Original Article

A case–control study to examine the association between breastfeeding during late pregnancy and risk of a small-for-gestational-age birth in Lima, Peru

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Abstract

Excessive demands on maternal nutritional status may be a risk factor for poor birth outcomes. This study examined the association between breastfeeding during late pregnancy (≥ 28 weeks) and the risk of having a small-for-gestational-age (SGA) newborn, using a matched case–control design (78 SGA cases: birthweight <10th percentile for gestational age; 150 non-SGA controls: 50th percentile <birthweight <90th percentile for gestational age). Between March 2006 and April 2007, project midwives visited daily three government hospitals in Lima, Peru and identified cases and matched controls based on hospital, gestational age, and inter-gestational period. Mothers were interviewed and clinical chart extractions were completed. Factors associated with risk of SGA were assessed by their adjusted odds ratios (aOR) from conditional logistic regression. Exposure to an overlap of breastfeeding during late pregnancy was not associated with an increased risk of having a SGA newborn [aOR = 0.58, 95% confidence interval (CI): 0.10–3.30]. However, increased risk was associated with having a previous low-birthweight birth (aOR = 6.53; 95% CI: 1.43–29.70) and a low intake of animal source foods (<25th percentile; aOR = 2.26; 95% CI: 1.01–5.04), and tended to be associated with being short (<150 cm; aOR = 2.05; 95% CI: 0.92–4.54). This study found no evidence to support the hypothesis that breastfeeding during late pregnancy increases the risk for SGA; however, studies with greater statistical power are needed to definitively examine this possible association and clarify whether there are other risks to the new baby, the toddler and the pregnant woman.

Keywords: breastfeeding, pregnancy, small-for-gestational-age, maternal weight gain, diet.

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Introduction

Low birthweight for gestational age, commonly referred to as small for gestational age (SGA), not only represents a significant risk factor for infant morbidity and mortality (United Nations Children's Fund (UNICEF) & World Health Organization 2004; Valero de Bernabe *et al.* 2004) but has also been associated with long-term consequences such as central obesity (Rasmussen *et al.* 2005; Ibanez *et al.* 2006),

higher levels of fasting insulin (Soto & Mericq 2005) and coronary heart disease (Eriksson *et al.* 1999). Birthweight is an important indicator of the intrauterine environment that can be compromised by poor maternal nutritional status (Ramakrishnan 2004; Valero de Bernabe *et al.* 2004; Lasker *et al.* 2005). Inadequate maternal body mass index and weight gain during pregnancy and poor quality diet (macronutrient and micronutrient deficiencies) may have an effect on birth outcomes (Ricci *et al.* 2010). Fetal

growth and development may be affected by maternal nutritional status as early as the time of conception (King 2003); however, most studies have focused on maternal nutritional status during pregnancy.

Micronutrient requirements increase with pregnancy and can be difficult to meet from dietary sources alone. Consequently, it is not surprising that rates of nutritional deficiency are highest among pregnant women (Lindström *et al.* 2011). A prenatal health project conducted on 2313 Canadian pregnant women who completed a food frequency questionnaire (FFQ) reported that only 3.5% of women consumed the number of servings for all food groups recommended by the Canada's Food Guide (Fowler *et al.* 2012). The Peruvian National Survey of Food Consumption conducted in 2003 reported that the median intakes of iron, folic acid, vitamin C, thiamin, niacin and riboflavin among women of childbearing age were under the Estimated Average Requirement for each nutrient (Calderón 2005). According to the 2010 Peruvian Demographic and Health Survey (DHS), 33% of pregnant women were anaemic (INEI & Programa Measure DHS+/ORC Macro, 2011).

As maternal nutritional status can play such an important role on birth outcomes, factors that can affect maternal nutrition should be examined. A short inter-pregnancy interval is one factor that has been suggested to be detrimental to maternal nutrition and thus birth outcomes, but more research in this area is needed (King 2003; Dewey & Cohen 2007). In addition to limiting repletion of women's nutrient stores, a short inter-pregnancy interval may lead to an overlap of breastfeeding with a new pregnancy. The macro- and micronutrient requirements of these two physiologically demanding states may exceed a woman's intake and place her further at nutritional risk. As in pregnant women, micronutrient deficiencies have been reported in lactating women. Anaemia was

reported among 27% of Peruvian lactating women in 2010 (INEI & Programa Measure DHS+/ORC Macro, 2011).

