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Risk factors and placental histopathological findings of term born low birth weight neonates

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ABSTRACT

Introduction: Low birth weight (LBW) is associated with increased neonatal morbidity and mortality. Hence, this condition should be well studied. The aims of this study were to identify the risk factors for term born LBW, as well as the placental histopathological lesions observed.

Methods: This case control study was carried out in the University Teaching Hospital and the Central Maternity, both of Yaoundé, Cameroon, from November 1st, 2013 to April 30th, 2014. Maternal medical records and placentas of term born (≥37 completed weeks) LBW (<2500 g at birth) or normal weight (3000–3500 g) were compared. The main variables recorded included maternal age and parity, maternal height, complications that occurred during pregnancy, maternal pre-gestational body mass index, the number of antenatal visits, the sex and birth weight of the newborn, the umbilical cord length, the placental weight and placental histology. Data were analyzed using Epi info 3.5.4. Fisher exact test, t-test and logistic regression were used for comparison. $P < 0.05$ was considered statistically significant.

Results: and Discussion: A total of 30 cases of LBW and the same number of controls were examined. Significant risk factors for LBW were primiparity (aOR 14.0, 95%CI 2.1–92.7), hypertensive diseases of pregnancy (aOR 18.1, 95%CI 1.02–322.5) and <4 antenatal visits (aOR 9.5, 95%CI 1.3–67.5). Significant placental lesions were placental infarction (aOR 19.5, 95%CI 2.9–130.1) and chronic villitis (aOR 35.9, 95% CI 1.2–1034.3). Our study showed that primiparous women, those with pregnancy-induced hypertensive diseases and those with <4 antenatal visits were more at risk for LBW. Significant placental lesions observed among LBW were placental infarcts and chronic villitis. Since LBW has the tendency to recur, and given that some causes such as placental infarcts are preventable, we recommend that a histological examination of the placenta should always be carried out in cases of LBW.

1. Introduction

Low birth weight (LBW) is defined as a birth weight less than 2500 g. Prevalence of LBW varies widely worldwide, ranging from approximately 7%–18% [1], with a rate of term born LBW between 1.1% and 6.1% [2–5].

LBW is associated with increased neonatal morbidities such as hypothermia, neonatal sepsis, respiratory, gastro-intestinal, hematologic, metabolic disorders as well as increased perinatal mortality [4–6].

Although the diagnosis of LBW is easy at delivery, its risk factors are not all known. These risk factors include hypertensive diseases of pregnancy, maternal anemia, severe maternal malnutrition, maternal cardiac and respiratory diseases, myomatous uterus, maternal alcohol and tobacco consumption, urinary tract infections, maternal infestations such as malaria, congenital infections like rubella and cytomegalovirus, and fetal chromosomic abnormalities [1,2,4–7].

Placental causes exist as well, and include: placental infarcts, microscopic chorionic cysts, decidual arteriopathy, chronic villitis, placental hemangiomas, placenta abruptio, circumvallate placenta and umbilical cord abnormalities [8–13]. In 20–30% of cases, no

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cause is found. In some women, LBW has the tendency to recur, especially when due to placental infarcts.

No study in our country has been conducted on the placental aspects of LBW neonates. Hence, this study was aimed at identifying the sociodemographic and obstetric characteristics of women with LBW neonates, as well as the associated placental histopathological findings observed.

2. Methods

This case control study was carried out in the maternities of the University Teaching Hospital and the Central Maternity, both of Yaoundé, Cameroon, from November 1st, 2013 to April 30th, 2014. Placentas of term born LBW (<2500 g at ≥37 completed weeks) were recruited. For each case, the placenta of the neonate born at term just after the delivery of the case with birth weight between 3000 and 3500 g was recruited as control. An informed consent was obtained from each woman. This study was approved by the two institutional ethics committees. Variables recorded on a pre-established and pretested questionnaire by the principal investigator included maternal age and parity, marital status, maternal height, complications that occurred during pregnancy, gestational age at delivery (confirmed by an ultrasound scan performed before 20 weeks gestation), maternal pre-gestational body mass index, gestational weight gain (difference between the weight just before delivery and the weight just after she realized that she was pregnant, but before 10 weeks), the number of antenatal visits, the sex and birth weight of newborn, the umbilical cord length (the distance from the point of cord insertion on the placenta to the point of insertion on neonate's umbilicus), the placental weight (measured just after the cord has been clamped and sectioned) and placental histology. The membranes and the umbilical cord were not removed prior to weighing because the entire placenta had to be taken to the pathologist or to the principal investigator who were the ones to carry sampling.

Placental histological examination was obtained through the following steps; six specimens of about 15 × 15 × 5 mm each were taken immediately after the placental weight has been obtained, the first two specimens (I and II) were taken at the placental margin with the latter on the maternal surface. Secondly, the two other specimens (III and IV) were taken at the central part of the placenta with the latter on the maternal surface. Thirdly, one (V) was taken on suspicious lesions and lastly, one (VI) on the umbilical cord. All the specimens were immediately fixed in a 10% formaldehyde solution for 48 h. Thereafter, serial sections of 0.3–0.5 mm were done and fixed for 24 h following the same procedure. All specimens were progressively dehydrated (with an histokinet LEICA TP 1020) in a 70% up to 100% ethanol solution, thereafter in Xylen solution, then embedded in a 61 °C paraffin solution and kept in a refrigerator. Sections of 2–5 μm were later done (with the apparatus LEICA RM 2125 RT) and kept in Barnstead/Electrothermal and lastly put on slides. After removing paraffin solution (with heat or Xylen solution), rehydration was later done by including slides progressively in solutions of 90% down to 70% ethanol and in distilled water. Slides were stained with hematoxylin-eosin solutions. Later on, the slides were dehydrated, following the same procedure described above. Preparations were put on slides using a synthetic resin (PERTEX) and all the slides were read, without knowing the group allocation, by the same pathologist.

