second stage, operative vaginal delivery, and cesarean delivery. Neonates were found to have substantially increased risk of requiring NICU admission and mechanical ventilation or CPAP, and increased risk of experiencing seizures, sepsis, and neonatal death. Importantly, metabolic acidemia was associated with an almost 100-fold increased risk of HIE requiring whole-body hypothermia. These findings persisted when using the more sensitive NICHD criteria for metabolic acidemia. The NICHD criteria identified 4513 (4.9%) neonates with metabolic acidemia, a greater number due to the broader definition compared with that of the ACOG criteria. This translated into approximately 16 more neonates being diagnosed with HIE requiring whole-body hypothermia. The sensitivity and specificity of the NICHD criteria were 86.7% and 92.2%, respectively, whereas sensitivity and specificity of the ACOG criteria were 74.2% and 97.2%.

The ACOG criteria were able to identify 5.6% of neonates born at <35 weeks of gestation with metabolic acidemia. Similar to their term counterparts, these neonates were also at considerably increased risk for NICU admission, mechanical ventilation or CPAP, seizures, and neonatal death. Expected preterm comorbidities such as PVL, IVH, BPD, NEC, and sepsis were not associated with metabolic acidemia in this preterm gestational age group. Despite a small incidence, these preterm neonates also experienced a markedly increased risk for HIE. The NICHD criteria identified 187 (6.5%) preterm neonates with metabolic acidemia. In contrast to their term counterparts, an equal number of neonates (n=3; 1%) were identified to have HIE when using the ACOG and the NICHD criteria for diagnosis. Neonates born to women with hypertensive disorders of pregnancy were noted to have increased risk of metabolic acidemia. Similar obstetrical complications and intrapartum events were noted in the preterm neonatal cohort.

Results in the context of what is known

Similar to previous findings by Morgan et al,[15,16] umbilical cord gas measurements collected at delivery that identified metabolic acidemia (by either ACOG or NICHD criteria) were associated with serious adverse neonatal outcomes. Expanding on the work by Nelson et al,[14] which examined intrapartum events associated with increased risk for whole-body hypothermia, our study found that placental abruption was strongly associated with metabolic acidemia. Furthermore, diabetes mellitus, hypertensive disorders of pregnancy, chorioamnionitis, a prolonged second stage, and mode of delivery were associated with increased risk for metabolic acidemia. With respect to mode of delivery, surprisingly, repeated cesarean delivery and scheduled cesarean delivery were predictive of metabolic acidemia. Possible explanations include events related to neuraxial anesthesia, as previously described by Rimsza et al.[17] Whereas lactate levels were not specifically examined in this study, the work by Tuuli et al[18] suggests that umbilical cord arterial lactate measurements taken after delivery may be superior to cord pH values in predicting short-term neonatal morbidity at term.

TABLE 3
Relative risks (95% confidence intervals) of metabolic acidemia for selected obstetric complications and interventions in neonates born with and without metabolic acidemia according to American College of Obstetricians and Gynecologists criteria