An overlap of breastfeeding and pregnancy is not an uncommon occurrence in many areas of the world. Data from the National Health and Nutrition Examination Survey III, for example, showed that 5% of lactating US women were pregnant (Briefel *et al.* 2000). Merchant *et al.* reported that among rural Guatemalan women participating in a nutrition supplementation trial, 50% of the women who had a child <7 years were breastfeeding during at least the first trimester of the next pregnancy (Merchant *et al.* 1990). In addition, Ramachandran (2002) found that around 30% of Indian women who became pregnant did so while still lactating. In the same year, Marquis *et al.* (2002) reported breastfeeding during the last trimester of pregnancy in 10% of Peruvian pregnant women who had a child less than 4 years of age. Given the reported links between maternal diet and birthweight, and the high prevalence of nutrient deficiencies among pregnant women, we hypothesized that the additional nutritional demands of breastfeeding during the third trimester of pregnancy would increase the risk of having a SGA infant. This study was designed to test this hypothesis.

Materials and methods

Study site and study design

This study was conducted between March 2006 and April 2007 at three government hospitals in Lima, Peru: Hospital de Apoyo Maria Auxiliadora (southern Lima), Hospital Nacional Docente Madre Niño San Bartolome (central Lima) and Hospital Nacional Hipolito Unanue (eastern Lima). The sites were chosen because each hospital had a high number of

Key messages

- Excessive demands on maternal nutritional status may be a risk factor for poor birth outcomes.
- There was no evidence of an association between breastfeeding during late pregnancy and increased risk for SGA, but further studies are warranted.
- Women who continue to breastfeed during pregnancy need more evidence-based advice regarding potential consequences of this behaviour.

births and an overlap of breastfeeding during late pregnancy was commonly reported among their pre-natal clients. A case-control study design was used as the SGA incidence rate in Peru was unknown but was expected to be low as the national low-birthweight rate was 10% (United Nations Children's Fund (UNICEF) & World Health Organization 2004) and global SGA rates were estimated to range between 2.3% and 10% (Saenger *et al.* 2007).

Ethical approval

The study received ethical approval from the Institutional Review Board of Iowa State University, the Research Ethics Committee of the Instituto de Investigación Nutricional and the ethics committees and/or authorities of the three hospitals.

Definition of cases and controls

All eligible women were at least 18 years of age, had a child <4 years old who had been breastfeeding and was living with her, started labour spontaneously and gave birth to a single, live newborn with a gestational age >32 weeks and ≤41 weeks. Within this defined population, cases were identified as those women whose newborns had a birthweight for gestational age <10th percentile (SGA). A control was defined as a woman whose newborn's birthweight for gestational age was >50th percentile and <90th percentile (non-SGA). The Latin American Center of Perinatology and Human Development (CLAP) established cut-off values for the 10th, 50th and 90th percentiles for birthweight for gestational age; no differentiation was made by sex (Fescina *et al.* 1996). These values were used to define the cases and controls in this study. The 50th percentile was chosen as the lower limit to avoid possible misclassification of the controls. To assure that control mothers had had the same potential risk of giving birth to a SGA newborn and newborns in the control group had the same potential for exposure to a breastfeeding-pregnancy overlap as the population, each case was matched to two controls according to hospital of delivery, week of gestational age of the newborn and inter-gestational interval (time between delivery of the mother's last child and birth of

newborn). The inter-gestational interval was categorized into three levels: 9–21 months, 22–34 months and 35–47 months. The use of two controls for every case enhances the study's power and the precision of the estimates (Grimes & Schulz 2005).

Definition of exposure variable

Exposure to a breastfeeding-pregnancy overlap was defined as continued breastfeeding until at least the 28th week of gestation, the period that represented the third trimester of pregnancy when the greatest fetal weight gain occurred.

Sample size

We assumed that 40% of pregnant women had a toddler <4 years of age and 12% of eligible women breastfed during late pregnancy (unpublished prenatal clinic pilot data). The sample size was calculated using Lachin's (2008) method for binary covariates using $\alpha = 0.05$ and a power of 80%. The annual number of births at the three hospitals (24 468 in 2006) with a SGA rate of at least 5% of all births was expected to meet the sample size of 183 cases and 366 controls needed to detect an odds ratio of 2.

