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Placental histology in clinically unexpected severe fetal acidemia at term

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ABSTRACT

Background: Fetal acidemia at birth is defined as a newborn condition wherein the cord blood pH value is less than 7.0. It could represent an association with newborn brain damage; therefore, it is important to investigate which conditions precipitate its occurrence. No extensive placental analysis has been performed in cases of acidotic newborns delivered from low-risk pregnancies.
Aims: To study placental characteristics in cases with severe fetal acidemia.
Study design: Retrospective case–control study.
Subject: 34 cases, 102 controls.
Outcome measures: Umbilical artery pH was measured at delivery from a doubly clamped portion of the cord. Placental characteristics were compared between cases with severe fetal acidemia (cord pH at birth <7.0) and controls (normal pH at birth) in term low-risk pregnancies.
Results: Macroscopic placental and umbilical cord characteristics were comparable in cases and controls whereas histological characteristics exhibited differences: diffuse villous edema, increased number of syncytial knots and villous branching abnormalities significantly affected cases more frequently than controls. Diffuse villous edema is related to fetal vascularization and associated with an increase of venous pressure; in our low-risk population, it is conceivable that these changes of fetal flow and pressure occurred in labor during the alteration of fetal heart rate. An increased number of syncytial knots and villous branching abnormalities have been previously associated with chronic placental hypoxic condition; in our low-risk population they could reflect a clinically undetectable hypoxic situation that acted during pregnancy reducing fetal resources to bear labor and delivery.
Conclusions: Placental histology provides useful information related to fetal acidemia in low-risk term pregnancy.

1. Introduction

Fetal pH is maintained within the normal narrow range thanks to placental exchanges that supply oxygen and remove respiratory and metabolic waste [1].

Pathological pH at birth, defined as fetal acidemia, corresponds to a cord blood pH value less than 7.0 [2,3]. Acidemia at birth could represent an association with newborn brain damage [2], therefore it is important to investigate which conditions precipitate its occurrence.

Several maternal and fetal diseases have been related to cord blood acidemia at birth [4] and maternal–fetal illness could also affect placental anatomy and function [5,6]: for example, maternal diabetes mellitus could impair acid–base balancing and could modify placental villous tree branching and angiogenesis.

Moreover, placental lesions could impair the ability of the fetus to compensate stress at the time of labor and delivery [7,8].

To our knowledge, no extensive placental analysis has been performed in cases of acidotic newborns delivered from low-risk pregnancies. The aims of this study were to evaluate placental histology in term low-risk pregnancies, and to verify if placental examination could provide useful information for the comprehension of the genesis of fetal acidemia. Taking into account what it was demonstrated in placentas from neurologically impaired newborns [9], we tested the hypothesis that clinically silent placental chronic

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lesions can reveal antepartum processes that could progress during the intrapartum period and predispose the fetus to an abnormal neonatal outcome.

2. Methods

2.1. Patients and data collection

Placentas from term singleton pregnancies were collected in four Italian Department of Obstetrics and Gynecology, during a two year period. The study is a retrospective review of a cohort of cases submitted to histopathology departments as part of clinical practice.

Criteria for inclusion in the study were: deliveries occurred after active labor at >37 weeks of gestation in healthy women with uneventful pregnancies, birth-weight appropriate for gestational age and normal fetal heart rate monitoring at admission. Exclusion criteria were any maternal or fetal diseases or pre-labor gestational complication or cesarean section before delivery.

Fetal umbilical cord arterial blood was measured at the time of delivery from a doubly clamped portion of the cord. Cases include

Table 1
Characteristics of our population.

