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Maternal Demographic and Placental Risk Factors in Term Low Birth Weight in Ghana

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Abstract

Background: Several studies report on factors that associate preterm birth and intrauterine growth restriction with low birth weight (LBW). However, few studies discuss risk factors that associate with LBW for full-term births. No such studies exist that involve a population from Ghana.

Method: We used a nested case-control study approach to examine maternal socio-demographic and placental factors that contribute significantly to term LBW in Ghana. We assessed also the incidence of LBW in general at a major teaching hospital facility in Ghana.

Results: Univariate and multivariate logistic regression analysis were used to investigate maternal socio-demographic and placental factors that associate with LBW. Following the preliminary univariate analysis, a stepwise logistic regression analysis showed that unstable income source, single motherhood, combined effect of pre-eclampsia and anaemia; ORs of 5.366 (95% CI: 1.986 to 14.497), 21.390 (95% CI: 3.610 to 126.734) and 3.246 (95% CI: 1.074 to 9.814), respectively, and placental weight and irregular insertion of the umbilical cord (variables scaled by a factor of 10-2 to aid interpretation) ORs 0.28 (95% CI: 0.115 to 0.683), 0.010 (95% CI: 0.001 to 0.173 respectively) on the chorionic plate, were risk factors for LBW. The socio-demographic and placental factors reveal a core role of maternal and infant nutritional deficiencies in term LBW in Ghana. The general prevalence of LBW in the Hospital facility was 6.2%.

Conclusion: We conclude that poor maternal and infant nutrient supply is key factors in term LBW in Ghana. These factors are amenable to appropriate nutritional and educational interventions.

Keywords: Term low birth weight; Maternal nutrition; Fetal nutrition

Introduction

Low birth weight (LBW) is defined as birth weights that are less than 2500 g at birth, and it is the single most important risk factor in neonatal and infant health [1-3]. LBW occurs in 15.5% of all live births or about 20.5 million infants per year worldwide [2,3]. LBW occurs in preterm babies (less than 37 completed weeks of gestation), infants with intrauterine growth restriction (IUGR) and full-term infants (greater or equal to 37-41 completed weeks of gestation) [4,5]. Although many sources in the literature consider risk factors specifically for preterm and/or IUGR on LBW infants [1,6,7], few studies consider those factors that associate with LBW in full-term births or "term LBW". Term LBW is the focus of the present study [8-10].

LBW babies are in general at a higher risk of long-term adverse health consequences, including cardiovascular, renal, metabolic disorders, and learning disabilities [11-13]. Two primary factors are

known to correlate with LBW, namely: Maternal nutrient availability; and, placental structure and health [14,15]. The developing fetus is obligatorily dependent on the mother for nutrient supply and so maternal adequate nutrition is critical for the provision of the required amounts of nutrients (carbohydrates, proteins and lipids) for the developing fetus [15]. On the other hand, the placenta must be well developed and healthy to ensure that the available nutrients from the mother are delivered to the fetus [16,17]. Comparative studies of maternal socio-demographic factors in various countries and in sub-Saharan Africa show that young age (and/or maternal age greater than 35), a single motherhood and lifestyle behaviours (e.g. physical activities and smoking) are high risk factors to poor fetal growth and pregnancy outcomes [18,19]. Maternal occupations that require prolonged standing, walking or vigorous physical exertion and psychological factors such as stress and anxiety may also contribute to LBW. However, these effects vary between populations [20,21]. It has been reported that placental factors alone contribute to neonatal growth retardation in 36% of LBW cases [12,22]. Placental factors include changes in placental morphology and insults to the placenta such as infarcts, chronic villous inflammation, and vascular vessel

thrombosis. Placental morphological changes include the length, breadth, weight and any shifts from central insertion of the umbilical cord on the chorionic plate to an irregular velamentous insertion [23,24]. Such changes affect the placental efficiency with regards to adequate development of the vasculature to meet the nutrient and oxygen supply to the fetus [25,26]. The placental weight serves as a marker of the available surface area for maternal-fetal nutrient exchange [27,28]. In our study, we examined firstly the incidence rate of LBW in general at the Korle-Bu Teaching Hospital, Accra, Ghana, retrospectively. Secondly, we investigated the socio-demographic and placental factors of prospective mothers that associate with term LBW in a nested case-control study at the hospital. We provide evidence that maternal socio-demographic and placental factors that impact on nutrient supply to the fetus are important contributors to low birth weight in term infants.

