Neonatal complications in newborns with an umbilical artery pH <7.00

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OBJECTIVE: Our purpose was to determine the significance of an umbilical artery pH <7.00 in relation to neonatal morbidity and mortality.

STUDY DESIGN: Between 1986 and 1993 acid-base assessment of the umbilical artery was performed routinely in 10,699 deliveries. In a retrospective cohort study 84 nonanomalous neonates with an umbilical artery pH <7.00 were individually matched with 84 neonates with an umbilical artery pH >7.24. Matched variables included year of delivery, gender, parity, maternal age, delivery mode, fetal presentation, gestational age, and birth weight. Differences in morbidity between the two groups during the neonatal period (until 28 days after delivery) were investigated.

RESULTS: Neonates with an umbilical artery pH <7.00 versus >7.24 showed significant differences in the following: neonatal condition directly post partum; neurologic, respiratory, cardiovascular, and gastrointestinal complications; and neonatal intensive care unit admissions. No significance was found in renal dysfunction and mortality rate. The proportion of premature infants (<37 weeks) was 17% in both groups. In the acidotic group a 1-minute Apgar score ≤3 and a 5-minute Apgar score <7 was predictive for neonatal complications.

CONCLUSIONS: Severe intrapartum asphyxia, quantified by an umbilical artery pH <7.00, poses a threat to the neonate's health. (Am J Obstet Gynecol 1996;175:1152-7.)

Key words: Fetal acidosis, neonatal morbidity, neurologic dysfunction

Neonatal multiple organ dysfunction is often considered to be a consequence of intrapartum asphyxia.[1] To identify the relationship between fetal intrapartum asphyxia and neonatal complications, many investigators have used the cord blood acid-base balance as a measure of intrapartum asphyxia.[2-6] Although inconsistent results have been published,[2, 6] recent studies indicated that there is a significant increase in neonatal multiorgan morbidity and neurologic dysfunction if acidemia is severe (pH <7.00).[3-5] Low et al.[7] showed a high base deficit (>16 mmol/L) to be the decisive parameter.

Apart from intrapartum asphyxia, many fetal and intrapartum variables such as infection, trauma, gestational age, birth weight, and others may influence the neonatal condition. To avoid confounding variables, most authors exclude low-birth-weight and premature infants from analysis.

In this study a retrospective matched cohort design was chosen to further clarify the association between severe acidosis and neonatal morbidity and to reduce the influence of confounding factors. An umbilical artery pH <7.00 was taken as a measure of severe intrapartum asphyxia.

Methods

Between January 1986 and December 1993, 14,025 infants were born alive at the University Hospital of Nijmegen. Umbilical cord blood samples were routinely obtained during this period. Immediately after delivery the umbilical cord was double clamped; arterial and venous blood samples were taken by the obstetric floor personnel with a preheparinized syringe. These samples were analyzed within 20 minutes after delivery on a blood gas analyzer (Ciba-Corning 288, Medfield, Mass.). Results of these analyses together with demographic and clinical data were entered into a computerized database.

The umbilical artery blood pH of each sample was checked for its reliability by comparing it with the pH of the umbilical vein. If the difference was <0.03 pH units (indicating the probability that venous blood was obtained twice), the case was eliminated. Reliable cord blood samples were available from 10,699 (76.6%) neonates. One hundred thirty (1.3%) had an umbilical artery pH <7.00. From seven cases there was only an umbilical

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Table I. Maternal and fetal demographic and intrapartum characteristics

	Total population (n = 14,025)	*Matched cases*		*Unmatched acidotic cases (n = 33)*
		Study group (n = 84)	*Control group (n = 84)*	
Age (yr) (mean ± SD)	29.6 ± 4.6	29.1 ± 4.5	29.1 ± 3.6	30.6 ± 5.1
Nulliparous (%)	51†	64	64	72
Gestational age (days) (mean ± SD)	270 ± 26	270 ± 21	270 ± 20	235 ± 31‡
Immature (%)	3	0	0	13‡
Premature (%)	13	18	18	66‡
Term (%)	78	81	81	19‡
Postmature (%)	6	1	1	3
Presenting part (caput/breech) (%)	89.6/10.4†	81/19	81/19	52/48
Delivery method				
Not operative (%)	67†	48	48	27‡
Vacuum extraction (%)	9†	16	16	0‡
Forceps (%)	6	10	10	9
Elective cesarean (%)	11	14	14	42‡
Emergency cesarean (%)	8†	13	13	21
Birth weight (gm) (mean ± SD)	3049 ± 845	2935 ± 772	2909 ± 717	1926 ± 765‡
$<P_{2.3}$ (%)	3	6	6	6
Sex (female/male) (%)	48/53†	33/67	33/67	50/50
Multiple gestation (%)	4†	10	10	26‡

*Total investigated population delivered in University Hospital Nijmegen between 1986 and 1993.
†Significant difference ($p < 0.05$) between total population and study group.
‡Significant difference ($p < 0.05$) between study group and group of acidotic neonates that could not be matched.

vein pH <7.00 available. Because the umbilical artery pH is always lower than the umbilical vein pH, these cases were included.

