Received: 7 August 2020 | Revised: 19 September 2020 | Accepted: 22 September 2020

DOI: 10.1111/aogs.14007

ORIGINAL RESEARCH ARTICLE

Intrapartum zigzag pattern of fetal heart rate is an early sign of fetal hypoxia: A large obstetric retrospective cohort study

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Funding information
Mikko Tarvonen has received a grant for his doctoral studies from Olga & Vilho Linnamo Foundation. Sture Andersson has received research grants from a Special Governmental Subsidy for Clinical Research, Finska Läkaresällskapet, and the Foundation for Pediatric Research in Finland.

Abstract

Introduction: The aim of the present study was to identify possible associations of fetal heart rate (FHR) patterns during the last 2 hours of labor with fetal asphyxia expressed by umbilical artery acidemia at birth and with neonatal complications in a large obstetric cohort.

Material and methods: Cardiotocographic recordings from 4988 singleton term childbirths over 1 year were evaluated retrospectively and blinded to the pregnancy and neonatal outcomes in a university teaching hospital in Helsinki, Finland. Umbilical artery pH, base excess and pO_2, low Apgar scores at 5 minutes, need for intubation and resuscitation, early neonatal hypoglycemia, and neonatal encephalopathy were used as outcome variables. According to the severity of the neonatal complications at birth, the cohort was divided into three groups: no complications (Group 1), moderate complications (Group 2) and severe complications (Group 3).

Results: Of the 4988 deliveries, the ZigZag pattern (FHR baseline amplitude changes of >25 bpm with a duration of 2-30 minutes) occurred in 11.7%, late decelerations in 41.0%, bradycardia episodes in 52.9%, reduced variability in 36.7%, tachycardia episodes in 13.9% and uterine tachysystole in 4.6%. No case of saltatory pattern (baseline amplitude changes of >25 bpm with a duration of >30 minutes) was observed. The presence of the ZigZag pattern or late decelerations, or both, was associated with cord blood acidemia (odds ratio [OR] 3.3, 95% confidence interval [CI] 2.3-4.7) and severe neonatal complications (Group 3) (OR 3.3, 95% CI 2.4-4.9). In contrast, no significant associations existed between the other FHR patterns and severe neonatal complications. ZigZag pattern preceded late decelerations in 88.7% of the cases. A normal FHR preceded the ZigZag pattern in 90.4% of the cases, whereas after ZigZag episodes, a normal FHR pattern was observed in only 0.9%.

Conclusions: ZigZag pattern and late decelerations during the last 2 hours of labor are significantly associated with cord blood acidemia at birth and neonatal complications. The ZigZag pattern precedes late decelerations, and the fact that normal FHR pattern

Abbreviations: BE, base excess; CI, confidence interval; CTG, cardiotocography; FHR, fetal heart rate; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value; UA, umbilical artery.

precedes the ZigZag pattern in the majority of the cases suggests that the ZigZag pattern is an early sign of fetal hypoxia, which emphasizes its clinical importance.

KEYWORDS

cardiotocography, fetal heart rate, fetal hypoxia, fetal monitoring, neonatal complications, saltatory pattern, ZigZag pattern

1 | INTRODUCTION

Cardiotocography (CTG) is the most common fetal surveillance method during labor. The main purpose of CTG registration is to identify fetuses at risk of hypoxia during labor. Ideally, intrapartum fetal surveillance should predict and diagnose fetal hypoxia before fetal compromise occurs.

Despite substantial utilization of the CTG, its use is related with uncertainty and disagreement about effectiveness,[1,2] recognition,[3] and classification[4] of fetal heart rate (FHR) abnormalities. Abnormal CTG registrations are common during the last 2 hours of labor.[5] Moreover, inter- and intraobserver agreement is generally low.[6,7] Misinterpretation of signs of fetal hypoxia and failure to act timely on abnormal CTG patterns are leading causes of severe intrapartum asphyxia among term infants.[8,9] In addition, unnecessary operative interventions based on wrong interpretation of FHR patterns can increase the risk of maternal complications[1] and may have adverse effects on the newborn infant.[10]

The aim of the present study was to examine possible associations of FHR patterns during the last 2 hours of labor with fetal asphyxia expressed by umbilical artery (UA) acidemia at birth and with clinical outcomes of the newborn infant in a large obstetric cohort.

Key message

Intrapartum ZigZag pattern and late decelerations are significantly associated with cord blood acidemia and neonatal complications. ZigZag pattern precedes late decelerations in the majority of the cases and is an early sign of fetal hypoxia, which emphasizes its clinical importance.

2 | MATERIAL AND METHODS

We evaluated retrospectively, continuously monitored FHR tracings from all eligible singleton childbirths with gestational age of ≥37 weeks in a 1-year cohort at the Maternity Hospital of the Helsinki University Hospital in 2012. In the Capital Region of Finland, the Maternity Hospital predominantly took care of low-risk childbirths, excluding, for example, preterm births <33 weeks of gestation and childbirths of women with type 1 diabetes, who were treated at the tertiary care center of the Helsinki University Hospital. All women in the cohort were in the active phase of labor with regular uterine contractions. After exclusion for preterm labor, noncephalic presentation, elective cesarean section, twin delivery, cases without CTG registration or UA blood gas results, and cases with major congenital malformations, the study cohort comprised of 4988 deliveries (Figure 1).

In the cohort, FHR was recorded via a scalp electrode in 91.4% of the cases. UA blood was collected from a double-clamped cord for pH and blood gas analyses in all cases. Pregnancy and intrapartum maternal, fetal and neonatal data were obtained from the patient records.