Materials and Methods

The study site

The study was conducted at the Department of Pathology and Maternity Wards of the Obstetrics and Gynecology Department of the Korle-Bu Teaching Hospital (KBTH), Accra, Ghana. KBTH is a leading tertiary referral hospital that serves the city of Accra, the surrounding urban population and the Southern part of Ghana.

Extraction of incidence data and Case-control study

The records of all deliveries and weights of babies occurring at the KBTH between May 2000 and January 2006 were documented. As part of the nested case-control study (i.e., a case-control study “nested” within a cohort study), prospective mothers were recruited at the antenatal clinic of the Obstetrics and Gynaecology wards during their normal visit after 12 weeks of gestation. At recruitment, the study objective was first explained to each prospective mother, after which a consent form was signed if consent to participate was given. Subsequently, a structured questionnaire assessing socio-demographic characteristics, maternal diseases and past obstetric outcome(s) was completed. A total of 200 expectant mothers were recruited consecutively within a 1.7 year period from May 2004 to January 2006. These mothers were followed until delivery, at which time babies were classified as either cases or controls based on their birth weight. We defined pre-eclampsia as blood pressure greater or equal to 140/90 mm Hg with proteinuria of at least 1 plus on dipstick in two samples taken 6 h apart. Anaemia in pregnancy is defined as haemoglobin concentration less than 10 g/dl after 8 to 10 weeks of gestation. Finally,

term birth refers to those births that occurred during or after 37 weeks of gestation. This study was approved by the Protocol and Ethical Review Committee of the University of Ghana Medical School.

Collection of placental samples at delivery

The neonates were weighed during the first hour after delivery using manually calibrated scales by nurses of the maternity wards. All placentas were collected and placed in labelled containers, and then they were transported to the Pathology Department, KBTH. The placentas were washed with water and cleaned of blood clots in the laboratory.

Placental measurements (see below for details) of both low birth weight (<2500 g) neonates (designated as “cases”) and of normal birth weight neonates (i.e., in the range: 2500 g to <4300 g) (designated as “controls”). Samples were included for analysis if the mother had a singleton, delivery of a live neonate birth without major gross abnormalities at or after 37 weeks of gestation. Out of the 200 subjects that were enrolled, 56 delivered outside of the hospital. Thus, 144 subjects were used in this analysis, consisting of 72 “cases” and 72 “controls”.

Examination and processing of placenta

Gross examination of the placenta

All fresh and cleaned placentas were examined immediately or kept in a refrigerator (1-3°C) and examined within 24-48 h after delivery. Morphometric data was documented covering the weight of the placenta, length, width, thickness and the largest or smallest distance from the point of insertion of the umbilical cord to the edge of the placental disc, as is shown schematically in Figure 1. The dimensions of the placenta were taken as follows: horizontal and vertical lines serving as perimeter markers were drawn and the largest horizontal line taken as the length while the vertical line was taken as the breadth., The largest and smallest distances from the point of the insertion of the umbilical cord to the perimeter were measured, as shown in Figure 1. The placenta (excluding the umbilical cord and membranes) was weighed. After a detailed gross examination, the placenta was cut in serial slices ½ cm to 1 cm thick parallel to a line through the insertion of the umbilical cord. Samples of tissue were taken for histology as follows: (a) from the site of insertion of the umbilical cord (UC); (b) from each margin of the central slice including both placental tissue and chorionic membrane; and, (c) from all representative lesions or random slices throughout the placental tissue if no lesion could be identified grossly.

