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Types of intrapartum hypoxia in the newborn at term with metabolic acidemia: A retrospective study

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Abstract

Introduction: In the most recent recommendations of the International Federation of Gynecology and Obstetrics (FIGO), a chapter was dedicated to the physiological approach and to the description of fetal mechanisms developed to respond to hypoxia. Our objective was to classify the type of hypoxia in the case of metabolic acidemia and to describe the order of appearance of fetal heart rate abnormalities in cases of gradually evolving hypoxia.

Material and methods: 132 neonates born between 2018 and 2020 with acidemia were included. We excluded preterm birth, fetuses with congenital anomaly and twin pregnancies. Intrapartum cardiotocography traces were assigned to one of these four types of labor hypoxia: acute, subacute, gradually evolving and chronic hypoxia. For gradually evolving hypoxia, fetal heart rate abnormalities were described according to the FIGO classification.

Results: 36 cardiotocography traces (27.3%) were classified as acute hypoxia, 14 (10.6%) as subacute hypoxia, and 3 (3.2%) as chronic hypoxia; gradually evolving hypoxia occurred in 62 cases (47%). In 77.4% of cases of gradually evolving hypoxia, deceleration was the first anomaly to appear, with loss of variability and bradycardia appearing later. Increased fetal heart rate was observed immediately after late deceleration in 46.8% of cases and was followed by a loss of variability or saltatory rhythm in 37.1% of cases.

Conclusions: In cases of metabolic acidemia at term, the most frequent situation observed was gradually evolving hypoxia, with an initial occurrence of decelerations. The sequence of fetal heart rate modifications was variable.

KEYWORDS

chemoreflex, deceleration, fetal heart rate, hypoxia, intrapartum CTG, neonatal acidemia, variability

Abbreviations: CTG, cardiotocography; FHR, fetal heart rate; FIGO, International Federation of Gynecology and Obstetrics.

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1 | INTRODUCTION

Evaluation of fetal well-being during labor is assessed by intermittent or continuous cardiotocography (CTG).¹ The analysis of fetal heart rate (FHR) has an inter- and intra-observer variability, despite the use of many classifications,^{2,3} and it has resulted in a significant increase in intrapartum cesarean section and operative vaginal delivery rates, without improving neonatal outcomes.⁴ Furthermore, the prediction of neonatal acidemia or cerebral palsy with CTG analysis is poor to moderate.^{5,6}

Therefore, a more physiological approach is proposed by many authors to better understand the fetal response to the stress during labor.⁷⁻⁹ In the most recent recommendations of the International Federation of Gynecology and Obstetrics (FIGO), a chapter was dedicated to the physiological approach and to the description of fetal mechanisms developed to respond to hypoxia.^{10,11} Hypoxia is described by Pinas & Chandraran⁷ using the following four categories: type 1, corresponding to acute hypoxia; type 2, corresponding to subacute hypoxia; type 3, as gradually evolving hypoxia; and type 4, as chronic hypoxia.

However, the physiological interpretation is mainly derived from experimental models in sheep (ewes),¹²⁻¹⁵ and few studies clearly describe the sequence of FHR abnormalities in cases of progressive hypoxia.¹⁶ Thus, the purpose of this study was to evaluate the type of hypoxia and the FHR evolution in cases of intrapartum gradually evolving hypoxia in case of metabolic acidemia.

2 | MATERIAL AND METHODS

This was a monocentric (Lille, France, level III maternity hospital with 5500 births per year), retrospective, observational study, from January 2018 to December 2020. We included all women with living newborns with arterial umbilical pH of <7.0. The exclusion criteria were premature birth (<37 weeks), the presence of a severe congenital malformation or a twin pregnancy.

The CTG traces were systematically evaluated from labor onset until delivery and, according to the physiological interpretation,⁷ the FHR features were used to assign each case to one of the following four subtypes of labor hypoxia:

Acute hypoxia, characterized by a sudden prolonged deceleration lasting more than 10 min under 80 bpm and requiring birth within 15 min.

Subacute hypoxia, corresponding to hypoxia developing between 30 and 60 min, characterized by the deepening and widening of ongoing decelerations, whereby the fetus spends more time within the deceleration (>90 s) than at baseline (<30 s).