Two experienced perinatologists (SS and KT) evaluated the CTG recordings independently and blinded to the pregnancy and neonatal outcomes in order to assess the following CTG changes: ZigZag pattern, saltatory pattern, late decelerations, episodes of tachycardia and bradycardia, reduced FHR variability and uterine tachysystole. Each of the CTG changes was considered separately and only CTG changes that were concordant between the two perinatologists were used in the study. The findings were classified according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines on intrapartum fetal monitoring, with the exception of the ZigZag pattern (see below).[11,12]

Normal baseline FHR was defined as a baseline between 110 and 160 bpm. Normal FHR variability was defined as baseline amplitude changes of 5-25 bpm. ZigZag pattern was defined as FHR baseline amplitude changes of >25 bpm with a duration of 2-30 minutes.[12] The definition of saltatory pattern was FHR baseline amplitude changes of >25 bpm with a duration of >30 minutes. Late decelerations were defined as U-shaped decreases of FHR of >15 bpm occurring late in relation to uterine contractions. In the presence of a tracing without accelerations and reduced variability, the definition of late decelerations included also those with an amplitude of 10-15 bpm. Tachycardia was defined as a baseline frequency >160 bpm lasting for more than 10 minutes, and bradycardia episodes as a baseline frequency <100 bpm lasting for more than 3 minutes. The reduced variability was defined as an amplitude <5 bpm for >10 minutes, and that of uterine tachysystole as the occurrence of more than five contractions during a 10-minute period.

Apgar scores at 1 and 5 minutes were routinely assessed. The pH, base excess (BE) and pO_2 were measured from UA blood at birth by Siemens RAPIDLab 248/348 Blood Gas System (Siemens Healthineers, Erlangen, Forchheim, Germany). The lowest plasma glucose value obtained during the first 24 hours after birth was used for the evaluation of neonatal hypoglycemia.

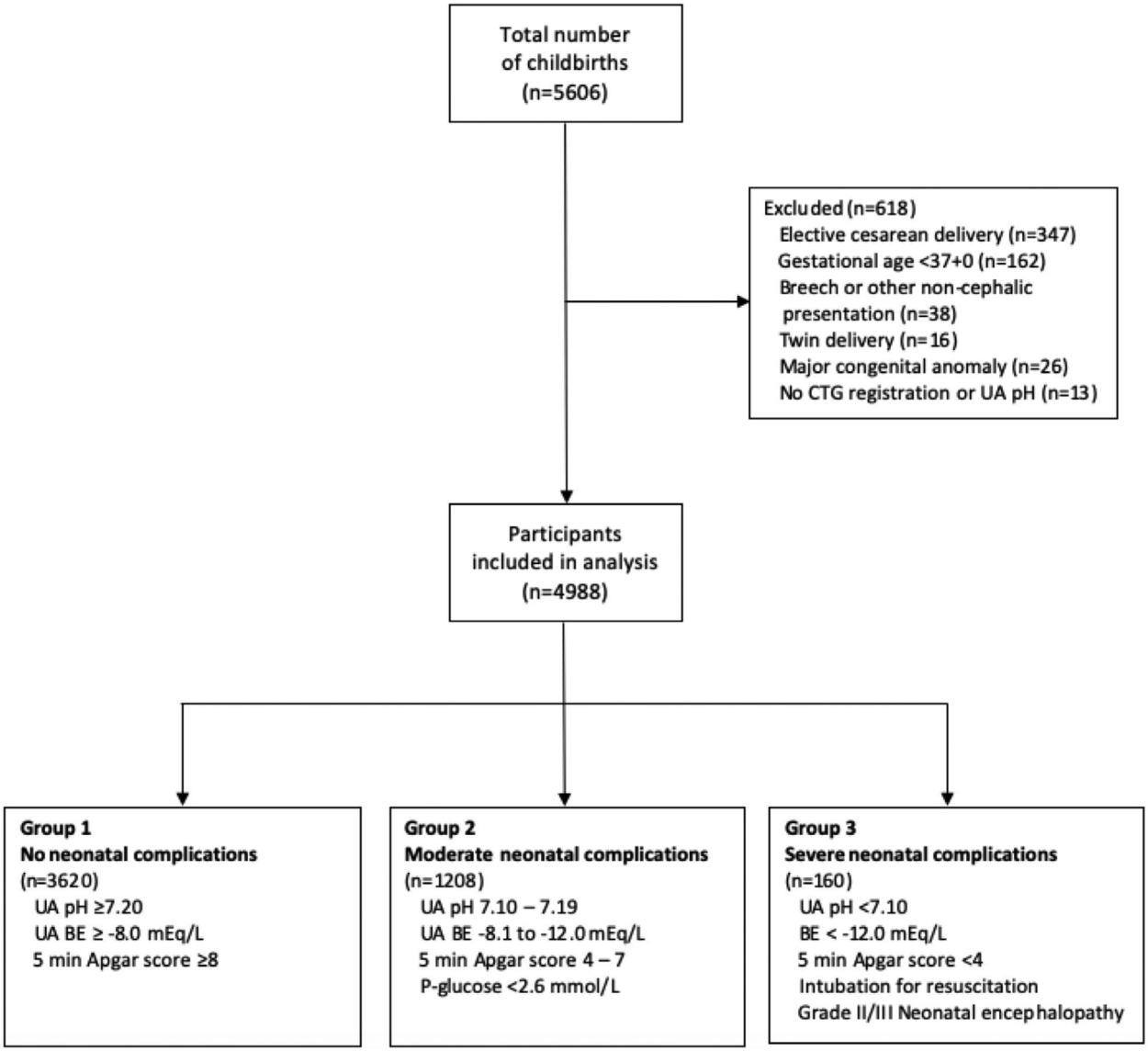

FIGURE 1 Flow chart of the study participants and grouping of the newborn infants according to the severity of complications. BE, base excess; CTG, cardiotocography; P-glucose, plasma glucose; UA, umbilical artery

According to the severity of the neonatal complications at birth, the cohort was divided into three groups: Group 1 (n = 3620) consisting of cases with no neonatal complications (ie UA pH ≥7.20 and UA BE ≥−8.0 mEq/L and 5-minute Apgar score ≥8) and no hypoglycemia, Group 2 (n = 1208) consisting of cases with moderate neonatal complications (ie UA pH 7.10-7.19 and/or UA BE −8.1 to −12.0 mEq/L and/or 5-minute Apgar score 4-7 and/or plasma glucose <2.6 mmol/L during the first 24 hour) and Group 3 (n = 160) consisting of cases with severe neonatal complications (ie UA pH <7.10 and/or BE <−12.0 mEq/L and/or 5-minute Apgar score <4 and/or intubation for resuscitation and/or Grade II/III Neonatal encephalopathy) (Figure 1).

