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Title:

Short interpregnancy interval and low birth weight: a role of parity

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ABSTRACT

Objectives: Short interpregnancy intervals (IPI) and high parity may be synergistically associated with the risk of unfavorable pregnancy outcomes. This study tests if the effect of short IPI on the odds ratio for low birth weight (LBW, <2,500 g) differs across parity status.

Methods: The study was carried out on the birth registry sample of almost 40,000 singleton, live-born infants who were delivered between the years 1995 and 2009 to multiparous mothers whose residence at the time of infant's birth was the city of Krakow. Multiple logistic regression analyses were used for testing the effect of IPI on the odds ratio (OR) for LBW, after controlling for employment, educational and marital status, parity, sex of the child, maternal and gestational age. Stratified analyses (according to parity) and tests for interaction were performed.

Results: Very short IPI (0–5 months) was associated with an increased OR for LBW, but only among high parity mothers with three or more births (OR = 2.64; 95% CI 1.45–4.80). The test for interaction between very short IPI and parity on the OR for LBW was statistically significant after adjustment for multiple comparisons (P = 0.04). Among low parity mothers (two births) no statistically significant associations were found between IPI and LBW after standardization.

Conclusion: Parity may modify the association between short birth spacing and LBW. Women with very short IPI and high parity may have a higher risk of having LBW infants than those with very short IPI but low parity.

Low birth weight (LBW) poses a crucial epidemiological problem, mainly because it contributes strongly to infant mortality and increased risk of many diseases in adult life (Barker, 1995; Jasienska, 2009a; Wells, 2000). LBW, defined as birth weight below 2500 g, is a consequence of preterm birth, that is a birth before 37 weeks of gestation, or retarded fetal growth (known also as hypotrophy – small for gestational age babies born at term), or is a result of both factors combined (Glinianaia et al., 2004).

Higher probability of delivering an infant with LBW may be also associated with parity. Life-history theory predicts that increased allocation into current pregnancy may lead to reduced future pregnancy outcomes, especially when resources are limited (Jasienska, 2009b; Lycett et al., 2000). Multipara mothers are predisposed to adverse pregnancy outcomes because they are more likely to have additional health problems, such as chronic anemia, diabetes mellitus and hypertension which are known to influence fetal growth (Aliyu et al., 2005). Aliyu et al. (2005) in a review article pointed out that more frequent incidences of placenta previa, abruption, abnormal presentation, and hemorrhagic complications in grand multiparous and great grand multiparous mothers make them more prone to have an offspring with LBW.

Birth spacing is also a factor contributing to adverse birth outcomes. Both very short and very long intervals between pregnancies (typically defined as intervals shorter than 6 months and longer than 60 months) have been found to increase the risk of LBW and other pregnancy health problems (Adams et al., 1997; Conde-Agudelo et al., 2006; de Weger et al., 2011; Gibbs et al., 2012; Kozuki et al., 2013; Wendt et al., 2012; Zhu and Le, 2003). The mechanism of the changes in fetal development as a result of birth spacing is still not clear. However, it is likely that pregnancies that occur before restoration of maternal hormonal and energy balance, and repletion of maternal resources, especially energy, proteins, essential fatty acids, folate and iron, can lead to health complications for subsequent offspring (Conde-Agudelo et al., 2012; van Eijsden et al., 2008). Maternal depletion syndrome is defined as deterioration of maternal condition occurring in women with high lifetime costs of reproduction, especially when they live in energy poor environment (Jasienska, 2013). High lifetime costs of reproduction may have long-term negative health consequences for the mother, such as increased risk of coronary heart disease (Lawlor et al., 2003) or diabetes (Simmons et al., 2006), and consequently result in reduced lifespan (Jasienska et al., 2006).

We hypothesized that interaction between parity and birth spacing may be associated with the risk of low birth weight. We expected that the effect of short interpregnancy intervals will differ across the parity status with the impact of short birth spacing being stronger for high parity than for low parity mothers. The results of previous studies suggest synergistic effect of short interpregnancy intervals and high parity on the risk of unfavorable pregnancy outcomes (Hinkle et al., 2014; Miller, 1994), but this problem has not been adequately addressed. Therefore, it is important to examine the effect of such interaction on the odds ratio for LBW.

