



Morphometric characteristics of the umbilical cord and vessels in fetal growth restriction and pre-eclampsia



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ARTICLE INFO

Article history:

Received 22 June 2015

Received in revised form 14 November 2015

Accepted 17 November 2015

Keywords:

Umbilical cord

Pregnancy complications

Fetal growth restriction

Preeclampsia

Umbilical vessels

ABSTRACT

Background: Reports on the morphometric analysis of umbilical cord (UC) and its vessels have been inconsistent due to varying inclusion criteria and methodology. The current study tried to overcome the limitations of previous studies by comparing the UC in pregnancies complicated by fetal growth restriction (FGR), preeclampsia (PE) and FGR + PE, to healthy controls.

Aims: Analyze the morphometric attributes of the UC in pregnancies complicated by FGR and PE.

Study design: Case–control.

Subjects: The study groups consisted of 36 patients with FGR + PE, 72 with FGR (without PE) and 15 with PE (without FGR). They were compared to 50 patients without FGR or PE.

Outcome measures: Histological cross-sections of the UC were photographed and measured. The following variables were recorded: cross-section area of UC, thickness and surface area of umbilical vessel walls, shortest distance between cord surface and nearest artery (DSA), distance between the arteries (DBA) and placental weight and measurements. The area of the Wharton's jelly (WJ) area was calculated.

Results: UC and WJ cross-section areas were significantly smaller in FGR + PE and FGR, but not in PE. The umbilical vessel wall area was decreased in FGR + PE, but the thickness was not significantly decreased in all three study groups, compared to controls. DSA was smaller in all three groups, whereas DBA was not significantly different, compared to controls.

Conclusions: Smaller UC cross-section areas were seen in FGR and FGR + PE, but not in PE without FGR. However, there is no evidence to determine whether this reduction is a cause or consequence of FGR. Reduced DSA in PE, whose UC cross-section area was not smaller as in FGR and FGR + PE, might reflect alterations in UC induced by PE.

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1. Introduction

Recent research concerning the umbilical cord (UC) has evaluated hemodynamic flow patterns with ultrasound [1–4], biochemical composition using various assays [5], mechanical properties [6,7], structure and function [8,9]. Ultrasound studies found that the UC was thinner in pregnancies complicated by fetal growth restriction (FGR) [10] and preeclampsia (PE) [11]. Histological sections of the UC were used to develop nomograms [12] and revealed alterations in the umbilical vessels

and Wharton's jelly (WJ) in pregnancies with FGR [13,14] and PE [15–18]. Due to differing inclusion criteria, the results were not comparable or were contradictory [13–18]. In addition, PE is not always associated with FGR, which may have diverse etiologies. Our hypothesis was that FGR and PE might have different effects on the UC. The aim of the current study was to analyze the morphometric attributes of the UC and its constituent parts in pregnancies complicated by FGR and PE.

2. Methods and materials

This case–control study assessed the effect of FGR and PE on the characteristics of the UC and its vessels. FGR was diagnosed as birth weight <10th percentile for this specific population according to gestational age and gender [19]. PE was defined as blood pressure above 140/90 and proteinuria above 300 mg/24 h [20].

Abbreviations: DBA, shortest distance between the arteries; DSA, shortest distance between cord surface and nearest artery; FGR, fetal growth restriction; H&E, hematoxylin and eosin; PE, preeclampsia; UC, umbilical cord; WJ, Wharton's jelly.

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The cord was clamped immediately at the end of the second stage of delivery while the newborn was placed on the mother's abdomen. Of note, during the study period, the timing of cord clamping and its position relative to the maternal pelvis were the same in all cases.

2.1. Study population

Patients with a clinical diagnosis of FGR and/or PE comprised the study groups. Maternal age, parity, gestational age at delivery (weeks), birth weight (grams), placental weight (grams) and newborn gender were recorded for each case.

Control cases were chosen as the next parturient with similar delivery age (± 1 week), parity (± 1), maternal age (± 3 years) and uneventful pregnancy whose placentas were also submitted for pathology evaluation for other reasons e.g., suspected placental abruption or maternal fever. Inclusion criteria were singleton gestation with no fetal malformations, gestational age ≥ 30 weeks, and the presence of a 3-vessel umbilical cord.

2.2. Pathology study of the UC and placenta

The placentas which were submitted for pathology examination were fixed in 4% buffered formaldehyde. The general examination included evaluation of umbilical cord, membranes and placental disc [21]. The umbilical cord was grossly examined for length and diameter and inspected for appearance, coiling, and focal lesions. Three slices, grossly perpendicular to the long axis were sectioned from either end and from the center of the UC. They were submitted for histological tissue processing and embedded in paraffin. The histological sections were 4 μ m thick, and stained with hematoxylin and eosin (H&E) (Fig. 1). The three cross-sections (proximal end, distal end, center of the cord) were analyzed separately but with no indication of the specific origin. For uniformity and considering that a blood clot may increase the cross-sectional size, the smallest of the three cross-sections of the UC was selected for analysis.