Continuous variables were analyzed by analysis of variance (ANOVA) and Mann-Whitney U-test. Pearson's chi-square and Fisher's exact probability test were used for categorical variables. In Tables 1 and 2, the Kruskal-Wallis test was used to compare maternal and neonatal variables among the three neonatal outcome groups. The differences in FHR patterns and neonatal outcome variables were measured by independent samples t test (Table 2). In addition, logistic regression analysis was performed with IBM SPSS 26.0 (IBM Corp., Armonk, NY, USA). All tests were two-sided. Values of P <.05 were considered statistically significant.

2.1 | Ethical approval

The study was approved by the Institutional Review Board and the Ethics Committee of the Helsinki University Hospital, Finland (no. 361/13/ 03.03.2010, TMK03§210/ 15.12.2010).

3 | RESULTS

From the 4988 CTG recordings a total of 20 129 CTG changes were identified. The overall concordance of CTG patterns between the

TABLE 1 Maternal and delivery-related characteristics by neonatal outcome groups

Maternal variables	Group 1 No neonatal complications	Group 2 Moderate neonatal complications	Group 3 Severe neonatal complications	*P* value
Number	3620 (72.6)	1208 (24.2)	160 (3.2)	
Age (y)	30.9 (± 5.2)	31.0 (± 5.1)	32.6 (± 4.9)	<.001
Maternal age ≥35 years	917 (25.3)	266 (22.0)	56 (35.0)	.001
Nulliparous	1883 (52.0)	720 (59.6)	104 (65.0)	<.001
Multiparous	1737 (48.0)	488 (40.4)	56 (35.0)	
Gestational age at delivery (wk)	40.2 (± 1.0)	40.2 (± 1.1)	40.5 (± 1.2)	.03
Smoking	340 (9.4)	112 (9.3)	14 (8.8)	.96
Preeclampsia	109 (3.0)	36 (3.0)	1 (0.6)	.21
Gestational diabetes				
Diet-treated	397 (11.0)	146 (12.0)	26 (16.3)	.16
Metformin-treated	34 (0.9)	16 (1.3)	1 (0.6)	
Maternal fever at delivery ≥38.0°C	75 (2.0)	31 (2.6)	11 (6.9)	<.001
Labor type				
Spontaneous onset	2836 (78.3)	914 (75.7)	116 (72.5)	.05
Induction	784 (21.7)	294 (24.3)	44 (27.5)	
Mode of delivery				
Spontaneous vaginal	2963 (81.9)	952 (78.8)	2227 (63.1)	.002 .01
Vacuum extraction	346 (9.6)	144 (11.9)	25 (15.6)	
Cesarean (elective excluded)	311 (8.6)	112 (9.3)	18 (11.3)	

Data are mean ± SD or number (%).

P value expresses the difference between Groups 2 and 3.

two perinatologists was 86.3%. Only concordant CTG changes were used in the analyses. For the separate CTG changes, the concordance was as follows: 87.2% for ZigZag pattern, 82.1% for late decelerations, 92.1% for tachycardia episodes, 94.0% for bradycardia episodes, 78.3% for reduced variability and 85.4% for uterine tachysystole.

No case of saltatory pattern was observed.

Tables 1 and 2 show the clinical characteristics of the cohort. Most pregnancies (84.7%) were uncomplicated, with no maternal or fetal prelabor risk factors. The incidence of FHR changes according to the neonatal outcome groups is shown in Table 2. FHR changes occurred in Group 1 in 75.9% (2749/3620), in Group 2 in 87.1% (1052/1208) and in Group 3 in 99.4% (159/160) of the cases during the last 2 hours of labor. In Group 3, FHR changes occurred significantly more frequently than in Group 1 (P <.001) or Group 2 (P <.001). The risk for Group 3 was 24.2-fold higher (95% confidence interval [CI] of odds ratio [OR], 6.0-97.6) in cases with CTG changes than in cases with normal intrapartum CTG. Furthermore, taking all the groups together, none of the 1133 (22.7%) cases with normal CTG had cord blood acidemia at birth. The negative predictive value of normal CTG tracing for severe neonatal complications (Group 3) was 99.9%.

The presence of ZigZag pattern or late decelerations, or both, in the CTG recordings during the last 2 hours of labor significantly increased the likelihood of severe complications (Group 3) in newborn infants (OR 3.3, 95% CI 2.4-4.9) (Table 2). In contrast, no significant association was found among cases with episodes of bradycardia, tachycardia or reduced variability and severe neonatal complications (Group 3) (Table 2). A CTG recording with both ZigZag pattern and late decelerations occurred in 76.9% (123/160) of Group 3 cases and in only 5.6% (201/3620) of Group 1 cases (P <.001).

In the total study population, late decelerations occurred in 91.2% (531/582) of the CTG recordings together with ZigZag pattern (Figure 2). ZigZag pattern preceded late decelerations in 88.7% (471/531) of the cases. A normal FHR preceded the ZigZag pattern in 90.4% (526/582) of the cases, whereas after ZigZag episodes, a normal FHR pattern was observed in only 0.9% (5/582).