MATERIALS AND METHODS

The study was carried out on a group of life born infants who were delivered between 26 and 42 weeks of gestation between October 1st, 1995 and the end of December 2009 to mothers whose residence at the time of infant's birth was the city of Krakow. The data was obtained from the birth registry (Central Statistical Office in Poland). The registration record included: month and year of birth, birth weight (in grams), infant's sex, maternal age (in years), gestational age (in weeks), parity, maternal education (primary, lower secondary, basic vocational, upper general or specialized secondary and academic education), maternal employment status (employed vs. not employed) and maternal marital status (married vs. not married, that is single, widow, divorced or in separation). Because the date of birth in registration records was restricted to month and year, the day of birth had to be assigned as 15^{th} of given month to each newborn. Low birth weight (LBW) was defined as birth weight below 2,500 g, and all infants with birth weight ≥ 2,500g were classified as having a normal birth weight (NBW). By using the recorded gestational age and date of birth, we estimated last interpregnancy interval (IPI) for each pregnancy, that is the time (in months) between the last birth and the approximate date of conception of the current pregnancy.

The birth registry data included 88,476 singleton newborns, of which we excluded stillbirths (N=387), births with unknown gestational age (N=2), born below 26 or above 42 weeks of gestational age (N=256), those with extremely high or low birth weight for a given gestational age (N=5) and born by primiparous mothers (N=47 857). That exclusions left 39,968 eligible subjects and among them 1,715 (4.3%) infants had LBW.

Statistical analysis

We examined the distribution of several known risk factors for LBW across different exposure categories in order to identify potential confounders. Women were divided into two categories according to parity (number of births): low parity, i.e. women with two births (reference category), and high parity, i.e. women with three or more births. Maternal employment status was divided into two categories: employed vs. not employed. Maternal education was stratified into two levels: higher education (passed at least final high school exams, which corresponds to British A-levels, such as: upper general or specialized secondary and academic education) and lower education (secondary education without final high school exams, such as: primary education, lower secondary or basic vocational education). Because maternal employment status and education were strongly associated, we calculated Emp & Edu indicator, which allowed to categorize women into four groups: “Not Employed - Low Education” (NE-LE), “Not Employed – High Education” (NE-HE), “Employed - Low Education” (E-LE) and “Employed - High Education” (E-HE), with the last one being the reference group.

We also tested the distribution of characteristics of singleton births among low and high parity mothers using Student’s t-test for independent samples for continuous variable with normal distribution (maternal age), Mann-Whitney *U* test for not normally distributed continuous variable (gestational age) and Chi-square test for categorical variables (sex of the offspring, marital, employment and educational status and Emp & Edu indicator). In order to test the distribution of characteristics of singleton births among IPI groups we used ANOVA for continuous variable with normal distribution, Kruskal-Wallis test for not normally distributed continuous variable and Chi-square test for categorical variables.

After a descriptive analysis of the maternal-infant characteristics and their distribution among LBW-NBW, among strata of parity, and among IPI groups, we performed simple and multiple logistic regression analyses to estimate the association of IPI as a categorical variable with the odds ratio (OR) for LBW. For interpregnancy intervals we used the categories previously defined in the literature (Zhu, 2005; Ball et al., 2014) that is IPI of 0–5, 6–11, 12–17, 18–23, 24–59, 60-119 and ≥120 months. Firstly, only the IPI was entered as a predictor of LBW (crude effect). In the second stage, we built the full model by entering biological factors, such as: maternal age and gestational age (both continuous), sex of the child, and parity, and social factors: Emp & Edu groups and marital status, and tested whether there was a significant change in the log likelihood of delivering an infant with LBW after adding these factors to the simple model.

Because the main research question of our study was to determine if high parity mothers are more susceptible to the effect of short IPI on the OR for LBW than low parity mothers, we conducted the same procedure, after stratification for parity. The influence of parity on the observed association, i. e. effect modification by parity, was further tested by adding the product term (IPI x parity) into the full logistic regression model. The interaction (effect modification) referred to the state when the effect of one exposure (IPI) on an outcome (LBW) differs across strata of another exposure (low and high parity). The interaction effect was interpreted on the multiplicative scale and it indicates to what extent the effect of IPI differs between high and low parity mothers (Buis, 2010).

Presentation of stratum specific estimates together with a statement of statistical significance based on appropriate test for interaction, as we provided in our study, is the most frequently used approach when reporting interaction in case-control and cohort studies (Knol et al., 2009).