Data collection

Each hospital was visited daily by a project midwife who screened all births that had occurred since the last visit. After the midwife enrolled a case, she identified and enrolled two matched controls. Hospital policy dictated that mothers be discharged 24 h after a vaginal birth and within 72 h after a caesarean delivery. The midwife approached all mothers at least 6 h after delivery to allow them some time to rest and facilitate a relaxed dialog during the project interview. After explaining the study and obtaining informed written consent from the mother, the midwife used a structured questionnaire to interview the mother about her socio-demographic characteristics, obstetric and health history including use of supplements during pregnancy, birthweight and gestational age of her last child, and recommendations that she received during pregnancy. A brief FFQ adapted from previous studies

included 17 foods and food groups (chicken, beef/pork, chicken liver, beef liver, other organ meat, fish, shellfish, dairy products, eggs, beans, quinoa/wheat, rice, pasta, bread, vegetables not in soup or stew, potatoes/sweet potatoes/cassava and fruit) that were the primary sources of micronutrients (including iron, zinc and calcium) commonly deficient in this population (Sacco *et al.* 2003). Mothers reported the number of days per week or month that the food or food group was consumed. To obtain information about exposure to a breastfeeding-pregnancy overlap, mothers were asked if their previous child (the toddler) was currently breastfeeding. If the response was 'yes', mothers were asked how many times a day she breastfed the previous week; if the response was 'no', they were asked at what age the child had been weaned (Gillespie *et al.* 2006).

Next, the midwife completed a clinical chart review and extracted information about the mother (obstetric history including previous LBW births, prenatal controls including haemoglobin analyses and anthropometric measurements, gestational age documented from last menstrual period or ultrasound and progression of stages of labour) and the newborn (birth anthropometry, gestational age determined by Capurro's method which uses five physical parameters to calculate a newborn's gestational age: skin texture, shape of the ear, size of the mammary nodule, formation of the nipple and the folds of the sole of the foot (Capurro *et al.* 1978), Apgar scores and medical procedures and pathologies present at birth). Birthweight was measured by hospital staff using a digital regularly calibrated scale (SORES, Lima, Peru) with a capacity of 22 kg and a precision of 5 g that was provided by the project. Gestational age was calculated using the date of the beginning of the last normal menstrual period (LNMP). LNMP is widely used in research; although it has been reported to be prone to error (Kramer *et al.* 1988), it was the most consistently reliable method available for study mothers. In cases where the mother was not sure about the LNMP date (22% of SGA and 12% of non-SGA mothers; $P = 0.052$), we compared the gestational age from any available ultrasound to the gestational age recorded using Capurro's method. If the difference between the two methods was greater than 2 weeks, the mother was not enrolled.

Data analysis

A dichotomous variable for exposure was coded based on a mother's response to questions about breastfeeding and weaning her toddler. Exposure existed if the mother stated that she presently was breastfeeding or reported that she had weaned the toddler after 27 weeks of pregnancy.

Pregnancy weight gain was estimated only for those women whose clinical chart included a pre-pregnancy weight and a final pregnancy weight taken no more than 9 days before delivery ($n = 128$). Weight gain was calculated as the difference between the two weights. Maternal height was categorized as a dichotomous variable, $<$ or $\geq$ to the 25th percentile for height (150 cm) for this sample.

Responses to individual FFQ questions were converted to average daily frequency of intake. Total intake of animal source foods (ASF) was calculated as the sum of all nine ASF categories (chicken, beef/pork, chicken liver, beef liver, other organ meat, fish, shellfish, dairy products, eggs). Low ASF daily intake in this study was defined as <25 th percentile for all participants (equivalent to 1.9 ASF foods per day).

Group differences in the exposure variable (breastfeeding-pregnancy overlap) and the variables that were possible confounders but not used in the matching procedure were tested individually using unadjusted conditional logistic regression. Those variables that were significantly associated with risk in the unadjusted analysis were included in the conditional multiple logistic regression analysis that tested the adjusted risk associated with a breastfeeding-pregnancy overlap on the occurrence of SGA. Unadjusted and adjusted odds ratios (OR and aOR, respectively) and 95% confidence intervals (CI) are reported. An unmatched logistic regression analysis was also run to analyse data from all participants, including cases that had no matched control.