The presence of ZigZag pattern or late decelerations, or both, was associated with cord blood academia: UA pH <7.10 and/or UA

TABLE 2 Neonatal characteristics and fetal heart rate patterns during the last 2 hours in labor in three neonatal outcome groups

Neonatal variables	Group 1 No neonatal complications	Group 2 Moderate neonatal complications	Group 3 Severe neonatal complications	*P* value	Differences (95% CI) Group 1 vs Group 3	Differences (95% CI) Group 2 vs Group 3
Number	3620 (72.6)	1208 (24.2)	160 (3.2)			
Neonate sex						
Female	1813 (50.1)	567 (46.9)	72 (45.0)	.09		
Male	1807 (49.9)	641 (53.1)	88 (55.0)			
Birthweight (g)	3545 (± 470)	3509 (± 474)	3459 (± 442)	.005		
Birthweight z-score (SD units)	−0.1 (± 1.0)	−0.2 (± 1.0)	−0.4 (± 1.0)	.002		
Post-term (≥42.0 wk)	333 (9.2)	132 (10.9)	23 (14.4)	.03		
FHR patterns						
ZigZag pattern	241 (6.7)	278 (23.0)	63 (39.4)	<.001	32.7 (25.4–40.5)	16.4 (8.7–24.4)
Late decelerations	1358 (37.5)	576 (47.7)	111 (69.4)	<.001	31.9 (24.2–38.7)	21.7 (13.7–28.9)
Bradycardia episodes	1988 (54.9)	572 (47.4)	79 (49.4)	<.001	−5.5 (−13.4 to 2.3)	2.0 (−6.1 to 10.2)
Reduced variability	1322 (36.5)	437 (36.2)	72 (45.0)	.09	8.5 (0.8–16.4)	8.8 (0.8–17.0)
Tachycardia episodes	552 (15.2)	119 (9.9)	23 (14.4)	<.001	−0.8 (−5.6 to 5.5)	4.5 (−0.4 to 11.0)
Uterine tachysystole	176 (4.9)	41 (3.4)	11 (6.9)	.04	2.0 (−1.1 to 7.1)	3.5 (0.3–8.6)
5-min Apgar score <7	NA	NA	12 (7.5)	NA	NA	NA
UA pH	7.29 (± 0.06)	7.18 (± 0.06)	7.06 (± 0.05)	<.001	0.227 (0.218–0.236)	0.116 (0.107–0.126)
UA BE (meq/L)	−2.8 (± 1.9)	−6.2 (± 2.3)	−8.9 (± 3.4)	<.001	6.10 (4.63–5.02)	2.70 (2.30–3.20)
UA pO_2 (kPa)	3.2 (± 1.0)	3.0 (± 0.9)	2.7 (± 1.0)	<.001	0.54 (0.38–0.69)	0.32 (0.14–0.45)
UA acidosis						
UA pH <7.10	NA	NA	146 (91.3)	NA	NA	NA
UA BE <−12.0 (meq/L)	NA	NA	39 (24.4)	NA	NA	NA
Hypoglycemia, P-glucose <2.6 mmol/L	NA	62 (5.1)	31 (19.4)	<.001	NA	14.3 (8.7–21.2)
Intubation for resuscitation	NA	NA	17 (10.6)	NA	NA	NA
NICU admission	119 (3.3)	74 (6.1)	31 (19.4)	<.001	16.1 (10.7–22.9)	13.3 (7.7–20.2)
Neonatal encephalopathy	NA	NA	2 (1.3)	NA	NA	NA

Data are mean ± SD or number (%).

P value expresses the difference between Groups 2 and 3.

Differences for FHR patterns and neonatal outcome variables are %-units (95% CI), with the exception of UA blood gases, which are expressed as variable units (95% CI).

BE, base excess; FHR, fetal heart rate; NA, not applicable due to selection criteria; NICU, neonatal intensive care unit; UA, umbilical artery.

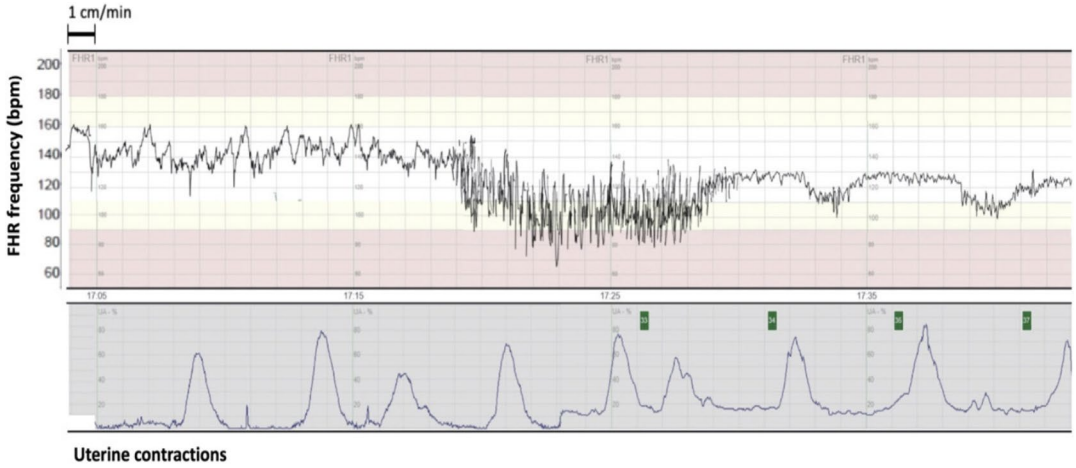

FIGURE 2 Intrapartum CTG recording of a 35-year-old nullipara at 42^{+1} weeks' gestation. At left, normal baseline fetal heart rate (FHR) with normal variability and accelerations followed by a 10-minute ZigZag pattern. The ZigZag episode is followed by repetitive late decelerations and decreased FHR baseline. Normal frequency of uterine contractions (2-3 contractions in 10-minute periods). ZigZag pattern occurred 105 min before a male fetus was spontaneously born in vertex position. Umbilical cord blood gas analysis showed acidemia: umbilical artery (UA) pH 7.09, UA base excess −12.9 mmol/L, UA pO_2 1.9 kPa. Apgar scores of 7 and 7 at 1 and 5 min, respectively. FHR was recorded via scalp electrode. Paper speed 1 cm/min [Color figure can be viewed at wileyonlinelibrary.com]