Gradually evolving hypoxia, with a slower course of a few hours with the onset of different successive FHR abnormalities, which allowed time for FHR abnormalities to appear. Pinas & Chandraran⁷ described the sequence of this type as onset of deceleration, loss of accelerations, followed by a baseline heart rate increase, then a loss of variability, and finally heart failure with terminal bradycardia.

Key message

In the case of severe neonatal acidosis, gradually evolving hypoxia is the most frequent type of hypoxia observed, with an initial occurrence of decelerations.

Chronic hypoxia, corresponding to exposure of the fetus over a prolonged period to hypoxia, often associated with uteroplacental insufficiency. The features observed on the CTG trace in chronic hypoxia include an increase in the baseline rate with reduced variability and the presence of shallow decelerations.

FHR was performed by external fetal monitoring and analyzed with a scrolling speed of 1 cm/min by two different investigators (a fellow and an expert trained in the pathophysiology interpretation of the CTG) at the same time. Once the FHRs were classified into the four different categories described, the sequence of FHR abnormalities was determined for the gradually evolving hypoxia type. Features were noted as described in the FIGO classification¹⁷ in seven different categories:

- Variable deceleration, reflecting the baroreflex response, defined as “decelerations that exhibit a rapid drop (onset to nadir in less than 30 s), good variability within the deceleration, rapid recovery to the baseline, varying size, shape, and correlation to uterine contractions”.
- Late deceleration, reflecting the chemoreflex response, defined as decelerations with a gradual onset and/or a gradual return to the baseline and/or reduced variability within the deceleration. Gradual onset and return occur when more than 30 s elapses between the beginning/end of a deceleration and its nadir. When contractions are adequately monitored, late decelerations start more than 20 s after the onset of a contraction, have a nadir after the acme, and a return to the baseline after the end of the contraction.
- Loss of accelerations.
- Increase of baseline heart rate (increasing 20 bpm above the fetal heart baseline) or tachycardia (fetal heart baseline over 160 bpm lasting more than 10 min).
- Loss of variability (amplitude below 5 bpm for more than 50 min) or a saltatory pattern (a bandwidth value exceeding 25 bpm, lasting more than 30 min).
- Return to baseline.
- Bradycardia (baseline value below 100 bpm, lasting more than 10 min).

Umbilical artery pH is measured routinely in our center. Blood samples were collected into pre-heparinized syringes after cord clamping and within 5 min after birth, and were analyzed in the labor ward with an ABL 90 Flex Plus analyzer (Radiometer).^{18,19}

For cesarean sections during labor, the degree of emergency was defined according to a color code (green, orange and red) as described.^{20,21} Late-term pregnancy was defined by a delivery after 41 weeks of gestation.

2.1 | Statistical analysis

Qualitative variables were described in terms of frequency and percentage. Numerical variables were described as the mean and standard deviation or as the median and interquartile range. The normality of numerical variables was checked graphically and tested with the Shapiro–Wilk test. Statistical analyses were performed with SAS software (SAS Institute version 9.4).

2.2 | Ethics statement

This study was approved on June 25, 2020, by CEROG, Ethics Committee for Research in Obstetrics and Gynecology (CEROG 2020-OBST-0506).

3 | RESULTS

From 15045 live births after 22 weeks during the study period, 195 (1.3%) neonates had an umbilical cord pH under 7.0 (Figure 1).

Sixty-three were excluded due to prematurity ($n = 52$), severe congenital anomalies ($n = 5$) or twin pregnancy ($n = 6$). Among the remaining 132 cases, 36 (27.3%) were interpreted as acute hypoxia, 14 (10.6%) as subacute hypoxia, 62 (47%) as gradually evolving hypoxia, and three (3.2%) as chronic hypoxias. For 16 cases (12.1%), interpretation of FHR was impossible because of the poor quality of the signal or rapid delivery. In one case, FHR was normal during labor.

Table 1 presents the maternal, labor and neonatal characteristics. Almost half of the women were nulliparous (48.8%), with prior cesarean section in 22.7% of cases, and 17% had a body mass index $>30\text{kg/m}^2$. About one-fifth of the population were late-term pregnancy (22%). Labor was induced in 36.4%.