The probability that breastfeeding-pregnancy overlap is associated with decreased risk of SGA (i.e. an odds ratio <1) was estimated also using a Bayesian formulation of the conditional logistic regression model (Appendix A). The posterior distribution of the log odds ratio was estimated by Markov Chain Monte Carlo sampling using 10 000 samples and a

burn-in of 1000 samples. Convergence was monitored by the Brooks–Gelman–Rubin statistic with three chains and inspection of trace plots. The probability that the odds ratio is <1 was estimated as the proportion of posterior samples of the log odds ratio that were less than 0. We used diffuse proper prior distributions for all parameters. Sensitivity to choice of prior was assessed by changing the prior distribution for the log odds ratio to more informative priors with positive means (mean of 2 and variance of 1000, and mean of 5 and variance of 100).

The analyses were conducted using SPSS/PASW version 18 (SPSS, Inc., Chicago, IL, USA), SAS version 9.2 (SAS Institute, Inc., Cary, NC, USA) and OpenBUGS version 3.2.1 (OpenBUGS Project Management Team). Statistical significance was set at $P < 0.05$.

Results

Study participants

A total of 21 534 deliveries were screened; 1248 women met all of the inclusion criteria and 20 286 births were excluded because they had one or more of the following conditions: first live birth (50%); sibling >48 months (24%), mother <18 years old (6%), not a singleton birth (1%), induced labour (6%) or pathologies at birth (16%). The refusal rate was low (5%) and did not differ between cases and controls ($P = 0.40$). All women with an eligible SGA newborn ($n = 102$) were invited to enrol in the study and 95 accepted. Among the 1146 women in the non-SGA group, 157 women were invited to participate and 150 accepted. The remaining 989 women met the inclusion criteria but were not invited primarily because they were not selected as one of the matched controls for a case (93%). Six cases had only one matched control; 17 cases were excluded from the matched analysis due to the lack of at least one matched control. Controls were difficult to find for some cases because of the strict matching criteria and infrequent occurrence of certain combinations of gestational age, inter-gestational period and adequate weight for gestational age. Of the 17 cases without controls, nine were premature (35 and 36 weeks) and one had a

Table 1. Descriptive characteristics of Peruvian newborn SGA cases and their non-SGA controls extracted from medical chart*

	SGA	Non-SGA
	<i>n</i> = 78	<i>n</i> = 150
Birthweight, g	2529.1 $\pm$ 173.9	3534.2 $\pm$ 175.5
Birth length, cm	46.9 $\pm$ 1.4	50.5 $\pm$ 1.4
Apgar scores		
1 min	8.0 $\pm$ 1.0	8.1 $\pm$ 1.0
5 min	8.9 $\pm$ 0.5	9.0 $\pm$ 0.5
Use of incubator	4 (5.1)	3 (2.0)
Presence of pathology	5 (6.4)	4 (2.7)
Use of oxygen	6 (7.7)	5 (3.3)

*Values shown as mean $\pm$ SD or *n* (%). SGA, small for gestational age: <10 th percentile birthweight for gestational age; non-SGA: 50th percentile $>$ birthweight for gestational age <90 th percentile (Fescina *et al.* 1996).

short and three had long inter-gestational periods. In addition, four cases were enrolled late in the study and controls were not found prior to closing enrolment. Two of the cases without controls were exposed to the practice of breastfeeding during late pregnancy. Data from 78 SGA and 150 non-SGA participants were included in this matched analysis.

Newborn characteristics

Group differences in birthweight for gestational age were defined by the study design (Table 1). In addition to the expected difference in weight, the mean birth length of SGA newborns was 3.6 cm less than that of non-SGA newborns ($P < 0.001$), demonstrating that the SGA newborns were overall smaller, not just thinner, than the non-SGA newborns. Few newborns were premature ($n = 3$ sets of matched case–controls) and none were post-term; the mean gestational age was 38.7 ± 0.2 weeks. Although a small number of newborns required an incubator, these were all transitory; none of the infants were in a neonatal intensive care unit. The only other group difference in newborn characteristics was in sex; there was a higher proportion of females in the SGA than the non-SGA group ($P = 0.001$; Table 2).