BE <−12.0 meq/L (OR 3.3, 95% CI 2.3-4.7). Table 3 shows that UA pH, BE and pO_2 were worse in those cases with ZigZag pattern than in whom late decelerations, episodes of bradycardia or tachycardia, reduced variability or uterine tachysystole were present. The finding was similar in cases with a ZigZag pattern and in those in which the ZigZag pattern was absent (Table 4).

Newborn infants with ZigZag pattern or late decelerations had a significantly higher risk for 5-minute Apgar score <7 compared with cases without these patterns (OR 13.9, 95% CI 1.8-108.3). Moreover, the risk of low 5-minute Apgar score was 6.7-fold higher in cases with both ZigZag pattern and late decelerations than in cases with only late decelerations (95% CI of OR, 1.7-26.1).

The risk of intubation for resuscitation was 11.0-fold higher (95% CI of OR, 4.2-29.0) in cases with ZigZag pattern than in cases without ZigZag pattern. The frequencies for intubation were lower for those with late decelerations, episodes of bradycardia or tachycardia, reduced variability or uterine tachysystole (Table 3).

In addition, the presence of intrapartum ZigZag pattern was associated with higher risk for admission to NICU when compared with cases without ZigZag pattern (OR 2.0, 95% CI 1.4-2.8) (Table 4). The finding was similar for those with late decelerations (OR 2.5, 95% CI 1.9-3.3) (Table 4).

Newborn infants with ZigZag pattern during the last 2 hours of labor had hypoglycemia (plasma glucose <2.6 mmol/L) significantly more often during the first 24 hours after birth than did those without ZigZag pattern (OR 8.7, 95% CI 5.8-13.2) (Table 4). The finding was similar for cases with late decelerations (OR 3.9, 95% CI 2.6-6.1) than cases without (Table 4).

In all three neonatal outcome groups, bradycardia episodes occurred in approximately half of the cases. The highest incidence of 54.9% occurred in cases without neonatal complications (Group 1) (Table 2). The majority (74.7%) of bradycardia episodes took place in the last 30 minutes before birth. The presence of episodes with reduced baseline variability was relatively common in all three neonatal groups (Table 2). The vast majority (92.4%) of the episodes of reduced variability were preceded and followed by normal baseline variability and FHR accelerations. However, the presence of episodes of reduced variability or tachycardia was associated with a higher risk for admission to NICU when compared with cases in which reduced variability or tachycardia were absent (Table 4).

We also evaluated FHR patterns in terms of first occurrence before birth. The FHR patterns occurring between 120 and 0 minutes and between 120 and 90 minutes before birth in Group 3 are listed in Tables 5 and 6, respectively. Tables 5 and Table 6 also give the sensitivity and specificity, and the estimated positive predictive value (PPV) and negative predictive value (NPV) of FHR patterns predicting severe neonatal complications (Group 3).

We also examined the effects of parity, gestational age at delivery ≥42 weeks, maternal age ≥35 years, gestational diabetes mellitus, preeclampsia, maternal fever ≥38.0°C, smoking, fetal sex and birthweight z-score on how well ZigZag pattern and late decelerations predicted severe neonatal complications (Group 3). Logistic regression analysis revealed that adjustment attenuated the OR only marginally (for Group 3 crude OR was 3.3, 95% CI 2.4-4.9; adjusted OR was 2.9, 95% CI 2.0-4.1). After adjustments, the effects of ZigZag pattern and late decelerations remained statistically significant (P <.001). In these models, the presence of ZigZag pattern had an adjusted OR of 33.0 for severe neonatal complications between 120 and 90 minutes before birth, and OR of 5.4 at birth.

Mean duration of a single ZigZag episode was 4.8 minutes in Group 1, 6.5 minutes in Group 2 and 10.7 minutes in Group 3. The mean duration of a single ZigZag pattern was significantly longer in Group 3 than in Group 1 (P <.001) or Group 2 (P <.001). In six (1.0%) of

TABLE 3 Neonatal outcome characteristics when ZigZag pattern is compared with other CTG changes present