In more than one-third of cases, oxytocin was used during labor and in 39.2% of cases, a uterine hyperstimulation occurred (with or without oxytocin). Cesarean during labor occurred in 60 cases, mostly in code red (63.3%). The characteristics of the gradually evolving hypoxia population are mostly similar to the global population (Table S1). Hyperthermia occurred in five cases. In only two cases, intrauterine infection was confirmed with placenta examination. In those two cases, FHR abnormalities occurred before diagnosis of hyperthermia and late deceleration were observed first (before tachycardia).

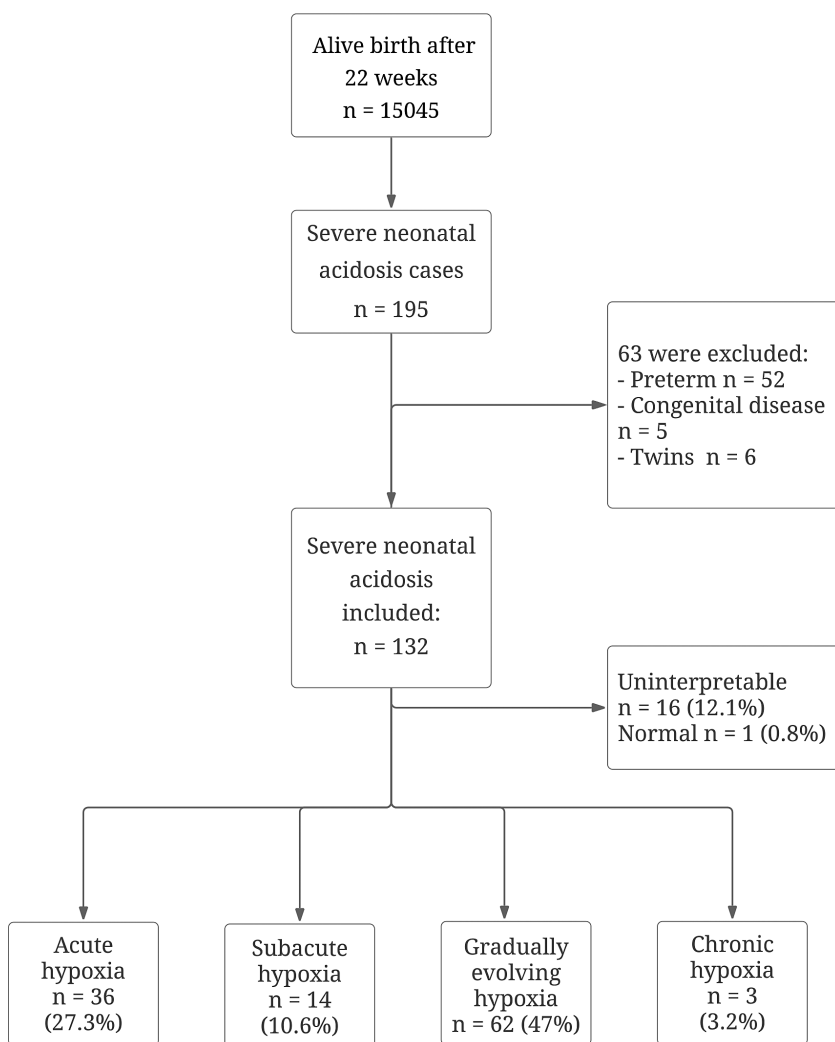


FIGURE 1 Flow chart.