Multiple hypothesis tests were controlled by false discovery rate (FDR), which is an expected proportion of false positives among the tests declared significant (false plus true). We set the maximum acceptable FDR at the level of 5%, and calculated the FDR-adjusted p-values at this level to assess whether the resulting p-values were still statistically significant after multiple comparisons. For the results of simple logistic regression analyses (crude effects), the adjustment was performed for 18 comparisons, including: six effects of each category of IPI in two subgroup of parity and six effects of each category of IPI among all births. For the results of multiple logistic regression analyses (adjusted effects), the adjustment was performed for 19 comparisons, including: six effects of each category of IPI in two subgroup of parity, six effects of each category of IPI among all births and one effect of interaction. The results of logistic regression analyses and test for interaction were considered statistically significant when the FDR-adjusted p-value was <0.05. The Benjamini-Hochberg method was used to calculate the FDR-adjusted p-values (Benjamini and Hochberg, 1995).

Statistica version 12.0 was used for the statistical analyses.

RESULTS

The univariate analysis suggested that the odds ratio for LBW was significantly associated with parity, sex of the offspring, gestational and maternal age, maternal educational and employment status, and marital status (Table 1). Mothers who had male offspring had a 22% lower OR for LBW than those who gave birth to females. Each week of gestation was associated with decreasing OR for LBW by 59%, whilst each year of maternal age was associated with increasing OR by 4%. Unmarried women had a 2.6 times higher OR for delivering infant with LBW than married women. Having a lower education level was associated with above twofold increase in OR in comparison to higher education levels, whilst not being employed vs. employed elevated OR by 87%. When analyzing the educational and employment status together, women who simultaneously had lower education and no employment, had above 3 times higher OR for delivering a child with LBW than women with both higher education and employment. Mothers having three or more births in comparison to low parity mothers had elevated OR for LBW by 78% (Table 1). The strata of parity differed according to maternal and gestational age, marital, employment and educational status, and Emp & Edu indicator (Table 2). The IPI groups differed according to the same factors and also to parity (Table 3).

From January 1, 1995 to December 31, 2009 a total of 38 775 interpregnancy intervals were recorded from multiparous women aged 17-49 years. Of these, 2.5% of the women (N=986) became pregnant within 5 months after the previous delivery, and 8.3% of the women (N=3 313) had interpregnancy intervals of ≥120 months. In univariate analyses, both short (<6 months and 6-11 months) and long (60-119 months and ≥120 months) interval categories were associated with elevated OR for LBW in comparison to the IPI between 18-23 months (Table 4). However, after adjustment for maternal and infant characteristics, these associations did not reach the level of statistical significance. Stratified analysis showed that, in low parity mothers no statistically significant associations were found between categories of IPI and LBW after standardization. In contrast, among strata of high parity mothers the elevated OR for LBW was associated with very short IPI (0-5 months), after adjustment to biological and social factors (Table 4). The effect of very long (≥120 months) IPI on the OR for LBW, although present before standardization, was no longer statistically significant after accounting for other factors. Results of logistic regression analyses were interpreted after adopting the false discovery rate (FDR) controlling approach.

The test for interaction between very short IPI (0-5 months) and parity on the odds ratio for LBW was statistically significant, after using multiple comparison correction (FDR-adjusted $p=0.04$). The effect of very short IPI for high parity mothers was almost 4 times higher than the effect of very short IPI for low parity mothers in multiplicative scale (OR for interaction = 3.64; 95% CI 1.50 – 8.83).

DISCUSSION

An elevated odds ratio for low birth weight associated with short interpregnancy intervals was observed in multiparous mothers, but only among those who delivered 3 or more children. Interaction analyses indicated that parity modified the association between IPI and the odds ratio for LBW. Several causal mechanisms have been proposed to explain the effects of short IPI on maternal-fetal condition (Conde-Agudelo et al., 2012). One of the most studied explanations is related to nutritional depletion hypothesis which states that short birth spacing provides insufficient time to restore the energetic and nutritional reserves needed to support fetal growth and development during the subsequent pregnancy (Dewey and Cohen, 2007; Bereczkei et al., 2000; Jasienska, 2009b). Because the maintenance of pregnancy and lactation is energetically costly (Butte and King, 2005), very short birth spacing (below 6 months) and high parity (3 or more births) may contribute to insufficient energetic resources of the mother, and consequently lead to a reduced birth weight of her infant.