		Cases (pH < 7.0) n = 34	Controls (pH ≥ 7.0) n = 102	p
Maternal characteristics	Maternal age (years)	33.2 ± 5.1	30.9 ± 4.5	**0.01**
	Pre-pregnancy BMI (kg/m^2)	22.0 ± 5.1	23.3 ± 4.5	0.2
	Obese (BMI ≥ 30 kg/m^2)	2 (5.8)	10 (9.8)	0.7
	Caucasian	31 (91.2)	85 (83.3)	0.4
	First pregnancy	21 (61.8)	56 (54.9)	0.5
	Gestational age (weeks)	40.2 ± 1.1	39.8 ± 1.4	0.06
Labor and delivery	Spontaneous onset of labor	21 (61.8)	74 (72.6)	0.2
	Induced labor	13 (38.2)	28 (27.4)	0.3
	Vaginal delivery	17 (50)	90 (88.2)	<**0.0001**
	Operative delivery with vacuum	10 (29.4)	10 (9.8)	**0.01**
	Cesarean section	17 (50)	12 (11.8)[a]	<**0.0001**
Intrapartum risk factors	Maternal pyrexia	1 (2.9)	3 (2.0)	1.0
	Meconium staining of AF	7 (20.6)	16 (15.7)	0.6
	Sentinel event	2 (5.9)[b]	0	0.06
	Placental abruption[c]	4 (11.3)	0	**0.002**
	Abnormal FHR[d]	23 (67.4)	1 (0.9)	<**0.0001**
Neonatal characteristics	Umbilical artery pH	6.91 ± 0.06	7.26 ± 0.09	<**0.0001**
	Birth-weight (grams)	3438.8 ± 431.0	3381.6 ± 348.2	0.4
	Male	19 (55.9)	52 (50.9)	0.7
	Intubation	6 (17.6)	0	<**0.0001**
	Apgar score at 5 min	7.17 ± 2.15	9.8 ± 0.6	<**0.0001**
	Apgar score ≤ 5 at 5 min	7 (20.6)	0	<**0.0001**
Umbilical cord abnormalities	Nuchal cord	3 (8.8)	5 (4.9)	0.4
	Hypercoiling (>3 coils/10 cm)	4 (11.3)	10 (9.8)	0.7
	Achirality (absence of coiling)	0	0	1.0
	Torsion	2 (5.9)	0	0.06
	Furcate insertion	0	1 (0.9)	0.6
	Velamentous insertion	1 (2.5)	3 (2.9)	1.0
	False knots	3 (8.8)	7 (6.9)	0.7
	True knots	0	0	1.0
Placental macroscopic characteristics	Bilobate	1 (2.9)	5 (4.9)	1.0
	Accessories lobule	0	1 (0.9)	0.6
	Area (cm^2)	226.9 ± 54.9	229.5 ± 53.5	0.4
Placental histology	Inflammation			
	Acute chorioamnionitis	0	3 (2.9)	0.6
	Funisitis	0	3 (2.9)	0.6
	VUE	7 (20.6)	9 (8.8)	0.1
	Disruptive lesion			
	Abruption	4 (11.3)	0	**0.002**
	Rupture vasa praevia	0	0	1.0
	Feto-maternal hemorrhage	0	0	1.0
	Obstructive lesions			
	Infarction	3 (8.8)	1 (0.9)	0.05
	Decidual vasculopathy	3 (8.8)	5 (4.9)	0.4
	Massive fibrin deposition	3 (8.8)	7 (6.9)	0.7
	Diffuse villous edema	13 (38.2)	0	<**0.0001**
	Fetal thrombotic vasculopathy	0	0	1.0
	Adaptive lesions			
	Increased n. of syncytial knots	13 (38.2)	14 (13.7)	**0.005**
	Chorangiosis	3 (8.8)	3 (2.9)	0.3
	Villous branching anomalies	12 (35.3)	15 (14.7)	**0.02**

Data are expressed as mean ± standard deviation or number (percentage).
AF = amniotic fluid, BMI = body mass index, min = minute, n. = number, FHR = fetal heart rate, VUE = chronic villitis to unknown etiology.
Placental lesions are not mutually exclusive: in each case more than one abnormality may coexist.
[a] Cesarean section in controls were performed for labor dystocia: 8/12 failure to progress in the active first stage, 4/12 failure to progress in the second stage.
[b] Including 1 uterine rupture and 1 maternal shock for anaphylaxis after antibiotic administration.
[c] Placental abruption was identified clinically (by the presence of vaginal hemorrhage and FHR abnormality) and confirmed by histological examination.
[d] Abnormal fetal heart rate includes bradycardia or prolonged deceleration immediately before the delivery.