Maternal socio-demographic characteristics

Socio-demographic characteristics of case and control mothers were similar. About half of all mothers were

Table 2. Unadjusted odds ratios for SGA from conditional logistic regression for maternal and pregnancy characteristics that were possible confounding variables*

		SGA	Non-SGA	Unadjusted OR	(95% CI)
Maternal					
Age, y	78/149 [†]	26.2 ± 5.9	27.8 ± 6.0	0.96	0.92–1.01
Height, cm	77/146	151.8 ± 6.2	154.2 ± 6.2	0.95	0.91–0.99
Height <150 cm	77/146	25 (32.9)	26 (17.7)	1.98	1.08–3.61
Low ASF intake [‡]	72/140	26 (36.1)	32 (22.9)	1.87	0.98–3.56
Obstetric history					
Pregnancies [§] , <i>n</i>	78/150	2.0 ± 1.5	2.4 ± 1.5	0.90	0.74–1.09
Births [§] , <i>n</i>	78/150	1.8 ± 1.3	2.0 ± 1.3	0.89	0.70–1.12
Last birthweight, g	70/139	2860 ± 527	3309 ± 531	0.90 [¶]	0.90–0.95
Previous LBW ^{**}	70/126	16 (22.9)	4 (2.9)	8.80	2.54–30.57
Current pregnancy					
Haemoglobin, g/dL ^{††}	62/134	11.0 ± 1.2	11.2 ± 1.2	0.94	0.71–1.23
Anaemia ^{‡‡}	62/107	22 (35.5)	53 (39.6)	0.87	0.42–1.82
Weight gain, kg	41/87	8.6 ± 5.2	11.7 ± 5.0	0.78	0.65–0.92
Wt gain <11 kg ^{§§}	41/87	28 (68.3)	33 (37.9)	4.20	1.39–12.67
Pre-eclampsia	78/150	5 (6.4)	5 (3.3)	2.00	0.58–6.91
Female newborn	78/150	52 (66.7)	66 (44.0)	2.75	1.48–5.10
Breastfed >28 weeks of pregnancy ^{¶¶}	78/150	3 (3.8)	14 (9.3)	0.41	0.11–1.47

*Values shown as mean ± SD or *n* (%). SGA, small for gestational age, <10th percentile birthweight for gestational age; non-SGA: 50th percentile <birthweight for gestational age <90th percentile (Fescina *et al.* 1996). Conditional logistic regression on cases and controls matched for hospital, gestational age and inter-gestational period (9–21 months, 22–34 months and 35–47 months). [†]Sample for SGA/non-SGA. [‡]ASF, animal source foods (chicken, beef/pork, chicken liver, beef liver, other organ meat, fish, shellfish, dairy products, eggs); low ASF intake: <25% percentile (= 1.9 ASF foods). [§]Does not include present pregnancy/birth. [¶]The estimate is for a birthweight interval of 50 g. ^{**}LBW, low birthweight in last pregnancy. ^{††}Haemoglobin values were available from different trimesters: SGA: 1st = 0%, 2nd = 27.4%, 3rd = 72.6%; non-SGA: 1st = 9%, 2nd = 29.8%, 3rd = 61.2%. ^{‡‡}Anaemia was defined as <11 g/dL. ^{§§}Weight gain <median of 11 kg. ^{¶¶}Distribution of the matched sets of cases and controls according to their exposure to breastfeeding during late pregnancy:

Controls	Cases	
	Exposed	Not exposed
Not exposed	3	62
One of the controls exposed	0	12
Two of the controls exposed	0	1

from Lima (50% of the SGA group and 55% of the non-SGA). Of the SGA and non-SGA groups, 56% and 62% had completed at least high school, 87% and 92% were married or living with a partner and 17% and 13% worked at the time of the study, respectively. The mean difference of 1.5 years in maternal age between groups did not reach significance ($P = 0.12$; Table 2).

Maternal nutrition and obstetrics characteristics

There were important group differences in the mothers' nutrition and obstetric history (Table 2).

Almost twice as many mothers in the SGA group were less than 150 cm in height compared to the non-SGA group ($P = 0.03$). The mean birthweight of the previous pregnancy in the SGA group was about 450 g lower and having had a previous LBW birth was much more common among SGA than non-SGA women ($P < 0.01$). Mothers with a SGA newborn had gained almost 3 kg less during the current pregnancy than the comparison group ($P < 0.01$). However, there were no group differences in the prevalence of smoking (5% SGA vs. 2% non-SGA), exposure to passive smoking (17% SGA vs. 11% non-SGA) or use of antibiotics (32% SGA vs. 28% non-SGA) or

vaginal suppositories (28% SGA vs. 37% non-SGA). The majority of women reported taking a vitamin and/or mineral supplement (85% SGA vs. 81% non-SGA). Iron supplements were most common (82% vs. 78%), whereas zinc (18% vs. 23%), calcium (28% vs. 26%) and folic acid (27% vs. 39%) supplements were reported by a minority of SGA and non-SGA women, respectively. No group differences were found regarding the use of any of the supplements.