	≥35 wk				< 35 wk			
	Acidemia	No acidemia			Acidemia	No acidemia		
Complications/Interventions	(n=2659)	(n=89,035)	*P* value	RR (95% CI)	(n=161)	(n=2737)	*P* value	RR (95% CI)
Diabetes mellitus	294 (11)	7372 (8)	<.001	1.34 (1.20–1.49)	31 (19)	389 (14)	.077	1.35 (0.97–1.88)
Severe preeclampsia	458 (17)	7104(8)	.001	2.16 (1.98–2.35)	99 (61)	1009 (37)	<.001	1.67 (1.46–1.90)
cHTN	101 (4)	2286 (3)	<.001	1.48 (1.22–1.80)	26 (16)	376 (14)	.390	1.18 (0.82–1.69)
gHTN	524 (20)	11,180 (13)	<.001	1.57 (1.45–1.70)	84 (52)	919 (34)	<.001	1.55 (1.33–1.82)
Previa	8 (0)	302 (0)	.866	0.89 (0.44–1.79)	2 (1)	71 (3)	.435	0.48 (0.12–1.93)
Abruption	94 (4)	347 (0)	<.001	9.07 (7.25–11.36)	35 (22)	145 (5)	<.001	4.10 (2.94–5.73)
42 wk gestation	85 (3)	2017 (2)	.002	1.41 (1.14–1.75)	0 (0)	0 (0)	—	—
Prolonged second stage	203 (8)	2971 (3)	<.001	2.29 (2.00–2.62)	3 (2)	43 (2)	.740	1.19 (0.37–3.78)
Chorioamnionitis	285 (11)	6627 (7)	<.001	1.44 (1.29–1.61)	5 (3)	70 (3)	.608	1.21 (0.50–2.97)
Shoulder dystocia	19 (1)	436 (0)	.104	1.46 (0.92–2.31)	0 (0)	0 (0)	—	—
Forceps delivery	187 (7)	1963 (2)	<.001	3.19 (2.76–3.69)	1 (1)	22 (1)	>.999	0.77 (0.10–5.70)
Cesarean delivery (total)	1559 (59)	26,367 (30)	<.001	1.98 (1.91–2.05)	119 (74)	1405 (51)	<.001	1.44 (1.30–1.59)
Cesarean delivery for fetal distress	465 (17)	4359 (5)	<.001	3.57 (3.27–3.90)	33 (20)	190 (7)	<.001	2.95 (2.11–4.12)
Repeat cesarean delivery	733 (28)	16,109 (18)	<.001	1.52 (1.43–1.62)	44 (27)	602 (22)	.114	1.24 (0.96–1.61)
Cesarean delivery for other reason	92 (3)	1120 (1)	<.001	2.75 (2.23–3.39)	23 (14)	155 (6)	<.001	2.52 (1.68–3.79)
Scheduled cesarean delivery	320 (12)	8280 (9)	<.001	1.29 (1.17–1.44)	0 (0)	46 (2)	.180	—
Stat cesarean delivery (within 10 min)	355 (13)	1374 (2)	<.001	8.65 (7.75–9.66)	40 (25)	159 (6)	<.001	4.28 (3.14–5.82)
Stat cesarean delivery (within 30 min)	535 (20)	2923 (3)	<.001	6.13 (5.64–6.66)	54 (34)	251 (9)	<.001	3.66 (2.86–4.68)

CI, confidence interval; *cHTN*, chronic hypertension; *gHTN*, gestational hypertension; *RR*, risk ratio.

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TABLE 4
Comparison of neonatal outcomes between neonates with and without metabolic acidemia at birth according to *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria