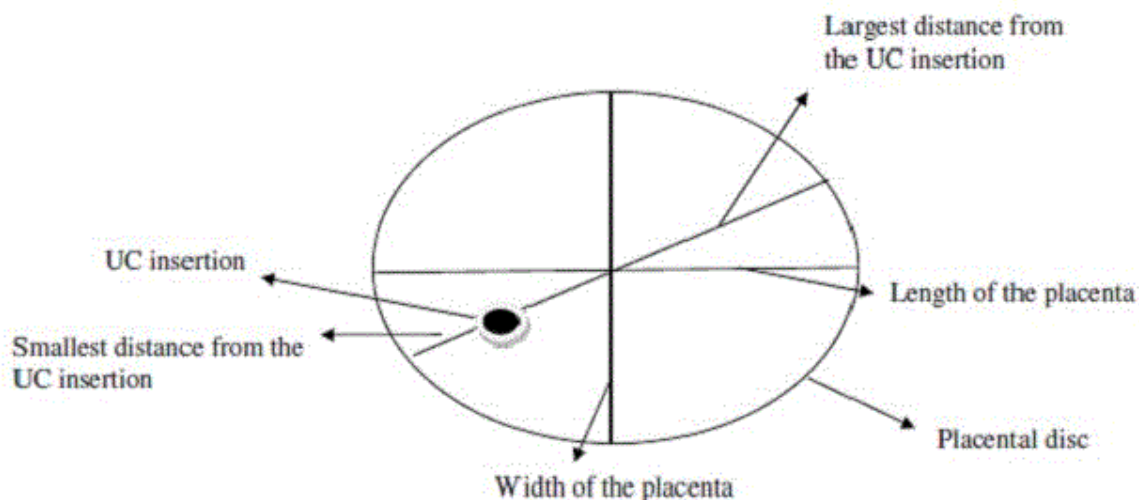


Figure 1: A schematic representation of the placental dimensions used in the study.

Histological evaluation

The tissue samples were soaked in 50-60 ml of 10% neutral buffered formalin for 2-3 days and they were embedded in paraffin wax after tissue fixation. Sections of tissue of 5 microns thickness were made and these tissues were then stained with hematoxylin, eosin and Giemsa stain for identification of chronic intervillitis.

The histological slides were examined by light microscopy under x40, x100, x400

Magnification with Leica DML type 020-518.500 DM/LS light microscope at the Department of Pathology, KBTH.

Statistical analysis

All calculations were carried out using either MS EXCEL (2013), SPSS V20 or STATA V13. Low birth weight was explored as a function of categorical (nominal) factors such as demographics and maternal characteristics by contingency tables. Associations between low birth weight and these factors were examined by chi-squared tests of the contingency tables. For those cases where sample sizes were low in a given class, and where this also meant that more than 20% of expected values had values less than 5), Monte Carlo simulation was used in SPSS V20 to establish accurate measures of probabilities (i.e., the p-values and their associated 99% confidence intervals). Odds ratios and their associated 95% confidence intervals were also determined for appropriate group-wise comparisons (described in the main text) using appropriate formula in MS EXCEL (also checked using univariate binary logistic regression in STATA V13). Low birth weight was also explored as a function of continuous factors such as placental

weight, length, width, thickness and distances from the placental disc of the umbilical cord insertions. Data was found to be slightly skewed only (due to a small number of outliers) and unpaired two-sample t-tests were used to detect differences in these continuous variables for the low birth weight group compared to the control group. As an additional and independent check, (non-parametric) Mann-Whitney tests were carried out and the results of these tests (not quoted here) were found to agree strongly with those results of the t-tests (i.e., in terms of detecting differences between the groups). Stepwise (multivariate) binary logistic regression was used to explore the data further and to account for any potentially confounding effects of the variables on each other. It was found that standardized residuals were generally small (i.e., less than 2) in all binary logistic regression calculations. Nominal factors were treated as binary variables (e.g., complications: yes or no) in order to reduce any potential problems of small sample sizes in specific groups. Furthermore, continuous variables (i.e., placental weight, length, age, etc.) were treated as (continuous) covariates. Note that odds ratios are determined with respect to a unit increase of these continuous variables, albeit scaled by a factor of 10⁻² to make odds ratios easier to interpret in Table 4. As there were a small number of outliers in these continuous variables, robust regression was used in multivariate logistic regression in STATA V13 in order to account for any possible model misspecification. However, any differences in final results for robust methods compared to non-robust (i.e., standard) methods were minimal. All measures of model fit (e.g. pseudo R-squared values) were found to increase very strongly for the multivariate model compared to equivalent univariate calculations, as expected.