Among nutritional factors that are important for fetal growth folate and n-3 fatty acids should be considered (Conde-Agudelo et al., 2012). In order to meet the increasing maternal and fetal demands during pregnancy, these nutrients are mobilized from maternal stores (Hornstra, 2000; van Eijsden et al., 2008). If dietary supply is low, concentrations of these nutrients are low after delivery, and repletion of maternal stores may take several months. Generally, repletion of folacin stores takes more than 6 months (Bruinse and van den Berg, 1995), whilst recovery of the functional DHA (docosahexaenoic acid) status, appears to still be incomplete after that time (Al et al., 1995). Therefore, mothers who conceive a subsequent child within 6 months after delivery are at greater risk of nutritional deficiency. Consequently, their offspring may be at higher risk of low birth weight.

Low supply of nutrients may be especially occurring among multiparous mothers, who have lower deposits of (n-3) fatty acids in maternal plasma phospholipids than primiparous mothers (Hornstra, 2000). In addition, the risk of folic acid deficiency among pregnant women with a parity of 2 or more was found to be 2.3 times higher compared with primiparous mothers (Pathak et al., 2004). These observations suggest biological mechanisms behind findings of our study showing that interaction between short IPI and parity explains LBW. Similar interactions were also described by other authors. For example, authors of a study conducted among Filipino infants have found that the unfavorable effect of short intervals (<6 months) and high birth order (fifth or higher) on birth weight, gestational age, weight-for-gestational age, infant length, weight-for-length and risk of neonatal mortality were confined to infants who had both attributes. There was no elevated risk associated with short previous intervals among lower-order infants, nor for high birth order infants conceived after longer intervals (Miller, 1994). The study conducted in Utah demonstrated that birth weight may decrease with increasing parity for women with a short interval (Hinkle et al., 2014).

In our study, crude analyses indicated that both short (≤11 mo) and long (≥60 mo) intervals were associated with elevated OR for LBW in comparison to the interval equal to 18-23 months, but after adjustment for maternal and infant characteristics these associations did not reach the level of statistical significance. It should be noted that IPI is not the best measure of whether a mother has had a chance to recover from the pregnancy, in terms of replenishing her nutritional status, because nutritional burden on the mother between pregnancies depends on the extent of breastfeeding (Butte and King, 2005; Dufour and Sauther, 2002; Jasienska, 2013). It was suggested that the "recuperative interval" (duration of the non-pregnant, non-lactating interval) instead, would be a more sensitive measure of maternal ability to recover from the previous reproductive event (Dewey and Cohen, 2007). However, due to a lack of data of duration of lactation we could not have used such indicator in our analyses. Moreover, the design of the present study limited our ability to assess other individual characteristics of women, such as preceding pregnancy outcomes or dietary habits which might provide additional information important to consider when assessing relationships between IPI and LBW risk. Problems with obtaining data on confounding factors may in part be responsible for not statistically significant effect of short interval on low birth weight found among all mothers irrespectively of their parity. Whereas, even interestingly designed study in which within-mother analyses were used (each mother was treated as her own control) there was no statistically significant association between short birth spacing (0-5 months) and risk of LBW (Ball et al., 2014). The Ball and colleagues (2014) suggested that the effect of short interpregnancy intervals on unfavorable birth outcomes may not be causal, but connected with maternal factors correlated with IPIs, or may be causally associated with each other, but much more weakly than previously thought. However, it is possible, that closely spaced births are related to low birth weight for multiparous mothers with higher parity in a more severe way than for mothers with lower parity, as our study has shown. Such effect of birth spacing modification by parity on birth weight has also been previously revealed in a within-mother designed study in Utah, described earlier (Hinkle et al., 2014).

Further, because parity is clearly an important factor influencing a risk of having a low birth weight infant (Aliyu et al., 2005; Hinkle et al., 2014; Shah et al., 2010) it would be interesting to investigate interactions between IPI and parity in more than two parity groups, as we have done in our study. However, because birth weight is affected by many factors, even in a study like ours that had a very large sample size, analyzes on groups of mothers with parity of four and more, and higher would not have reach a sufficient statistical power.

Our analyses should be repeated in future studies, especially among clinically defined term births, in order to avoid a problem of including preterm infants. A woman who gives birth to a preterm baby that subsequently does not survive will probably attempt to become pregnant again fairly quickly. Thus her IPI becomes very short. Due to that she may be at higher risk of another preterm birth. However, our analyses restricted to infants born at term (data not shown) revealed that the trends in the main results remained unchanged. Nonetheless the study on restricted group did not reach a sufficient statistical power because of too small number of newborns. As was shown advances in perinatal and neonatal care during the past two decades have improved the prognosis for most infants whose gestational age is as low as 23 weeks and the survival of infants who were born at 26 weeks reached 93% (Hoekstra and others, 2003) and is improving with advancing gestation.