Outcomes	≥35 wk				< 35 wk			
	Acidemia (n=7172)	No acidemia (n=84,522)	*P* value	RR (95% CI)	Acidemia (n=348)	No acidemia (n=2550)	*P* value	RR (95% CI)
Composite: seizure, IVH, PVL	46 (1)	43 (0)	<.001	12.61 (8.32–19.09)	19 (5)	60 (2)	.001	2.32 (1.40–3.84)
Admission to NICU	505 (7)	940 (1)	<.001	6.33 (5.70–7.04)	249 (72)	1366 (54)	<.001	1.34 (1.24–1.44)
Ventilator, first 24 h	120 (2)	152 (0)	<.001	9.30 (7.33–11.81)	69 (20)	320 (13)	<.001	1.58 (1.25–2.00)
CPAP	349 (5)	893 (1)	<.001	4.61 (4.08–5.20)	145 (42)	982 (39)	.257	1.08 (0.95–1.24)
Ventilator or CPAP, first 24 h	469 (7)	1045 (1)	<.001	5.29 (4.76–5.88)	214 (61)	1302 (51)	<.001	1.20 (1.10–1.32)
Infant seizures	44 (1)	43 (0)	<.001	12.06 (7.93–18.35)	11 (3)	14 (1)	<.001	5.76 (2.63–12.58)
PVL	1 (0)	0 (0)	.078	—	2 (1)	18 (1)	>.999	0.81 (0.19–3.49)
IVH, grade 3–4	1 (0)	0 (0)	.078	—	10 (3)	39 (2)	.068	1.88 (0.95–3.73)
Necrotizing enterocolitis, surgery	1 (0)	0 (0)	.078	—	2 (1)	3 (0)	.112	4.89 (0.82–29.13)
Bronchopulmonary dysplasia	0 (0)	1 (0)	>.999	—	41 (12)	226 (9)	.077	1.33 (0.97–1.82)
Culture proven sepsis	19 (0)	70 (0)	<.001	3.20 (1.93–5.31)	1 (0)	8 (0)	>.999	0.92 (0.11–7.30)
Neonatal death	7 (0)	8 (0)	<.001	10.31 (3.74–28.43)	11 (3)	38 (1)	.023	2.12 (1.09–4.11)
Cooled/HIE	111 (2)	17 (0)	<.001	76.95 (46.21–128.13)	3 (1)	0 (0)	.002	—

Cooled/HIE: only neonates born at ≥35 weeks diagnosed with HIE underwent treatment with whole-body hypothermia.

CI, confidence interval; *CPAP*, continuous positive airway pressure; *HIE*, hypoxic-ischemic encephalopathy; *IVH*, intraventricular hemorrhage; *NICU*, neonatal intensive care unit; *PVL*, periventricular leukomalacia; *RR*, risk ratio.

Kraus. Comparison of criteria for metabolic acidemia. Am J Obstet Gynecol 2023.