Maternal food frequency intake

The frequency of intake of many of the individual foods from the FFQ included the full range from 0 to 30 days per month. Only no consumption of pork/beef was associated with a risk of SGA (OR = 2.96, 95% CI: 1.15–5.90). The total ASF intake ranged from 0.75 to 4.5 ASF foods per day. SGA and non-SGA median values were 2.4 vs. 2.4, 0.5 vs. 0.6 and 0.9 vs. 1.0 times a day for total ASF, meats/poultry products and milk, respectively. Eggs and fish intake frequency in both study groups were 0.4 and 0.1 times a day, respectively. A low ASF daily intake (<25th percentile = 1.9 times a day) tended to be associated with a twofold increase in the risk of having a SGA newborn (OR = 1.87, 95% CI: 0.98–3.56; $P = 0.058$). The median of the daily consumption of fruits was 1 for both groups and of vegetables were 0.3 for SGA and 0.4 for non-SGA.

Maternal breastfeeding practice

Mothers in the SGA group weaned their toddlers when they were about 1.5 months younger than mothers in the non-SGA group (14.5 ± 8.0 vs. 16.1 ± 7.8 months); a one-month decrease in breastfeeding duration was associated with a 5% increase in risk of SGA (OR = 0.95, 95% CI: 0.92–0.99; $P = 0.02$). The median frequency of breastfeeding was low, at 3.0 times a day for both groups.

The number of months of overlap as a continuous variable (OR = 0.90; 95% CI: 0.79–1.02) as well as the presence or absence of any overlap during the entire pregnancy (OR = 0.65; 95% CI: 0.34–1.25) were not associated with risk of SGA. A similar proportion of SGA and non-SGA women reported breastfeeding

Table 3. Adjusted odds ratios for SGA from conditional logistic regression for maternal and pregnancy characteristics*

	Adjusted OR	(95% CI)
Breastfed ≥ 28 weeks of pregnancy	0.58	0.10–3.30
Maternal height <150 cm	2.05	0.92–4.54
LBW in last birth [†]	6.53	1.43–29.70
Female newborn	2.45	1.07–5.64
ASF <25th percentile [‡]	2.26	1.01–5.04

*Total $N = 164$; cases (SGA) = 62; controls (non-SGA) = 102. SGA, small for gestational age, <10th percentile birthweight for gestational age; non-SGA: 50th percentile <birthweight for gestational age <90th percentile (Fescina *et al.* 1996). Conditional logistic regression on cases and controls matched for hospital, gestational age and inter-gestational period (9–21 months, 22–34 months and 35–47 months). [†]LBW, low birthweight in last pregnancy. [‡]ASF, animal source foods (chicken, beef/pork, chicken liver, beef liver, other organ meat, fish, shellfish, dairy products, eggs); low ASF intake: <25% percentile of sample (1.9 ASF foods).

during the first and second trimester (23% SGA vs. 24% non-SGA during the first trimester; 10% SGA vs. 12% non-SGA during the second trimester); the twofold difference in reports of breastfeeding during the third trimester among those women who gave birth to a SGA baby compared to the non-SGA group did not reach significance (4% vs. 9%). In this study, there was no evidence of an association between an overlap of breastfeeding during late pregnancy and an increased risk of SGA. In fact, the unadjusted and aOR were opposite to the hypothesized direction (Tables 2 and 3). To determine if perception of risk of a SGA influenced breastfeeding duration, analysis of the data set without the women who had a previous LBW infant was conducted. This analysis showed similar results to that of all matched data points (OR = 0.46; 95% CI: 0.10–2.19). Conducting an unmatched analysis with all cases (78 matched + 17 not matched) and 150 controls showed results consistent with the matched analysis (OR = 0.54, $P = 0.25$, 95% CI: 0.19–1.55).