In our study we observed that parity is not a modifier of the association between other categories of IPI except for one - extremely short interval of 0-5 months. In analyses when multiple comparisons are performed it is possible that a single statistically significant result occurred by chance. However, we used a statistical approach that allows conducting multiple related hypotheses, that is False Discovery Rates (FDRs) procedures (Pike, 2011). These comparatively new statistical methods are potentially more powerful than Bonferroni-type approaches, and robust to the false positive paradox (which occurs when false positives are more common than true positives) to which traditional Bonferroni-type procedures are susceptible. We used classical one-stage method to calculate the FDR-adjusted p-values (Benjamini and Hochberg, 1995), however two other FDR methods described by Pike (2011), that is: two-stage sharpened method (Benjamini and others, 2006) and graphically sharpened method (Benjamini and Hochberg, 2000) gave the same results. Further, the statistically significant relationship that we observed is biologically plausible. Giving birth to third or subsequent child after a very short last interpregnancy interval (below six months) may lead to insufficient energetic and nutritional resources (maternal depletion syndrome, Conde-Agudelo et al., 2012). Undernourished women may have higher risk of delivering a child with LBW.

In summary, our study conducted on a very large population of infants suggests that the odds ratio for LBW associated with closely spaced births may vary with respect to parity. These findings provide the additional evidence for the relationship between interpregnancy intervals and birth outcomes (Conde-Agudelo et al., 2012), with identifying the vulnerable subgroup - multiparous mothers with three or more births.

CONFLICT OF INTEREST

We confirmed that we have no conflict of interest in relation to this work.

Table 1. Characteristics associated with LBW among singleton births of multiparous women

	level	N	LBW	NBW	OR (95%CI)	p-value
Maternal age [years]	(cont.)	N	1715	39968	1.04 (1.03 – 1.05)	<0.01
		mean	31.4	39.1		
		SD	5.7	1.7		
Gestational age [weeks]	(cont.)	N	1715	38253	0.41 (0.40 – 0.42)	<0.01
		median	36.0	39.0		
		Q1-Q3	33 - 38	38 - 40		
Sex of the child	male	N	773	19629	0.78 (0.71 – 0.86)	<0.01
		%	45.1%	51.3%		
	female	N	942	18624	1.00 [reference]	
		%	54.90%	48.7%		
Parity	high parity	N	685	10399	1.78 (1.61 – 1.97)	<0.01
		%	39.9%	27.2%		
	low parity	N	1030	27854	1.00 [reference]	
		%	60.1%	72.8%		
Marital status	unmarried	N	385	3844	2.59 (2.30 – 2.92)	<0.01
		%	22.5%	10.1%		
	married	N	1330	34409	1.00 [reference]	
		%	77.6%	90.0%		
Maternal education	lower	N	728	9795	2.18 (1.98 – 2.41)	<0.01
		%	43.1%	25.7%		
	higher	N	963	28294	1.00 [reference]	
		%	56.95%	74.3%		
Maternal employment	unemployed	N	679	10044	1.87 (1.69 – 2.07)	<0.01
		%	40.1%	26.4%		
	employed	N	1014	28037	1.00 [reference]	
		%	59.9%	73.6%		
Emp & Edu	E-LE	N	286	5237	1.71 (1.49 – 1.97)	<0.01
		%	16.9%	13.8%		
	NE-LE	N	440	4546	3.04 (2.69 – 3.43)	<0.01
		%	26.1%	11.9%		
	NE-HE	N	237	5493	1.35 (1.17 – 1.57)	<0.01
		%	14.0%	14.4%		
	E-HE	N	726	22789	1.00 [reference]	
		%	43.0%	59.9%		

Table 2. Distribution of characteristics of singleton births stratified for parity