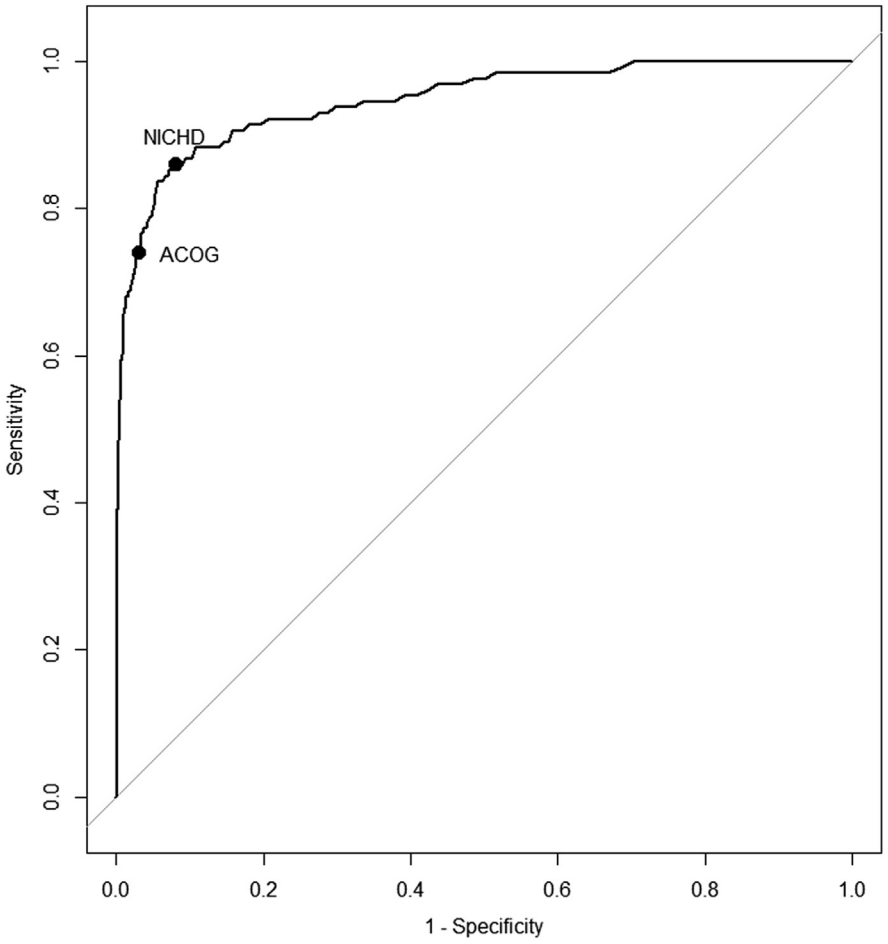
Clinical implications

These findings suggest that universal cord gas collection can be used to risk-stratify neonates who should undergo more intensive monitoring following delivery. This is particularly important for intrapartum cases of cesarean delivery for fetal compromise, placental abruption, and operative vaginal deliveries. Moreover, the use of the NICHD criteria should be considered by both obstetricians and pediatric providers given that risk for pathology persists with this more conservative and sensitive threshold. Universal cord gas collection can also be used as a measure for quality improvement within a L&D unit. Frequently, intrapartum events, such as placental abruption, emergent cesarean deliveries, and operative vaginal deliveries cannot be prevented; however, as previously described by Cahill et al,[19] active management of labor can reduce the rate of prolonged second stages, leading to improved maternal and neonatal outcomes.

Research implications

Future work should include a cost-effectiveness analysis for implementation of a universal cord gas collection protocol. Although we anticipate some increase in cost with such protocols, there will likely be advantages in early identification of infants at risk for adverse events and subsequent decreased NICU costs, as suggested by White et al.[20] Although correlating umbilical cord gas measurements to Apgar scores, as previous studies[10,21] have done, was not the primary focus of our study, this association with neonatal outcomes should be examined prospectively. Our study reinforces the findings of Sabol et al,[22] suggesting that neonates with reassuring Apgar scores have a residual risk of neonatal acidemia that is associated with higher rates of adverse outcomes. Moreover, a formal assessment of the safety and effectiveness of whole-body hypothermia in preterm infants is needed. Fortunately, a recent randomized control trial by the NICHD investigating the efficacy of whole-body hypothermia in neonates at 33 to 35

FIGURE
Receiver operating characteristic curves of diagnostic accuracy



ACOG, American College of Obstetricians and Gynecologists; *NICHD*, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

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TABLE 5
Diagnostic accuracy performance metrics for American College of Obstetricians and Gynecologists and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria

Metrics	NICHD	ACOG
Sensitivity	86.70%	74.20%
Specificity	92.20%	97.20%
Positive LR	11.2	26.5
Negative LR	0.14	0.265
PPV	1.50%	3.60%
NPV	99.9%	99.9%

ACOG, American College of Obstetricians and Gynecologists; *LR*, likelihood ratio; *NICHD*, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; *NPV*, negative predictive value; *PPV*, positive predictive value.

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weeks of gestation is currently undergoing analysis.[23] Finally, although short-term neonatal outcomes are significant, of equal importance is the long-term follow-up for these children. These neonates should be followed up into childhood given that long-term neurologic outcomes for acidemic umbilical cord gas measurements are still not well described. A substantial cohort (specifically those who underwent whole-body hypothermia) is being followed up at the affiliated Children's Medical Center Dallas, and continued work will investigate these cases in the future.

Strengths and limitations

Strengths of this study include the large size of our contemporary cohort, allowing us to detect rare events and to infer generalizability. Furthermore, our study was performed at a single center, facilitating the collection of universal cord gases for every delivery. Limitations of the study include the bias inherent to retrospective work. In addition, we did not collect data on the neonatal outcomes for those with missing cord gas samples, and although the anticipated effect of missing data is small, there may have been significant pathology within the missing cord gas samples. Finally, long-term follow-up of the identified neonates is possible but difficult within the Texas health care system because a considerable number of these neonates present at outside facilities for continued care.