From these 137 the cases with intrauterine infection (intrapartum maternal temperature >38° C and fetal tachycardia, $n = 8$), chromosomal and morphologic congenital anomalies ($n = 4$), no complete records available ($n = 8$), and no control case available ($n = 33$) were excluded.

This resulted in 84 cases (81 with an umbilical artery pH <7.00 and 3 with an umbilical vein pH <7.00) that could each be individually matched with a neonate with an umbilical artery pH >7.24, which is the 50th percentile for umbilical artery pH at Nijmegen University Hospital.[8] Matching variables included date of birth (same year or 1 year earlier or later, if not possible 2 years earlier or later), gender, parity (nulliparous or multiparous), gestational age (<26, 26 to 28, 28 to 30, 30 to 32, 32 to 34, 34 to 37, 37 to 42, >42 weeks of gestation), mode of delivery (spontaneous delivery, vacuum extraction, forceps delivery, elective cesarean delivery, cesarean delivery for dystocia or fetal indication), fetal presentation (cephalic or breech), birth weight according to the birth weight percentiles by Kloosterman[9] ($<P_{2.3}$, $P_{2.3}$ to P_{10}, P_{10} to P_{50}, P_{50} to $P_{97.7}$, $>P_{97.7}$). If several control cases were available, the one with the closest maternal age (at delivery) was selected.

The matched controls were selected without awareness of the neonatal outcome. The neonatal period was defined as the first 28 days of life. The following six categories of morbidity were noted from the newborn records: (1) fetal condition directly post partum (need for resuscitation or intubation, Apgar scores recorded after 1 and 5 minutes), (2) neurologic complications (abnormal tone >24 hours post partum, seizures, intracranial hemorrhage, periventricular leukomalacia, otherwise abnormal ultrasonography, abnormal electroencephalogram), (3) pulmonary complications (recurrent apnea, aspiration, pneumothorax, idiopathic respiratory distress syndrome [grade 1 to 4], bronchopulmonary dysplasia, persistent pulmonary hypertension), (4) cardiovascular complications (treated open ductus arteriosus, treated periods of bradycardia or tachycardia and hypotension), (5) renal dysfunction (serum creatinine levels >90 μmol/L after 3 days of life, and (6) gastrointestinal complications (alanine aminotransferase >25 U/L, aspartate aminotransferase >33 U/L, necrotizing enterocolitis). Sepsis, admission to the neonatal intensive care unit, and death were also noted.

Differences in neonatal complications between the study group (pH <7.00) and the control group (pH >7.24) were analyzed according to these parameters. To describe the study group, metabolic acidosis was defined according to Goodwin et al.[5] as $Pco_2 \leq 65$ mm Hg and base deficit ≥10 mmol/L; respiratory acidemia was defined as $Pco_2 > 65$ mm Hg and base deficit <10 mmol/L. Mixed acidosis was defined as $Pco_2 > 65$ mm Hg and base deficit ≥10 mmol/L.

Statistical significance was determined by 2 × 2 contingency tables and Fisher's exact tests. Differences in morbidity between the two groups were tested for significance