TABLE 1 Maternal, labor and neonatal characteristics of the global population

Characteristics	Global population n = 132
Maternal age, years (mean ± SD)	30.5 ± 5
Body mass index, kg/m ²	26.0 ± 6.1
Body mass index >30 kg/m ²	23 (17.42)
Nulliparous	64 (48.8)
Smoking	9 (6.8)
Diabetes	5 (3.8)
Scarred uterus	30 (22.7)
History of neonatal death	3 (2.3)
Gestational diabetes requiring insulin	15 (12.0)
Preeclampsia	3 (2.3)
Small-for-gestational age	13 (9.9)
Oligo/anamnios	9 (6.8)
Gestational age at birth, weeks	37.8 (36.8–38.9)
Prolonged pregnancy	29 (22.0)
Breech presentation	11 (8.3)
Labor induction	48 (36.4)
Hyperthermia	5 (3.8)
Meconium amniotic fluid	19 (14.6)
Oxytocin use	39 (29.5)
Uterine hyperstimulation	51 (39.2)
Elective cesarean	8 (13.3)
Cesarean during labor	
Green code	4 (6.7)
Orange code	10 (16.7)
Red code	38 (63.3)
Operative vaginal delivery	47 (35.6)
Uterine rupture	2 (1.5)
Cord prolapse	10 (7.6)
Shoulder dystocia	13 (9.8)
APGAR score <7 at 5 min	18 (14.0)
Lactates, mmol/L (mean ± SD)	10.5 ± 2.3
Base excess, mmol/L (mean ± SD)	13.9 ± 2.8
Base excess ≥12 mmol/L	95 (76.00)
Respiratory distress	53 (40.5)
Neonatal care unit transfer	21 (15.9)
Hypothermia	4 (3.1)
Death	3 (2.3)
Birthweight, g (mean ± SD)	3366 ± 532.5
Male neonate	79 (60.3)

Note: Data are presented as number (percentage) or mean ± standard deviation or median (interquartile).

Figure 2 illustrates the flow of the occurrence of the different FHR abnormalities. In 77.4% (48/62) of cases, a deceleration was the first anomaly to occur, with a variable deceleration occurring in

40.3% (25/62), and a late deceleration in 37.1% (23/62). The second most frequent anomaly was the occurrence of late decelerations (24/59 cases, 40.7%). In those cases, the previous anomaly was a variable deceleration ($n = 20$), a loss of acceleration ($n = 2$), a loss of variability ($n = 1$) or an increase in baseline heart rate ($n = 1$). A loss of variability and bradycardia occurred later in the FHR anomaly sequence. Among all the FHR abnormalities noted, whatever the sequence, late deceleration was present in 57 cases (91.9%) and FHR increased in 46 cases (74.2%). Loss of variability or saltatory rhythm was detected in 42 cases (67.7%) and bradycardia in only 26 cases (41.9%).

The sequence of appearance of FHR abnormalities is shown in two cases with the complete sequence described by Pinas & Chandraran⁷ (Table S2). The most frequent sequence of three different types of anomalies was (1) late deceleration, (2) FHR increase and (3) loss of variability or saltatory rhythm in 24.2% ($n = 15$). The most frequent sequence with four types of anomalies occurred in 14.5% ($n = 9$) of cases and was (1) variable deceleration, (2) late deceleration, (3) FHR increase, and (4) loss of variability or saltatory rhythm. Thus, an increase in FHR was observed just after a late deceleration in 46.8% ($n = 29$), followed by loss of variability or saltatory rhythm in 37.1% ($n = 23$).

4 | DISCUSSION

In cases of neonates born with metabolic acidemia at term, the most frequent situation observed was gradually evolving hypoxia. In that situation, the first FHR abnormality was deceleration in 77.4% of cases. The sequence of events preceding metabolic acidemia was variable, according to our findings. The most frequent sequence was late deceleration, followed by increased FHR and then loss of variability or saltatory rhythm (24.2%).

Gradually evolving hypoxia is the most frequent type of hypoxia observed in acidemic neonates, and the same proportions were found in a recent study.²² Indeed, Di Pasquo et al. found gradually evolving hypoxia in more than the half of their cohorts; they also noticed that this type of hypoxia is associated less with poor neonatal outcomes and that fetuses can tolerate much more time under hypoxic insult when hypoxia evolves gradually. The originality of our study is the CTG trace analyses describing the order of appearance of the different patterns in the case of gradually evolving hypoxia.

The first anomaly observed was the variable or late deceleration type, according to the FIGO classification. This is the first adaptive mechanism of the fetus to hypoxia, induced by uterine contraction by reducing its myocardial load. Indeed, blood flow decreases by 60% during the occurrence of uterine contractions, via uterine placental vessels and umbilical cord compression.⁹ The 2015 FIGO recommendations classify FHR decelerations as variable deceleration for the baroreflex type and late deceleration for the chemoreflex type.¹⁰ This point of view is discussed by physiologists and in the literature.²³ Indeed, the precise role of the baroreflex has been discussed in the literature for many years²⁴ and seems immature in the fetus. Moreover, according to