Conclusions

In our retrospective cohort of 91,694 deliveries, neonates born at ≥35 weeks of gestation with metabolic acidemia were at substantially increased risk for serious adverse neonatal outcomes, and had almost 100-fold increased risk for HIE requiring whole-body hypothermia. Preterm neonates born at <35 weeks of gestation had similar increased risk for serious adverse neonatal outcomes and HIE. When comparing the diagnostic accuracy of the ACOG and NICHD criteria, the NICHD threshold is more sensitive and identifies more neonates born at ≥35 weeks of gestation at risk for adverse neonatal outcomes, including

HIE requiring whole-body hypothermia. Furthermore, average Apgar scores (using either NICHD or ACOG acidemia criteria) at both 1 and 5 minutes remained reassuring in neonates born at ≥35 weeks of gestation, highlighting a residual risk of neonatal acidemia. This study adds to the literature supporting the association between adverse neonatal outcomes and metabolic acidemia, and suggests that providers should consider not only the use of the more conservative NICHD criteria for defining metabolic acidemia, but also implementation of universal cord gas collection policies on L&D wards. ■

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Author and article information

From the Department of Obstetrics and Gynecology, The University of North Carolina at Chapel Hill, Chapel Hill, NC (Dr Kraus); Department of Women's Health, Dell Medical School, The University of Texas at Austin, Austin, TX (Dr Saucedo); Department of Obstetrics and Gynecology, Joe R. and Teresa Lozano Long School of Medicine, The University of Texas Health Science Center at San Antonio, San Antonio, TX (Dr Byrne); Department of Pediatrics, Children's Medical Center Dallas, The University of Texas Southwestern Medical Center, Dallas, TX (Dr Chalak); Department of Obstetrics and Gynecology, The University of Texas Southwestern Medical Center, Dallas, TX (Drs Pruszynski and Spong); and Parkland Health and Hospital System, Dallas, TX (Drs Chalak and Spong).

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Corresponding author: Alexandria C. Kraus, MD. alexandria.kraus@unchealth.unc.edu

SUPPLEMENTAL TABLE 1

Maternal characteristics in women with umbilical artery blood gases analyzed at delivery by *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria

	≥35 wk			< 35 wk		
	Acidemia	No acidemia		Acidemia	No acidemia	
Characteristics	(n=7172)	(n=84,522)	*P* value	(n=348)	(n=2550)	*P* value
Age (y)	28.1 (6.7)	27.6 (6.3)	<.001	29 (7.2)	28.3 (6.9)	.086
Race			<.001			.243
Black	1184 (17)	11,352 (13)		81 (23)	545 (21)	
White	205 (3)	2468 (3)		12 (3)	122 (5)	
Hispanic	5515 (77)	67,641 (80)		243 (70)	1831 (72)	
Asian	120 (2)	1382 (2)		8 (2)	29 (1)	
Other	148 (2)	1679 (2)		4 (1)	23 (1)	
Parity	1 (0–2)	1 (0–2)	<.001	1 (0–2)	1 (0–2)	.352
Nulliparous	2619 (37)	23,067 (27)	<.001	113 (33)	792 (31)	.594
BMI at first PNC visit	28.5 (24.7–33.4)	27.8 (24.2–32.1)	<.001	29.3 (25.5–35.7)	28.9 (24.7–33.9)	.078
BMI at first PNC visit			<.001			.053
<25	1404 (27)	19,333 (30)		56 (23)	495 (27)	
25 to <30	1701 (32)	21,843 (34)		74 (30)	530 (29)	
30 to <35	1132 (22)	13,565 (21)		50 (20)	416 (23)	
35 to <40	588 (11)	5809 (9)		33 (13)	221 (12)	
>40	417 (8)	3555 (6)		34 (14)	154 (8)	

BMI, body mass index; *PNC*, prenatal care.