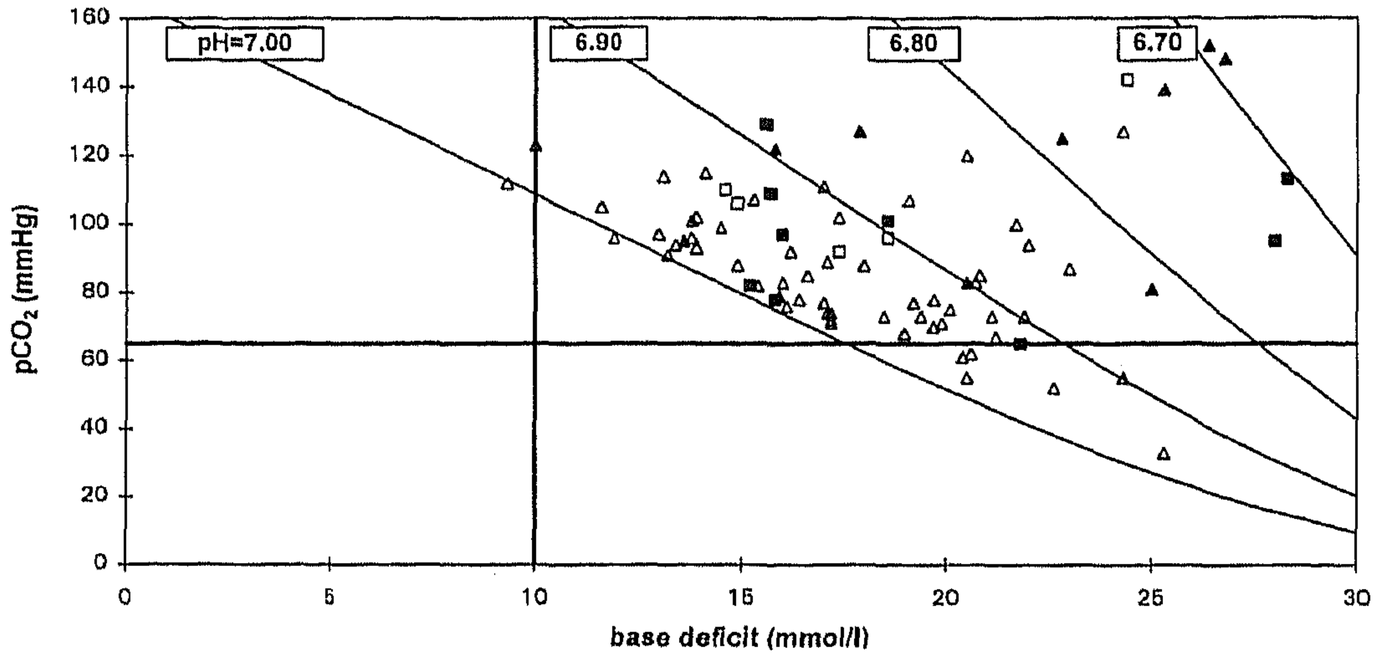

Fig. 1. Base deficit versus Pco_2 in umbilical artery with subdivision for gestational age and neurologic dysfunction. Iso-pH lines were drawn at pH 7.00, 6.90, 6.80 and 6.70. *Solid square*, Preterm infants with neurologic complications; *open square*, preterm infants without neurologic complications; *solid triangle*, term infants with neurologic complications; *open triangle*, term infants without neurologic complications.

Table II. Umbilical cord acid-base parameters

	Total population (N = 14,025)*	*Matched cases*		*Unmatched acidotic cases (n = 33)*
		Study group (n = 84)	*Control group (n = 84)*	
Arterial				
pH (mean ± SD)	7.24 ± 0.08 (*N* = 14,025)	6.91 ± 0.09 (81)	7.29 ± 0.03 (84)	6.87 ± 0.13 (31)
Pco_2 (mm Hg) (mean ± SD)		12.0 ± 3.3 (80)	6.6 ± 1.2 (77)	
Base deficit (mmol/L) (mean ± SD)		18.2 ± 4.3 (81)	3.6 ± 2.4 (78)	
Venous				
pH (mean ± SD)		7.02 ± 0.12 (84)	7.35 ± 0.04 (84)	
Pco_2 (mm Hg) (mean ± SD)		9.5 ± 3.1 (81)	5.2 ± 0.9 (78)	
Base deficit (mmol/L) (mean ± SD)		15.5 ± 4.3 (82)	3.8 ± 2.0 (79)	

Values in parentheses indicate number.
*Total investigated population delivered in University Hospital Nijmegen in between 1986 and 1993.

with the McNemar test. A p value <0.05 was considered significant.

Results

The demographic and intrapartum characteristics of the 84 pregnancies (70 term and 14 preterm neonates) in the acidotic and control groups are summarized in Table I and compared with the general obstetric population of the University Hospital of Nijmegen over the same time interval (1986 to 1993) and with the neonates in the acidotic group that could not be matched. In the study group the percentage of nulliparous patients, breech presentations, vaginal operative deliveries, multiple gestations, and male neonates was significantly higher than in the total population. In the group of acidotic neonates that could not be matched, the gestational age and birth weight were significantly lower; there were more premature and immature infants, and multiple pregnancies were more common. Also, significantly more operative deliveries were performed. In Table II the postpartum acid-base parameters in the umbilical artery of the total population, the unmatched cases, and the acidotic and control groups are shown.