Variables	ZigZag pattern present	Late decelerations present	*P* value	Bradycardia episodes present	*P* value	Reduced variability present	*P* value	Tachycardia present	*P* value	Uterine tachysystole present	*P* value
n	582 (11.7)	2045 (41.0)		2639 (52.9)		1831 (36.7)		694 (13.9)		228 (4.6)	
UA pH	7.19 (± 0.08)	7.25 (± 0.10)	<.001	7.27 (± 0.09)	<.001	7.26 (± 0.19)	<.001	7.27 (± 0.08)	<.001	7.28 (± 0.09)	<.001
UA BE (meq/L)	−5.8 (± 3.1)	−4.1 (± 3.0)	<.001	−4.0 (± 1.2)	<.001	−4.2 (± 4.4)	<.001	−3.9 (± 2.7)	<.001	−4.1 (± 2.8)	<.001
UA pO_2 (kPa)	2.9 (± 1.0)	3.0 (± 1.0)	<.001	3.2 (± 1.0)	<.001	3.2 (± 0.9)	<.001	3.2 (± 0.9)	<.001	3.2 (± 1.1)	<.001
UA acidosis											
UA pH <7.10	57 (9.8)	102 (5.0)	<.001	75 (2.8)	<.001	67 (3.7)	<.001	22 (3.2)	<.001	9 (3.9)	<.001
UA BE <−12.0 (meq/L)	21 (3.6)	31 (1.5)	.011	17 (0.6)	<.001	21 (1.1)	<.001	6 (0.9)	.001	3 (1.3)	.034
5-min Apgar score <7	7 (1.2)	10 (0.5)	.06	6 (0.2)	.028	4 (0.2)	.002	3 (0.4)	.14	0 (0.0)	.008
Hypoglycemia, P-glucose <2.6 mmol/L	48 (8.2)	76 (3.7)	<.001	36 (1.3)	<.001	47 (1.5)	<.001	19 (2.7)	<.001	5 (1.7)	<.001
Intubation for resuscitation	10 (1.7)	14 (0.7)	.014	7 (0.3)	<.001	7 (0.3)	<.001	1 (0.1)	.003	1 (0.4)	.02
NICU admission	45 (7.7)	140 (6.8)	.46	121 (4.6)	.008	114 (6.2)	.20	67 (9.7)	.23	10 (4.4)	.09
Neonatal encephalopathy	0 (0.0)	0 (0.0)	1.00	0 (0.0)	1.00	2 (0.1)	.43	0 (0.0)	1.00	0 (0.0)	1.00

Data are mean ± SD or number (%).

BE, base excess; CTG, cardiotocography; NICU, neonatal intensive care unit. UA, umbilical artery.

TABLE 4 Neonatal outcome characteristics when CTG changes are present or absent

Variables	ZigZag Pattern present	ZigZag Pattern absent	*P* value	Late Decelerations present	Late Decelerations absent	*P* value
Number	582 (11.7)	4406 (88.3)		2045 (41.0)	2943 (59.0)	
UA pH	7.19 (± 0.08)	7.28 (± 0.09)	<.001*	7.25 (± 0.10)	7.27 (± 0.09)	<.001*
UA BE (meq/L)	−5.8 (± 3.1)	−3.1 (± 3.0)	<.001*	−4.1 (± 3.0)	−3.9 (± 3.0)	<.001*
UA pO_2 (kPa)	2.9 (± 1.0)	3.1 (± 0.9)	<.001*	3.0 (± 1.0)	3.1 (± 0.9)	.004*
UA acidosis						
UA pH <7.10	57 (9.8)	89 (2.0)	<.001*	102 (5.0)	44 (1.5)	<.001*
UA BE <−12.0 (meq/L)	21 (3.6)	18 (0.4)	<.001*	31 (1.5)	8 (0.3)	<.001*
5 min Apgar score <7	7 (1.2)	4 (0.1)	<.001*	10 (0.5)	1 (0.03)	<.001*
Hypoglycemia, P-gluc <2.6 mmol/L	48 (8.2)	45 (1.0)	<.001*	76 (3.7)	17 (0.6)	<.001*
Intubation for resuscitation	10 (1.7)	7 (0.2)	<.001*	14 (0.7)	3 (0.1)	<.001*
NICU admission	45 (7.7)	179 (4.1)	<.001*	140 (6.8)	84 (2.9)	<.001*
Neonatal encephalopathy	0 (0.0)	2 (0.05)	.06	0 (0.0)	2 (0.07)	.24

Variables	Bradycardia present	Bradycardia absent		Reduced Variability present	Reduced Variability absent	
Number	2639 (52.9)	2349 (47.1)		1831 (36.7)	3157 (63.3)	
UA pH	7.27 (± 0.09)	7.26 (± 0.09)	<.001^	7.26 (± 0.19)	7.26 (± 0.09)	.51
UA BE (meq/L)	−4.0 (± 1.2)	−4.2 (± 2.9)	<.001^	−4.2 (± 4.4)	−4.1 (± 2.7)	.27
UA pO_2 (kPa)	3.2 (± 1.0)	3.1 (± 1.0)	<.001^	3.2 (± 0.9)	3.2 (± 0.9)	.72
UA acidosis						
UA pH <7.10	75 (2.8)	71 (3.0)	.42	67 (3.7)	79 (2.5)	.06
UA BE <−12.0 (meq/L)	17 (0.6)	22 (0.8)	.63	21 (1.1)	18 (0.6)	.08
5-min Apgar score <7	6 (0.2)	5 (0.2)	.60	4 (0.2)	7 (0.2)	.94
Hypoglycemia, P-glucose <2.6 mmol/L	36 (1.3)	57 (2.4)	.006^	47 (1.5)	46 (2.6)	.009^
Intubation for resuscitation	7 (0.3)	10 (0.4)	.80	7 (0.3)	10 (0.3)	.90
NICU admission	121 (4.6)	103 (4.4)	.21	114 (6.2)	110 (3.5)	<.001*
Neonatal encephalopathy	0 (0.0)	2 (0.09)	.84	2 (0.1)	0 (0.0)	.16