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SUPPLEMENTAL TABLE 2

Relative risks (95% confidence intervals) of metabolic acidemia for selected obstetric complications and interventions in neonates born with and without metabolic acidemia according to *Eunice Kennedy Shriver* National Institute of Child Health and Human Development criteria

	>35 wk				< 35 wk			
	Acidemia	No acidemia			Acidemia	No acidemia		
Complications/interventions	(n=7172)	(n=84,522)	*P* value	RR (95% CI)	(n=348)	(n=2550)	*P* value	RR (95% CI)
Diabetes mellitus	790 (11)	6876 (8)	<.001	1.35 (1.26–1.45)	68 (20)	352 (14)	.004	1.42 (1.12–1.79)
Severe preeclampsia	1080 (15)	6482 (8)	<.001	1.96 (1.85–2.08)	204 (59)	904 (35)	<.001	1.65 (1.49–1.83)
cHTN	269 (4)	2118 (3)	<.001	1.50 (1.32–1.70)	63 (18)	339 (13)	.015	1.36 (1.07–1.74)
gHTN	1278 (18)	10,426 (12)	<.001	1.44 (1.37–1.52)	174 (50)	829 (33)	<.001	1.54 (1.37–1.73)
Previa	21 (0)	289 (0)	.492	0.86 (0.55–1.33)	6 (2)	67 (3)	.313	0.66 (0.29–1.50)
Abruption	159 (2)	282 (0)	<.001	6.64 (5.48–8.06)	58 (17)	122 (5)	<.001	3.48 (2.60–4.66)
42 wk gestation	202 (3)	1900 (2)	.002	1.25 (1.09–1.45)	0 (0)	0 (0)	—	—
Prolonged second stage	454 (6)	2720 (3)	<.001	1.97 (1.79–2.17)	9 (3)	37 (1)	.112	1.78 (0.87–3.66)
Chorioamnionitis	740 (10)	6172 (7)	<.001	1.41 (1.31–1.52)	10 (3)	65 (3)	.721	1.13 (0.58–2.17)
Shoulder dystocia	57 (1)	398 (0)	<.001	1.69 (1.28–2.23)	0 (0)	0 (0)	—	—
Forceps delivery	444 (6)	1706 (2)	<.001	3.07 (2.77–3.40)	4 (1)	19 (1)	.348	1.54 (0.53–4.51)
Cesarean delivery (total)	3680 (51)	24,246 (29)	<.001	1.79 (1.74–1.83)	264 (76)	1260 (49)	<.001	1.54 (1.43–1.65)
Cesarean delivery for fetal distress	1049 (15)	3775 (4)	<.001	3.28 (3.07–3.49)	75 (22)	148 (6)	<.001	3.71 (2.88–4.79)
Repeat cesarean delivery	1772 (25)	15,070 (18)	<.001	1.39 (1.33–1.45)	96 (28)	550 (22)	.011	1.28 (1.06–1.54)
Cesarean delivery for other reason	202 (3)	1010 (1)	<.001	2.36 (2.03–2.74)	39 (11)	139 (5)	<.001	2.06 (1.47–2.88)
Scheduled cesarean delivery	838 (12)	7762 (9)	<.001	1.27 (1.19–1.36)	2 (1)	44 (2)	.107	0.33 (0.08–1.37)
Stat cesarean delivery (within 10 min)	672 (9)	1057 (1)	<.001	7.49 (6.82–8.23)	62 (18)	137 (5)	<.001	3.32 (2.51–4.38)
Stat cesarean delivery (within 30 min)	1052 (15)	2406 (3)	<.001	5.15 (4.81–5.52)	90 (26)	215 (8)	<.001	3.07 (2.46–3.82)

CI, confidence interval; *cHTN*, chronic hypertension; *gHTN*, gestational hypertension; *RR*, risk ratio.

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