The necessary sample size was calculated as needing at least 23 women in each group, using the following formula: $N = 2 \times (Z\alpha + Z\beta/P_0 - P_1)^2 \times P \times (1-P)$ where $Z\alpha = 1.65$ corresponding to a type I error of 5%, $Z\beta = 0.84$ corresponding to a type II error of 20% or a power of 80%, P_0 the prevalence of placental infarcts in women with LBW (50%), P_1 the prevalence of placental infarcts in women without LBW (15%) and P is $(P_0 + P_1)/2$. Data were analyzed using Epi info 3.5.4. Data of LBW neonates were compared to those of neonates of the control group. Fisher exact test was used to compare categorical variables and t-test to compare continuous variables. We used odds ratios with their 95% confidence intervals (CIs) to present the comparison between the two groups. Multiple logistic regression analysis was undertaken to control for potential confounders. $P < 0.05$ was considered statistically significant.

3. Results

During the study period, 46 term born LBW neonates were delivered out of 1492 singleton term deliveries (3.1%). Sixteen mothers refused their placentas from being taken away for cultural reasons. The remaining 30 placentas of LBW neonates and the same number of placentas of women of the control group were examined. Demographic and obstetrical characteristics are given in Table 1.

Regarding marital status, 22 women were single in the LBW group as against 18 in the control group ($P = 0.41$). Parity 1 was more frequently observed in both groups (Table 2). Odds Ratio (OR) for LBW was 3.4 (1.2–10) for women of parity 1 compared with women of parity >1 ($P = 0.03$).

Pre-gestational body mass index (BMI) is shown in Table 3. OR for LBW was 4.9 (95%CI 1.6–15.0, $P < 0.009$) when BMI <25 (23/30 cases in the LBW group as against 12/30 cases in the control group) was compared to ≥25.

Concerning maternal diseases that could have influenced the occurrence of LBW, chronic hypertension (blood pressure ≥140/90 mm Hg diagnosed before 20 weeks gestation in known hypertensive women) was present in two women (6.7%) in the LBW group as against zero (0%) among the controls, and pre-eclampsia (blood pressure ≥140/90 mm Hg developed after 20 weeks gestation associated with proteinuria ≥300 mg/24 h) was present in eight women (26.7%) in the LBW group as against two (6.7%) among the controls. OR for LBW was 5.1 (95%CI 0.98–26.4, $P = 0.08$) in women with pre-eclampsia. Sickle cell disease (Hemoglobin SS) was present in one woman (3.3%) of the LBW group as against none (0%) among the controls. Passive tobacco consumption was present in one woman in each group while HIV positive status was present in two women in each group.

A total of 16 female fetuses (53.3%) were observed in the LBW group as against 14 (46.7%) in the control group. OR for LBW was 1.3 (95%CI 0.4–3.6, $P = 0.79$) when the fetus was a female.

OR for LBW for umbilical cord length <50 cm was 3.7 (95%CI 1.04–13.6, $P = 0.07$) while OR for LBW for placentas weighing

Table 1
Distribution of some variables in both groups.

Variables		LBW group (<2500 g)	Control group (3000–3500 g)	P value
Number of women		30	30	
Maternal age in year (range)		26.2 ± 5.5 (16–40)	26.6 ± 4.7 (16–38)	0.76
Parity (range)		1.8 ± 1.5 (1–8)	2.2 ± 1.3 (1–6)	0.27
Maternal height (cm)	Mean ± SD (range)	161.8 ± 6.6 (148–180)	163.8 ± 7.5 (150–180)	0.27
	<165	23 (76.7%)	15 (50%)	
	≥165	7 (23.3%)	15 (50%)	
Number of antenatal visits	Mean ± SD (range)	4.0 ± 1.6 (0–8)	4.9 ± 1.5 (2–8)	0.028
	<4	11 (36.7%)	4 (13.3%)	
	≥4	19 (63.3%)	26 (86.7%)	
Gestational age in week (range)		38.1 ± 1.4 (37–42)	38.6 ± 1.4 (37–42)	0.17
Gestational weight gain (kg)		8.5 ± 5.5 (0–20)	8.0 ± 5.7 (0–22)	0.73
Pre-gestational BMI (kg/m^2)		22.6 ± 3.0 (15.2–28.8)	26.8 ± 6.0 (17.7–42.6)	0.0011
Birth weight (g)		2251 ± 283.1 (1500–2490)	3216 ± 195.8 (3000–3499)	<0.0001
Umbilical cord length (cm)	Mean ± SD (range)	51.8 ± 10.8 (31–74)	63.0 ± 11.3 (44–87)	0.0002
	<50	11 (36.7%)	4 (13.3%)	
	≥50	19 (63.3%)	26 (86.7%)	
Placental weight (g)		468.3 ± 87.9 (280–750)	655.6 ± 133.5 (370–920)	<0.0001

LBW: low birth weight, BMI: body mass index.