Neonatal complications for the matched acidotic and the nonacidotic groups are summarized in Table III. Neonatal morbidity (poor condition after delivery, neurologic, pulmonary, gastrointestinal, and cardiovascular complications) was significantly higher in the acidotic group than in the nonacidotic group, with the exception of renal complications. Neonatal intensive care unit admissions were also significantly higher. Two neonates in the acidotic group died. Conversely, 23 (27%) acidotic neonates with a pH between 6.80 and 7.00 did not show any signs of neonatal morbidity.

Of the acidotic newborns, 87.5% had a mixed, 2.5% a respiratory, and 10% a metabolic acidosis (Fig. 1, $n = 80$; in three cases no arterial blood sample was available, in one case Pco_2 was not measured). Regarding the neurologic complications, all were seen in the group with mixed acidosis and none in the metabolic acidosis group. Almost all (15/16) neurologic complications were found in acidotic neonates with a base deficit ≥15 mmol/L. All

Table III. Neonatal complications in newborns with umbilical artery pH <7.00 versus umbilical artery pH >7.24

Complication	*Study cohort (n = 84)*	*McNemar test (significance)*	*Control group (n = 84)*
Poor condition after delivery	63 (75)	$p < 0.001$	10 (12)
Resuscitation	51	$p < 0.001$	6
Intubation	24	$p < 0.001$	2
Apgar score <7 at 1 min	56	$p < 0.001$	8
Apgar score <7 at 5 min	26	$p < 0.001$	2
Neurologic	19 (23)	$p < 0.01$	6 (7)
Abnormal tone	12	$p < 0.02$	2
Seizures	9	$p < 0.01$	1
Intracranial hemorrhage	5	NS	2
Periventricular leukomalacia	2	NS	1
Abnormal EEG–cranial ultrasonography	12	$p < 0.05$	3
Pulmonary	26 (31)	$p < 0.01$	9 (11)
Recurrent apnea	4	NS	4
Aspiration	18	$p < 0.01$	3
Pneumothorax	3	NS	1
Idiopathic RDS	8	$p < 0.02$	3
Bronchopulmonal dysplasia	2	NS	1
Persistent pulmonary hypertension	1	NS	0
Cardiovascular	13 (15)	$p < 0.01$	7 (8)
Treated open ductus arteriosus	2	NS	1
Bradycardia or tachycardia	7	NS	6
Hypotension	9	$p < 0.02$	2
Renal	4 (5)	NS	1 (1)
Gastrointestinal	14 (17)	$p < 0.001$	0
High liver enzyme values	14	$p < 0.001$	0
Necrotizing enterocolitis	1	NS	0
Death	2 (2)	NS	1 (1)
NICU admission	27 (32)	$p < 0.001$	7 (8)

Values in parentheses indicate percent. *EEG*, Electroencephalogram; *NS*, not significant; *RDS*, respiratory distress syndrome; *NICU*, neonatal intensive care unit.

term neonates except one with neurologic dysfunction had an umbilical artery pH ≤6.90. With increasing hypercarbia or base deficit the proportion of neonates with neurologic complications increased. When the umbilical artery pH of the neonates ranged between 6.90 and 7.00, neurologic dysfunction was found in all but one case in preterm infants. In the acidotic group, for both preterm and term infants, the risk for neurologic complications was higher than in the nonacidotic group (Table III).

Of the 24 cases in the acidotic group with a 1-minute Apgar score ≤3, 15 cases had neurologic complications (positive predictive value 65%, Fig. 2). A 5-minute Apgar score <7 was found in 26 cases, of which 13 (50%) had neurologic complications (Fig. 3).

Below an umbilical artery pH of 6.80, all neonates were born severely depressed. Above this value there was no relationship between umbilical artery pH and the 1- or 5-minute Apgar score. Twenty-five percent of the acidotic neonates were born in good condition (1-minute Apgar score ≥7). In the nonacidotic group no 1-minute Apgar score ≤3 was found.