Variable	Unadjusted (univariate)		Adjusted (multivariate)		
	OR	95% CI	OR	95% CI	Wald: P=

Complications (none to pre-eclampsia or anaemia)	2.13	0.978 to 4.640	3.246	1.074 to 9.814	0
Stable income (unstable to stable)	3.824	1.871 to 7.813	5.366	1.986 to 14.497	0
Marital status (unmarried to married)	14.2	1.794 to 112.396	21.389	3.610 to 126.734	0
Placental weight (scaled by a factor of 10 ⁻²)	0.178	0.092 to 0.342	0.28	0.115 to 0.683	0
Largest distance (scaled by a factor of 10 ⁻²)	0.032	0.004 to 0.277	0.01	0.001 to 0.173	0
Smallest distance (scaled by a factor of 10 ⁻²)	0.122	0.020 to 0.742	0.04	0.004 to 0.445	0

Table 4: Odds ratios from univariate (unadjusted) analyses and multivariate (adjusted) analyses via stepwise logistic multivariate regression (via “robust” methods) of maternal demographics, placental complications and gross placental dimensions.

Results

The incidence of LBW within the period from May 2000 to January 2006, at the KBTH was 6.2% (50,574 term live births with 3109 weighing <2500 g). In a univariate analysis of the maternal demographic and reproductive health characteristics that impact LBW

(Tables 1 and 2), unstable source of income, age band, single motherhood, unplanned pregnancy and antenatal complications, were significantly associated with low birth weight (P=0.0003, 0.0006, 0.0036, 0.0003 and 0.021, respectively).

	Low birth weight N=172	Controls N=72
Occupation		
Unemployed	13	3
Small scale trader	41	30
Employed (self or receiving salary)	18	39
$\chi^2=15.691$, dof=2, P (1-tailed)=0.0004; OR (unemployed compared to small scale trader)=3.171 (95% CI: 0.830 to 12.119); OR (unemployed compared to employed)=9.389 (95% CI: 2.376 to 37.098)		
Parity		
0	38	28
01-Jun	34	44
χ^2 (continuity correction)=2.266, dof=1, P (1-tailed)=0.1323; OR (0 compared to 1-6)=1.756 (95% CI: 0.906 to 3.406)		
Age (years)		
<21	32	11
21-30	28	40
≥ 31	12	21
$\chi^2=14.828$, dof=2, P (1-tailed)=0.0006; OR (<21 compared to 21-30)=4.156 (95% CI: 1.797 to 9.609); OR (21-30 compared to ≥ 31)=5.091 (95% CI: 1.899 to 13.647).		
Marital status		
Single	12	1
Married	60	71
χ^2 (continuity correction)=8.456, dof=1, P (1-tailed)=0.0036; OR (Single compared to Married)=14.2 (95% CI: 1.794 to 112.396)		
Planned versus unplanned pregnancy		
Unplanned	16	1
Planned	56	71

χ^2 (continuity correction)=13.073, dof=1, P (1-tailed)=0.0003; OR (Unplanned compared to Planned)=20.286 (95% CI: 2.610 to 157.651)		
Income		
Stable	17	39
Unstable	55	33
χ^2 (continuity correction)=12.886, dof=1, P (1-tailed)=0.0003; OR (stable compared to unstable)=3.824 (95% CI: 1.871 to 7.813)		

Table 1: Maternal socio-demographic and reproductive health characteristics between cases and controls (univariate analysis).

Gross measurements	Low birth weight N=72	Controls N=72	t-test: P (2-sided)=
Weight (g)	327.8 ± 61.2	429.5 ± 105.6	0
Length (mm)	187.8 ± 44.1	200.9 ± 28.6	0.037
Width (mm)	154.8 ± 21.7	171.1 ± 19.0	0
Thickness (mm)	11.5 ± 4.7	11.2 ± 3.9	0.602
Largest distance (mm)	111.1 ± 17.1	123.1 ± 21.5	0
Smallest distance (mm)	56.1 ± 18.2	65.0 ± 21.0	0.015

Table 3: Gross placental dimensions (mean ± standard deviation) in cases and controls.

All continuous variables except “thickness” (i.e., placental weight, length, width and largest and smallest distances) were found to be significantly different for the low birth weight group compared to the control group (Table 3) in a univariate analysis. After adjusting for confounding effects in a stepwise (multivariate) logistic regression analysis, unstable income, single motherhood and antenatal complications (pre-eclampsia and anaemia) were the only maternal demographic and reproductive health variables that remained significantly associated with LBW (P=0.001, 0.001 and 0.037, respectively) (Table 4) with an ORs of 5.366 (95% CI: 1.986 to 14.497), 21.390 (95% CI: 3.610 to 126.734) and 3.246 (95% CI: 1.074-9.814), respectively. Interestingly, vessel tree abnormalities had no significant effect on LBW. All the gross placental measurements were significantly lower in LBW compared to controls (Table 3) in a univariate analysis. However, only the placental weight, and the largest and smallest distances from the point of insertion of the umbilical cord were highly associated with LBW in a stepwise logistic regression analysis (Table 4) adjusting for the effects of all other variables (P=0.005, 0.002, 0.001, respectively; ORs 0.28 (95% CI: 0.115 to 0.683), 0.010 (0.001 to 0.173) and 0.04 (95% CI 0.004 to 0.445), respectively).