Variables	Tachycardia present	Tachycardia absent		Uterine Tachysystole present	Uterine Tachysystole absent	
Number	694 (13.9)	4294 (86.1)		228 (4.6)	4760 (95.4)	
UA pH	7.27 (± 0.08)	7.26 (± 0.09)	.01^	7.28 (± 0.09)	7.26 (± 0.09)	.18
UA BE (meq/L)	−3.9 (± 2.7)	−4.2 (± 2.9)	.001^	−4.1 (± 2.8)	−4.2 (± 2.8)	.45
UA pO_2 (kPa)	3.2 (± 0.9)	3.1 (± 1.0)	.005^	3.2 (± 1.1)	3.2 (± 0.9)	.20
UA acidosis						
UA pH <7.10	22 (3.2)	124 (2.9)	.68	9 (3.9)	137 (2.9)	.42
UA BE <−12.0 (meq/L)	6 (0.9)	33 (0.8)	.80	3 (1.3)	36 (0.8)	.47
5-min Apgar score <7	3 (0.4)	8 (0.2)	.05	0 (0.0)	11 (0.2)	.001^
Hypoglycemia, P-glucose <2.6 mmol/L	19 (2.7)	74 (1.7)	.12	5 (1.7)	88 (1.8)	.72
Intubation for resuscitation	1 (0.1)	16 (0.4)	.18	1 (0.4)	16 (0.3)	.86
NICU admission	67 (9.7)	157 (3.7)	<.001*	10 (4.4)	214 (4.5)	.43
Neonatal encephalopathy	0 (0.0)	2 (0.09)	.57	0 (0.0)	2 (0.04)	.76

Data are mean ± SD or number (%). * Significant when present. ^ Significant when absent.

BE, base excess; NICU, neonatal intensive care unit; UA, umbilical artery;

TABLE 5 Sensitivity, specificity and positive and negative predictive values for the fetal heart rate patterns predicting severe neonatal complications (Group 3) in 120 to 0 min before birth

FHR Pattern	Number (n = 4988)	Sensitivity (95% CI)	Specificity (95% CI)	Positive (95% CI)	Negative (95% CI)
CTG with bradycardia episodes and/or tachycardia episodes and/or reduced variability and/or uterine tachysystole but without ZigZag pattern or late decelerations	1759 (35.3)	22.5 (16.4-29.9)	64.3 (62.9-65.7)	2.0 (1.5-2.9)	96.2 (95.4-96.8)
CTG with late decelerations (ZigZag pattern overlooked)	1934 (38.8)	69.4 (61.5-76.3)	59.9 (58.5-61.3)	5.4(4.5-6.5)	98.3 (97.8-98.8)
CTG with ZigZag pattern or late decelerations	1565 (31.4)	31.3 (24.3-39.1)	68.6 (67.3-69.9)	3.2 (2.4-4.2)	96.8 (96.1-97.3)
CTG with ZigZag pattern or late decelerations or both	2096 (42.0)	70.0 (62.2-76.8)	58.9 (57.5-60.3)	5.3 (4.4-6.4)	98.3 (97.8-98.8)
CTG with ZigZag pattern and late decelerations	531 (10.6)	38.8 (31.3-46.8)	90.3 (89.4-91.1)	11.7 (9.1-14.8)	97.8 (97.3-98.2)

Data are presented as %.

CTG, cardiotocography; FHR, fetal heart rate.

the 582 CTG recordings, the duration of a single ZigZag episode was between 15 and 25 minutes, and only in one (0.2%) case was the duration >25 minutes (28 minutes). In Group 3, during the last 2 hours before delivery, the incidence of ZigZag pattern decreased continuously towards delivery, whereas late decelerations first increased and then decreased, with the highest incidence occurring 1 hour before birth.

4 | DISCUSSION

The main finding of this study is that ZigZag pattern and late decelerations of FHR were associated with cord blood acidemia, low Apgar scores, need for intubation and resuscitation, NICU admission and neonatal hypoglycemia during the first 24 hours after birth. The ZigZag pattern preceded late decelerations, and the fact that normal FHR pattern preceded the ZigZag pattern in the majority of the cases suggests that ZigZag pattern is an early sign of fetal hypoxia, which emphasizes its clinical importance.

The strengths of the present study are: (i) the large number of the study subjects, (ii) the use of well-defined criteria of different FHR changes, (iii) the high number and quality of the scalp-monitored CTG recordings, and (iv) the high concordance between the two experts evaluating the CTG recordings, which was distinctly higher, both in interpretation of single CTG changes and in the overall concordance, than in previously reported studies.[6,7,13]

Limitations of the study are the retrospective study design and a relatively short duration of the evaluated CTG recordings. Furthermore, this study was performed in women delivering at ≥37 weeks, which limits the generalizability to term childbirths.

Our results are in accordance with findings of FHR changes in animal models. Experimental studies in term fetal sheep and monkeys have shown that the initial FHR response after an acute hypoxic episode is increased variability, after which the variability decreases when the hypoxia progresses.[14-16] The pathophysiology of increased FHR variability is incompletely understood but it has been linked to increased alpha-adrenergic activity and FHR decelerations in the fetal sheep with rapidly progressing hypoxia.[15,16] An increased FHR bandwidth of >25 bpm is presumed to be caused by instability or hyperactivity of the sympathetic and parasympathetic functions of the fetal autonomic nervous system.[17,18] As observed

TABLE 6 Sensitivity, specificity and positive and negative predictive values for the fetal heart rate patterns predicting severe neonatal complications (Group 3) in 120 to 90 min before birth

FHR Pattern	Number (n = 4988)	Sensitivity (95% CI)	Specificity (95% CI)	Positive (95% CI)	Negative (95% CI)
CTG with late decelerations (ZigZag pattern overlooked)	253 (5.1)	45.6 (37.8-53.7)	96.3 (95.7-96.8)	28.9 (23.4-34.9)	98.2 (97.7-98.5)
CTG with ZigZag pattern or late decelerations	214 (4.3)	26.3 (19.8-33.9)	96.4 (95.9-96.9)	19.6 (14.7-25.7)	97.5 (97.0-97.9)
CTG with ZigZag pattern or late decelerations or both	311 (6.2)	53.1 (45.1-61.0)	95.3 (94.7-95.9)	27.3 (22.5-32.7)	98.4 (98.0-98.7)
CTG with ZigZag pattern and late decelerations	97 (1.9)	26.9 (20.3-34.6)	98.9 (98.5-99.2)	44.3 (34.4-54.8)	97.6 (97.1-98.0)

Data are presented as %.