Comment

In numerous studies the role of labor and delivery as a cause of neonatal morbidity has been investigated. The relationship between umbilical artery pH as a measure of intrapartum asphyxia and newborn morbidity remains, however, unclear. This may be because there is no consensus on the definition of acidosis. Umbilical artery pH values defined as acidosis range from 7.20[6, 10] to 7.00.[3-5] Goldaber et al.[4] and Gilstrap et al.[3] proposed a pH of 7.00 as a reasonable definition of fetal acidemia. However, they did not further assess the group of neonates with an umbilical artery pH <7.00. Goodwin et al.[5] showed that in term acidotic neonates with an umbilical artery pH <7.00 there is an increase in multiorgan morbidity as the umbilical artery pH decreases. These results are in agreement with our findings. We found that neonates with an umbilical artery pH <7.00 required resuscitation and intubation more often, and they had significantly more chance of having respiratory, gastrointestinal, cardiovascular, and neurologic complications than did neonates with an umbilical artery pH >7.24.

Renal dysfunction was not significantly increased compared with the nonacidotic group. This contradicts with other findings.[10, 11] Different ways of defining renal dysfunction may be one of the causes. Our definition was consistent with that of Perlman et al.[10] (serum creatinine >90 μmol/L after third day of life). However, they include additional parameters such as hematuria and oliguria or anuria in the assessment of renal dysfunction.

Low et al.[7, 12] advised the use of the base deficit as a measure of asphyxia because it indicates the severity and duration of insufficient oxygen supply. They reported

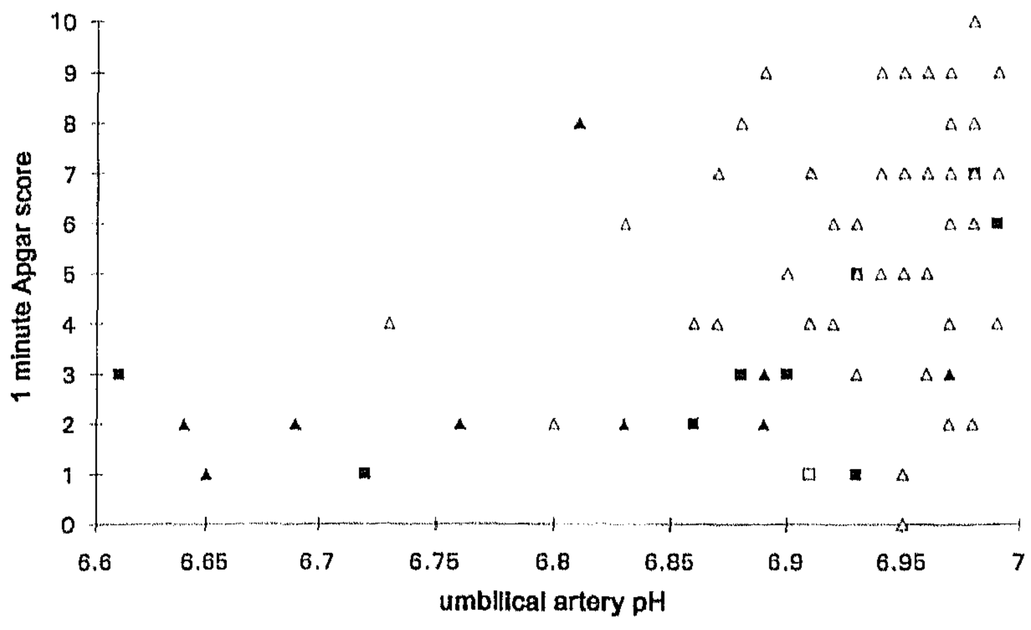

Fig. 2. Umbilical artery pH versus 1-minute Apgar score with subdivision for gestational age and neurologic dysfunction. *Solid square*, Preterm infants with neurologic complications; *open square*, preterm infants without neurologic complications; *solid triangle*, term infants with neurologic complications; *open triangle*, term infants without neurologic complications.