The probability that the odds ratio was less than 1 was estimated using the Bayesian model as 98.8%. The trace plots and the Brook–Gelman–Rubin statistics indicated no problem with convergence. The choice of prior had little impact on the estimated probability (estimates of 98.7% and 98.3% for the two other choices of prior).

Many women reported receiving recommendations regarding breastfeeding during pregnancy. Most of the recommendations were to wean the toddler because the overlap was believed to be harmful for the mother, the fetus or the toddler. Almost 20% of women in both groups reported that they received recommendations from health professionals or friends. However, a significantly higher proportion of mothers from the non-SGA group received recommendations from relatives compared to SGA group mothers (40.7% vs. 15.4%, respectively; $P < 0.001$). More than 70% of the non-SGA who breastfed until late pregnancy reported that they received recommendations from relatives.

In the multiple conditional logistic regression model (Table 3), only maternal and newborn factors remained significant predictors of risk of SGA newborn. Maternal nutritional factors and having a female baby more than doubled the risk of SGA; however, this was overshadowed by the sixfold increase in risk associated with previously having a LBW baby.

Discussion

To our knowledge, this is the first study designed to examine the association between the practice of breastfeeding during late pregnancy and SGA, although our study suggests that this practice may be common. We chose to use a case-control study design to examine the relationship between breastfeeding during late pregnancy and giving birth to a SGA infant as this design is efficient for low-incidence outcomes. We expected many more SGA and were surprised at the low incidence rates at the hospitals. This made it difficult to achieve our sample size. Contrary to our hypothesis, our conditional matched as well as the unmatched logistic analysis results showed no evidence that the practice of breastfeeding during late pregnancy increased the risk of SGA; the non-significant odds ratio was < 1 . The Bayesian analysis produced OR results that were also < 1 with high probability. Bayesian analyses with diffuse or uninformative priors often produce results that are very similar or identical to results from frequentist ('standard') methods. The two

approaches produce somewhat different results for the overlap-SGA association. The frequentist 95% CI for the unadjusted OR was 0.11–1.47, but the Bayesian 95% credible interval was 0.029–0.89 with an estimated probability of 98.8% that the OR was < 1 . The disparity arises from the small number of informative matched sets (see Table 2 footnote). In this situation, estimates from traditional conditional logistic regression can be biased and extremely variable (Greenland *et al.* 2000). Greenland *et al.* (2000) recommend that such data be analysed using Bayesian or empirical Bayes versions of the conditional logistic regression model.

The only other study that examined the association between birthweight and a breastfeeding-pregnancy overlap (at any trimester) reported a non-significant –57 g difference in birthweight in infants who were born to mothers who had an overlap compared to those with no overlap (Merchant *et al.* 1990). In contrast, in a small study of 57 women who breastfed during pregnancy, 43% of women overlapped until delivery; the average birthweight in the study (3.43 kg) was in the normal range (Moscone & Moore 1993).

Our study confirms other reports of associations between SGA including maternal characteristics (low maternal height, weight gain during pregnancy, previous children's birthweights). These results are consistent with reported risk factors associated with low birthweight (Lawoyin & Oyediran 1992; Vega *et al.* 1993; Abdulrazzaq *et al.* 1995; Strauss & Dietz 1999). The higher proportion of females in the SGA group could be explained by the fact that the table used to classify cases and controls did not have any differentiation by sex, thus overestimating SGA prevalence among female babies. Our finding of an increased risk of SGA with a low ASF daily intake is consistent with reports that associate the consumption of protein with the risk of SGA. Kramer and Kakuma reported results from 13 trials, demonstrating a substantially reduced incidence of SGA associated with a balanced energy/protein supplementation (Kramer & Kakuma 2003). Olsen *et al.* reported that higher milk intake in pregnancy was associated with a lower risk of SGA and that this outcome was related with the protein from dairy products (Olsen *et al.* 2007).