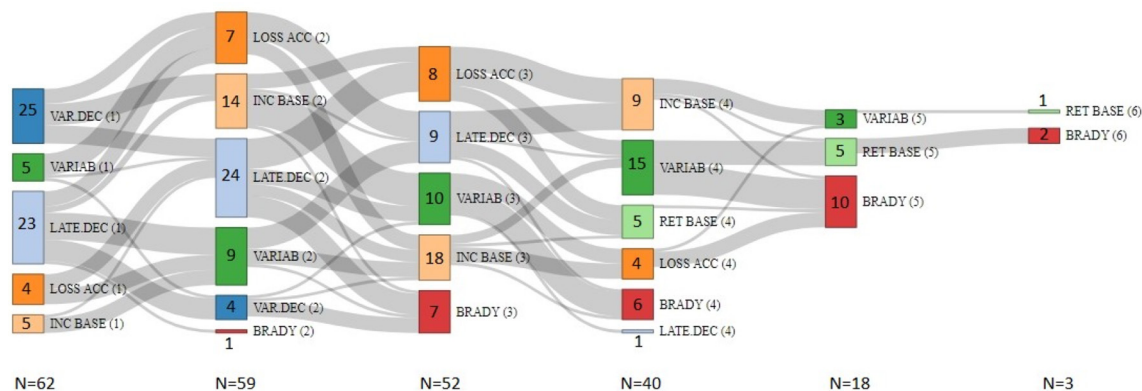


FIGURE 2 Schematic diagram of the order of appearance of the fetal heart rate (FHR) abnormalities.

Lear et al.,¹³ the chemoreflex is the homeostasis keeper. Other authors also suggest a Bezold-Jarish reflex in response to uterine contraction,²³ but this mechanism is also criticized.²⁵ Finally, FHR decelerations are, in this population, the first fetal adaptation sign and were mostly followed by FHR increases. Indeed, the increase in the baseline after late deceleration represents the response to the hypoxic stress.¹⁷ Chemoreceptors receive the signal for a decrease in the amount of oxygen in blood vessels and activate the sympathetic nervous system. The latter stimulates catecholamine production in the adrenal gland, inducing peripheral vasoconstriction and a positive chronotropic effect on myocardial cells, resulting in an increase in the basal heart rate. This FHR increase reflects a compensatory state, unlike the loss of variability or saltatory rhythm, which reflects the inability of the fetus to counteract this hypoxic stress fully. In our study, it was one of the last FHR abnormalities to appear before terminal bradycardia in 42.3% of cases, and in more than 40% of cases, it appeared after an increase in FHR. There were no identical full sequences found in the cases studied, probably because the sequence was variable according to the context, and because there was an intervention before the complete sequence could appear.

Gradually evolving hypoxia was observed in most cases, probably linked to the fact that an understanding of the mechanisms and FHR interpretation is not simple and the decision about a cesarean delivery not always straightforward. Few cases of chronic hypoxia were examined, probably because of the exclusion of preterm and congenital anomaly cases.

The main strength of this analysis is its originality. To date, a precise description of FHR in cases of rapidly progressive hypoxia has not been published.^{26–28} In fact, the sequences described mainly come from experimental studies in ewes using models of occlusion of varying lengths of the umbilical cord. Even though the ewe is the species most closely related to humans, the experimental conditions do not exactly mimic labor, and the placentation is different.^{29,30} Nevertheless, the current study has several limitations. It is a retrospective, unicentric study, with a limited number of cases. In addition, the interpretation of rhythms is subject to intra- and interobserver interpretation variability, and to knowledge of the outcome, namely, metabolic acidemia.^{3,31} Finally, the type of hypoxia is not universally accepted and the FIGO document does not mention these patterns. However, their use could be interesting and a recent

publication showed that type of hypoxia was associated with occurrence of neurological complications.²²

5 | CONCLUSION

In cases of metabolic acidemia at term, the most frequent situation observed was gradually evolving hypoxia, with an initial occurrence of decelerations. The sequence of FHR modifications was variable and could be one of the limits of FHR analysis to predict neonatal acidemia.

AUTHOR CONTRIBUTIONS

LD, CG and ED conceived and designed the study. LD and CG performed the literature search, checked the data and wrote the article. LD, CG and AS performed data extraction. ED and CM performed the data analysis. LG, DS and VHD were responsible for the revision.

CONFLICT OF INTEREST

None declared.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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