CTG, cardiotocography; FHR, fetal heart rate.

previously, repetitive late decelerations are most commonly caused by chemoreceptor-vagal reflex mechanisms and hypoxic myocardial depression due to uteroplacental insufficiency and reduced supply of oxygenated blood from the placenta to the fetus.[19,20]

Despite the shape similarity of the FHR patterns, the definition of the ZigZag pattern differs from the saltatory pattern in its duration. In the report by Gracia-Perez-Bonfils et al,[12] the ZigZag pattern was defined as fluctuation across the FHR baseline with amplitude of >25 bpm, with minimum duration of 1 minute. Previously, the saltatory pattern with a minimum duration of 1 minute was reported as a benign FHR change.[21] Furthermore, in our recent observation,[22] an increased variability of >25 bpm with a minimum duration of 2 minutes correlated significantly with neonatal acidosis and high cord blood erythropoietin (EPO) levels at birth, indicating fetal hypoxia. Therefore, in the present study, we limited the minimum duration of the ZigZag pattern to 2 minutes.

The 2015 CTG guideline of FIGO defines the saltatory pattern as a pathological finding if FHR baseline amplitude changes of >25 bpm last for >30 minutes.[11] The 2017 description of the saltatory pattern by the National Institute for Health and Care Excellence (NICE) categorizes this pattern as an abnormal FHR recording if the pattern lasts >25 mintues.[23] The National Institute of Child Health and Human Development (NICHD) 3-tier FHR interpretation guidelines do not define the exact duration of the saltatory pattern.[24] In the present cohort of 4988 deliveries and 582 cases with ZigZag patterns, there was only one case in which the duration of a single episode of increased variability lasted >25 minutes, and six cases with a duration of 15-25 minutes. Our finding is in agreement with a recent study that suggests that the saltatory pattern, as defined by FIGO and NICE, is an almost nonexistent phenomenon.[12] Based on our previous and present findings, even short episodes, that is, with a minimum of 2 minutes, of FHR baseline amplitude changes of >25 bpm are associated with unfavorable fetal and neonatal outcomes.[22]

The incidence of the ZigZag pattern in the present study was 11.7%. In the study by O'Brien and Benedetti (1992), the saltatory pattern was demonstrated in 3.5% of 286 term intrapartum CTG tracings.[21] Nunes et al[18] examined almost 14 000 CTG tracings during the last 30 minutes before birth and reported only four cases with UA metabolic acidosis and prolonged saltatory pattern lasting for more than 20 minutes. Gracia-Perez-Bonfils et al[12] reported that the ZigZag pattern with a minimum duration of 2 minutes was identified in 8.9% of 500 CTG tracings during the last hour of labor. In accordance with the findings of our study, the occurrence of the ZigZag pattern was associated with low 5-minute Apgar scores and UA acidosis at birth. In a recent study by Polnaszek et al[25], marked variability during the last 120 minutes before birth occurred in 4.5% of 8580 term deliveries. In agreement with our observations, FHR baseline amplitude changes of >25 bpm were associated with composite abnormal UA blood gas values.[22,25]

We also demonstrated that the ZigZag pattern and late decelerations were associated with neonatal hypoglycemia. Exposure to fetal hypoxia and anaerobic metabolism leads to depletion of glycogen stores of the fetus.[26] This may explain our observation that the cases with saltatory pattern or late decelerations during labor are associated with hypoglycemia (plasma glucose <2.6 mmol/L) during the first 24 hours after birth. In normally oxygenated newborn infants without these FHR patterns, a corresponding association was not observed.

In previous reports,[27-29] the interpretation of FHR patterns has shown a poor PPV but an excellent NPV when CTG recording was used as a screening tool for adverse neonatal outcomes. Importantly, in the present study, a CTG tracing with the combination of ZigZag pattern and late decelerations had a higher PPV and a similar NPV for the severe neonatal complications group (Group 3) compared with previous studies relating to the FHR patterns associated with fetal acidemia and adverse short-term neonatal outcome.[27,29] To our knowledge, the present study is the first in which the predictive accuracy of the combined occurrence of ZigZag FHR pattern and late decelerations has been demonstrated.

In all three neonatal outcome groups, bradycardia occurred in approximately 50% of the cases, the majority of which took place during the last 30 minutes before birth. This suggests that the bradycardia was caused by fetal head compression or by an overstretched or compressed umbilical cord.[30] Furthermore, episodes of reduced baseline variability were relatively common in all the three neonatal groups. In most cases, an episode of reduced variability was preceded and followed by normal baseline variability and FHR accelerations. This suggests that episodes of reduced variability in an intrapartum FHR tracing, when occurring with alternative phases of reactivity, are associated with normal fetal oxygenation.[29,31]

5 | CONCLUSION

The present study indicates that ZigZag pattern and late decelerations of FHR during the last 2 hours of labor are significantly associated with cord blood acidosis and neonatal complications. Of note, in the vast majority of the cases, the ZigZag pattern was preceded by a normal FHR pattern and followed by late decelerations, suggesting that the ZigZag pattern is an early sign of fetal hypoxia. This finding may improve the clinical decision-making on intrapartum CTG recordings and would enable the clinician to plan for possible interventions during labor. Future research should include neonatal and infant follow-up studies of offspring with the ZigZag pattern and other FHR changes during labor.

ACKNOWLEDGMENTS

We thank Antti Malmivaara, MD, PhD, for his participation in the planning of the study.

CONFLICT OF INTEREST

None.

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How to cite this article: Tarvonen M, Hovi P, Sainio S, Vuorela P, Andersson S, Teramo K. Intrapartum zigzag pattern of fetal heart rate is an early sign of fetal hypoxia: A large obstetric retrospective cohort study. *Acta Obstet Gynecol Scand*. 2021;100:252–262. https://doi.org/10.1111/aogs.14007