The proportion of mothers in the SGA group who reported an overlap during late pregnancy was much lower than a previous report among Peruvian women (Marquis *et al.* 2002), although the average 7.5% (cases and controls) reported in this study is still a sufficiently common practice to be of public health importance if associated with SGA. This feeding behaviour, at any trimester, is not supported by the Peruvian culture and generally discouraged by Peruvian health professionals and this may have led to biased reporting, with higher denial among mothers delivering an SGA baby. As mothers were interviewed after delivery, they were aware of their birth outcomes which might have influenced their openness about reporting breastfeeding during pregnancy. However, the existence of biased reporting is not supported by other data. If SGA mothers purposefully under-reported breastfeeding during pregnancy, then we might have expected them to also consistently under-report having received recommendations to stop this practice. The proportion of women who said that they received recommendations about breastfeeding during pregnancy from health professionals and friends was similar in the SGA and non-SGA groups. In contrast, the higher percentage of women who reported that family members discouraged the practice suggests that more non-SGA mothers may have been breastfeeding during pregnancy than SGA mothers.

Reported breastfeeding practices during the first and second trimesters of pregnancy also suggest that there was no biased reporting. An additional explanation could be reverse causality, that is, the perceived risk of SGA determined maternal breastfeeding behaviour. However, the analysis was unchanged when data from mothers with previous LBW births were excluded from the analysis, suggesting that reverse causality may not be relevant here. In this study, SGA mothers stopped breastfeeding almost two months before non-SGA mothers. Although there are no studies on SGA babies, researchers have reported shorter duration of breastfeeding among low-birthweight babies (including SGA) compared to normal-weight babies (Lefebvre & Ducharme 1989; Flacking *et al.* 2003). Low weight gain during pregnancy, a factor linked to SGA, may have also contributed to a mother's decision to wean.

In the present study, we found an average breastfeeding frequency of three times a day by the toddler, while the previous study that reported a lower weight gain in infants who were born from mothers who breastfed during late pregnancy reported an average breastfeeding frequency of five times a day (Marquis *et al.* 2002). One of the limitations of both studies was that breastfeeding practices were documented through recall, so no information was available on milk consumption at each breastfeeding event. We also were not able to look at more complex factors, including placental morphology and endocrine factors, among others, that have been reported to be related to the occurrence of SGA (Christian 2010). Analysis of interactions involving factors that may modify the association of a breastfeeding-pregnancy overlap and the risk of SGA was not feasible due to the limited sample size. There may be maternal physiological adaptations that enable adequate fetal growth (Merchant *et al.* 1990). A decrease in breast milk intake has been reported on a group of toddlers whose mothers were pregnant compared with non-pregnant women (Verney A., unpublished data) and a difference on breast milk composition for the newborn has also been reported by Marquis *et al.* (2003). More research is needed to understand these physiological adaptations and their effect on maternal body stores and also to explore if feeding demand and milk intake of the toddler modulates the observed relationship.

In conclusion, in this study, there was no evidence that there is an association between increased risk of SGA and an overlap of breastfeeding during late pregnancy. Some published evidence suggests that the practice may be detrimental to post-natal health and growth and more research is needed to further explore the consequences of this practice as we found that breastfeeding during pregnancy is common, and, in our population, 7.5% of pregnant women with toddlers breastfed up to the last trimester of pregnancy despite advice against the practice.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Contributions

All authors were involved in the design, analysis, interpretation and final approval of the manuscript. RP, GM and MP were involved in the data collection. RP wrote the first draft of the manuscript.

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Appendix A: The Bayesian conditional logistic regression model

The data are:

- N_i The number of SGA individuals (cases) in matched set i (always 1)
- Y_i The number of cases with overlap in matched set i (0 or 1)
- M_i The number of non-SGA individuals (controls) in matched set i (1 or 2)
- X_i The number of controls with overlap in matched set i (0, 1, or 2)

The parameters are:

- μ_i The log odds of overlap for controls in matched set i
- α The log odds ratio for overlap

We also define π_{0i} as the probability of overlap for a control individual in matched set i and π_{1i} as the probability of overlap for a case individual in matched set i .

The conditional logistic regression model for a single binary covariate is:

For control individuals:

$$\log\left(\frac{\pi_{0i}}{1-\pi_{0i}}\right) = \mu_i$$

$$X_i \sim \text{Binomial}(M_i, \pi_{0i})$$

For case individuals:

$$\log\left(\frac{\pi_{1i}}{1-\pi_{1i}}\right) = \mu_i + \alpha$$

$$Y_i \sim \text{Binomial}(N_i, \pi_{1i})$$

Our prior distributions are:

$$\mu_i \sim N(0, 1000000)$$

$$\alpha \sim N(0, 1000000)$$

Our two “more informative” priors for alpha are $N(2, 1000)$ and $N(5, 100)$.