Histological sections of the UC were photographed with an Olympus DP70 digital camera at $\times 12.5$ magnification. The morphometric

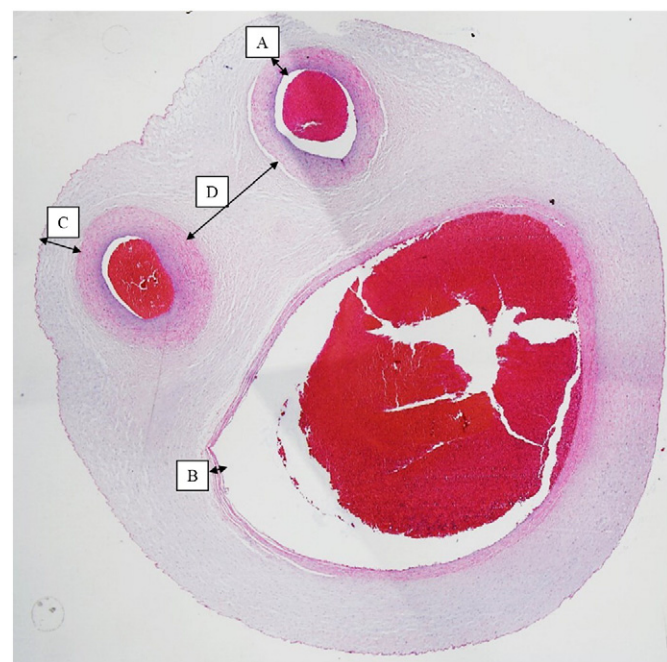


Fig. 1. Umbilical cord cross-section showing: (A) thickness of umbilical artery wall, (B) thickness of umbilical vein wall, (C) distance of the cord surface to the nearest artery (DSA), and (D) the distance between arteries (DBA).

measurements were blindly performed by two physicians (RS and DK) using two software programs (ImageJ and paint.net). An intraclass correlation coefficient (ICC) was used to estimate the inter-rater reliability. The following parameters were measured, calculated and re-recorded using ImageJ software (National Institutes of Health) and paint.net software (.NET frameworks): A) UC – cross-section area; B) umbilical vessels – wall thickness/wall surface area, calculated by subtracting the inner from the outer surface area; C) the shortest distance between cord surface and nearest artery (DSA); D) the shortest distance between the arteries (DBA) (Fig. 1); and E) placental weight and dimensions. The area of WJ was calculated by subtracting the vascular area from the total UC cross-sectional area.

2.3. Clinical data

Data collected from the patient records included pregnancy complications, maternal background medical history and drug therapy, fetal anomalies, gestational age at delivery, mode of delivery, neonatal gender and birth weight.

The study was approved by the local Institutional Review Board.

2.4. Statistical analysis

Power analysis, assuming 80% power, an α -error of 5% and 10% size change, determined that each arm of the study should include 36 cases. The complicated pregnancies were compared to the control group using one-way ANOVA to test significant differences between groups. $p < 0.05$ was considered significant. SPSS-17 statistical analysis software (Chicago, IL) was used.

3. Results

Among the 30,261 deliveries from January 2007 through December 2011, 173 singleton pregnancies at 30–41 weeks gestational age were included in the study. These included 36 cases of PE and FGR, 72 cases of FGR (without PE), 15 cases of PE (without FGR) and 50 controls. The clinical characteristics of the study groups are summarized in Table 1.

The morphometrics of the UC in the study and control groups are summarized in Table 2. An intraclass correlation coefficient (ICC) showed high inter-rater reliability (0.975).

In FGR (without PE), the UC and WJ cross-section areas were smaller than in the control and PE groups. The vessel wall thicknesses were not significantly decreased, but the wall area of the arteries (but not the vein) was smaller than in control and PE. The artery was closer to the cord surface (decreased DSA).

In PE (without FGR), the UC and WJ cross-section areas were not smaller than control. The vessel wall thickness was not significantly smaller than the control. The wall surface area of umbilical vessels was not significantly smaller than control. The artery was closer to the cord surface (decreased DSA).

Table 1

Clinical characteristics (mean + standard deviation) of the study groups.

Characteristic	FGR + PE N = 36	FGR N = 72	PE N = 15	Control N = 50
Maternal age	30.6 \pm 6.1	30.2 \pm 5.3	28.3 \pm 5.8	32.2 \pm 6.4
Parity	1.6 \pm 0.9	1.8 \pm 1.1	2.1 \pm 1.5	2.3 \pm 1.3
Gestational age (weeks)	34.1 \pm 3.1 ^a	37.8 \pm 1.6	35.2 \pm 4.5	36.8 \pm 2.6
Birth weight (grams)	1703 \pm 504 ^a	2363 \pm 396	2432 \pm 827	2966 \pm 568
Placental weight (grams)	290 \pm 77 ^a	365 \pm 71	438 \pm 109	463 \pm 115
Male/female	17/19	34/38	13/2	26/24

FGR fetal growth restriction; PE preeclampsia.

^a $p < 0.05$ vs. control.

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