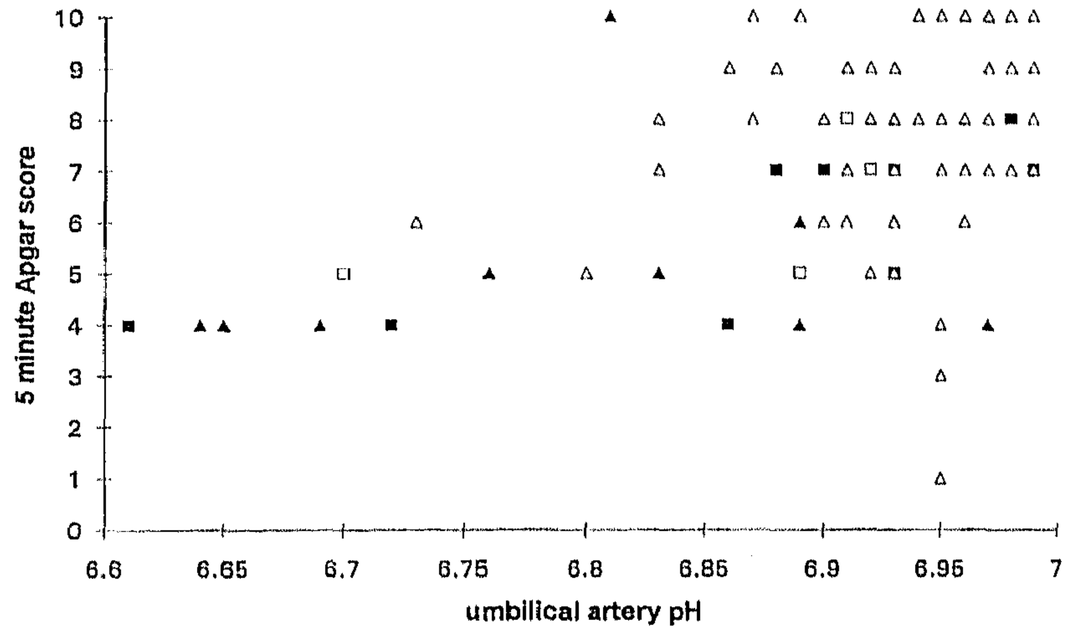

Fig. 3. Umbilical artery pH versus 5-minute Apgar score with subdivision for gestational age and neurologic dysfunction. *Solid square*, Preterm infants with neurologic complications; *open square*, preterm infants without neurologic complications; *solid triangle*, term infants with neurologic complications; *open triangle*, term infants without neurologic complications.

that only newborns (term and preterm) with metabolic acidosis (base deficit >16 mmol/L) showed an increase in neonatal complications. The respiratory component (hypercarbia) was considered unimportant in their analysis. Pure respiratory acidosis, defined as umbilical artery carbon dioxide tension >75 mm Hg, was not associated with either an increase in frequency or severity of newborn complications compared with nonacidotic controls. Goodwin et al.,[5] and the current results showed that neonatal complications are predominantly found when the base deficit is >15 mmol/L. They found that extreme hypercarbia (>100 mm Hg) was present in all neonates with major neurologic deficits, whereas no infants with pure metabolic acidosis had seizures. We found that neonates in the acidotic group who had neurologic problems all revealed a Pco_2 ≥65 mm Hg. Fetuses with prolonged intrapartum hypoxia (causing anaerobic metabolism to start) where placental gas exchange continues to be disrupted appear to be at the highest risk for neonatal morbidity. The absence of neurologic dysfunction in fetuses with pure metabolic acidosis (Fig. 1) may be explained by the restoring of oxygen supply (and placental carbon dioxide diffusion) at a time before tissue damage has occurred.

Twenty-seven percent of neonates born with a pH between 6.80 and 7.00 had no neonatal problems. Neonatal morbidity may not only depend on the duration and degree of exposure to hypoxia but also on the difference in fetal vulnerability determined by adequacy of adaptive responses (i.e., redistribution of blood flow to the vital organs), genetic factors, and maturity of the central nervous system.[13]

In this study the predictive value of a 1-minute Apgar ≤3 and a 5-minute Apgar score <7 in the acidotic group was high for neurologic dysfunction. Other authors also report sensitive predictions of newborn complications when severe acidemia and Apgar score are combined.[3, 14] Apgar scores should not be used as the sole index of asphyxia.[15] Using only low Apgar scores to indicate the need for acid-base assessment in the neonate would overestimate the role of acidemia as causative factor for neonatal morbidity. Therefore determination of the umbilical artery pH should be performed in every newborn.

Adverse events during labor and delivery appear to play only a limited role in the genesis of long-term neurologic disability.[16] Moreover, the scarcity of cerebral palsy (approximately 2 per 1000 deliveries) results in poor correlations with other measures of neonatal condition. This study has revealed that intrapartum asphyxia quantified by an umbilical artery pH <7.00 is not uncommon (in this study 1.3% of the total population), and a relationship with neonatal multiorgan morbidity was found. When adequate neonatal care is available, all the organ system effects may resolve in time. Only neonatal seizures have been found to be a marker for long-term neurologic sequelae.[17] However, these abnormal neonatal outcomes should be prevented, and therefore delivery of newborns with an umbilical artery pH <7.00 has to be avoided.

Further studies should determine the degree of asphyxia or acidemia that can be handled by the neonate without an increase in neonatal complications compared with nonacidotic controls.

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