Discussion

Much evidence exists in the literature relating to factors that associate with LBW in preterm births. By contrast, fewer studies consider risks factors relating to LBW in full-term births, and still fewer studies (or reviews) concentrate on a diverse range of subject populations [1,6,7]. These factors make it imperative for such data to be collated. Our study shows that, proxy factors on nutrition, particularly unstable income source and single motherhood, serve as high-risk factor for term LBW in term infants in Ghana. Studies in Pakistan and China showed that maternal low primary education, anaemia, hypertension and socio-economic factors were strong factors that influenced term LBW [8,9]. Intrauterine malnutrition as a result of poor maternal nutrition can lead to restricted growth in utero and it

can serve as a proxy to LBW [29,30]. A single mother in Ghana, especially in the low income range, will have difficulty obtaining adequate income to afford enough, well-balanced food to eat. Clearly, this will in turn affect her nutritional supply and concomitantly neonatal nutrition. It is well established that placental nutrient transport efficiency is a core maternal factor that associates with LBW. Furthermore, antenatal complications also associate with LBW [28,31]. It has been reported that the placenta may act as a nutrient sensor that adjust maternal nutrient supply to fetal growth [27,30]. In our study, the combined effect of pre-eclampsia and anaemia were the respective placental and antenatal complications seen associating strongly with term LBW. Recent reports have compelling evidence of the role of nutritional deficiencies and inadequacies in pre-eclampsia particularly micronutrients, iron supplementation and inadequate diversity in food sources [32-34]. Anaemia is a common maternal nutritional disorder that has also recently been shown to lead to fetal anaemia, poor growth and LBW [35-37]. Interestingly, there was little evidence in our study that vascular tree structure associated with LBW suggesting that the structure may not strongly impact the volume or available surface area for nutrient exchange in the study population. The vascular tree has been suggested to be the sole source of oxygen and nutrient to the fetus, thereby defining placental efficiency [23,24]. Thus, it appears that nutrient delivery to the fetus may be minimally affected if placental efficiency in nutrient delivery is not unduly compromised by the vascular tree morphology. This hypothesis is partially supported from the very strong association of placental weight with LBW in the present population. The placental weight is a proxy for the available surface area for materno-fetal nutrient exchange, and so the larger the weight the greater the nutrient exchange (and vice versa) [28,31].

Previous reports have suggested that a shift in the centrality of the umbilical cord insertion on the chorionic plate reflects the level of vasculature available for nutrient supply [17,23]. Thus, a greater shift leads to a lower level of vascular distribution available for nutrient exchange (and vice versa) [24]. The largest distance from the point of

centrality is a high risk factor to term LBW in our population. Our results suggest that such a shift may indeed affect nutrient supply to the fetus, probably from changes in the vascular tree surface area required for nutrient transport to the fetus [23]. However, further research is necessary to establish if this observation is seen in other study populations. The overall LBW incidence found in this study was 6.2% for our sample of those mothers attending the Maternity Wards of the Obstetrics and Gynaecology Department of the Korle-Bu Teaching Hospital (KBTH), Accra, Ghana. This result contrasts a previous study in the community that reported a prevalence of 11% [38]. The difference could be due to early mortality rates within the Health Facility that precluded inclusion in the data capture. The overall prevalence in sub-Saharan Africa is 14%, which is ranked second globally after South-East Asia with a prevalence of 26% [3].

Conclusion

Finally, we conclude that maternal nutrition is a core problem in term LBW in Ghana. LBW prevention or reduction in incidence can be partially amenable to improved maternal nutrition and education during pregnancy.

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Author Contribution

AL conceived the study. All authors contributed to the design of the study. AL carried out the work. AL, DFJJ and QIK wrote the paper.

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