	Level	Low parity		High parity		p-value
Maternal age (mean, SD)[2]	(cont.)	29.6	4.4	33.0	5	<0.01
Gestational age (median, Q1-Q3)[3]	(cont.)	39.0	38-40	39.0	38-40	<0.01
Sex of the child (N, %)[1]	girl	14158	49.0%	5408	48.8%	0.69
	boy	14727	51.0%	5676	51.2%	
Marital status (N, %)[1]	unmarried	2656	9.2%	1574	14.2%	<0.01
	married	26229	90.8%	9510	85.8%	
Maternal education (N, %)[1]	lower	6098	21.2%	4425	40.2%	<0.01
	higher	22687	78.8%	6570	59.8%	
Maternal employment (N, %)[1]	not employed	6673	23.2%	4050	36.9%	<0.01
	employed	22111	76.8%	6940	63.1%	
Emp & Edu (N, %)[1]	E-LE	3454	12.0%	2069	18.8%	<0.01
	NE-LE	2640	9.2%	2346	21.4%	
	NE-HE	4029	14.0%	1701	15.5%	
	E-HE	18648	64.8%	4867	44.3%	

[1] Chi-square test, [2] t test for independant samles, [3] Mann-Whitney *U* test, Q1-Q3 – interquartile range

Table. 3. Distribution of characteristics of singleton births stratified for interpregnancy intervals (IPI)

	level		Interpregnancy intervals (in months)							
			0-5	6-11	12-17	18-23	24-59	60-119	120+	p-value
Maternal age [1]	(cont.)	mean	26.5	28.0	28.8	29.1	29.8	32.0	36.3	<0.001
(years)		SD	5.2	4.9	4.8	4.5	4.2	4.0	3.7	
Gestational age [2]	(cont.)	median	40.0	40.0	39.0	39.0	39.0	39.0	39.0	<0.001
(years)		Q1-Q3	38-40	38-40	38-40	38-40	38-40	38-40	38-40	
Sex of the child [3]	boy	N	477	1534	1789	1707	7403	5177	1682	0.769
		%	48.38%	50.53%	51.28%	51.06%	51.13%	51.11%	50.77%	
	girl	N	509	1502	1700	1636	7075	4953	1631	
		%	51.62%	49.47%	48.72%	48.94%	48.87%	48.89%	49.23%	
Parity [3]	high parity	N	342	954	958	899	3431	2893	1298	<0.001
		%	34.69%	31.42%	27.46%	26.89%	23.70%	28.56%	39.18%	
	low parity	N	644	2082	2531	2444	11047	7237	2015	
		%	65.31%	68.58%	72.54%	73.11%	76.30%	71.44%	60.82%	
Marital status [3]	unmarried	N	213	414	343	290	1138	1032	616	<0.001
		%	21.60%	13.64%	9.83%	8.67%	7.86%	10.19%	18.59%	
	married	N	773	2622	3146	3053	13340	9098	2697	
		%	78.40%	86.36%	90.17%	91.33%	92.14%	89.81%	81.41%	
Maternal employment [3]	not employed	N	471	1110	1100	945	3778	2263	724	<0.001
		%	48.36%	36.83%	31.75%	28.40%	26.20%	22.41%	21.97%	
	employed	N	503	1904	2365	2382	10644	7836	2571	
		%	51.64%	63.17%	68.25%	71.60%	73.80%	77.59%	78.03%	
Maternal education [3]	lower	N	432	915	833	780	3442	2723	1130	<0.001
		%	44.31%	30.36%	24.02%	23.44%	23.87%	26.97%	34.28%	
	higher	N	543	2099	2635	2547	10977	7375	2166	
		%	55.69%	69.64%	75.98%	76.56%	76.13%	73.03%	65.72%	
Emp & Edu [3]	E-LE	N	139	356	333	407	1786	1642	745	<0.001
		%	14.29%	11.82%	9.61%	12.23%	12.39%	16.27%	22.63%	
	NE-LE	N	291	559	500	373	1653	1079	381	
		%	29.91%	18.56%	14.43%	11.21%	11.47%	10.69%	11.57%	
	E-HE	N	363	1548	2032	1975	8852	6191	1823	
		%	37.31%	51.39%	58.66%	59.36%	61.42%	61.33%	55.38%	

NE-HE	N	180	549	599	572	2122	1183	343
	%	18.50%	18.23%	17.29%	17.19%	14.72%	11.72%	10.42%

[1]one-way ANOVA, [2] Kruskal-Wallis test, [3] Chi-square test, Q1-Q3 – interquartile range

Table 4. Crude and adjusted odds ratios (OR) with 95% confidence intervals (CI) for low birth weight by categories of interpregnancy intervals (IPI) and parity

IPI (months)	OR (95%CI)	FDR-adjusted p-value [3]	OR (95%CI)	FDR-adjusted p-value [3]
All	Crude		Adjusted[1]	
0–5	2.05 (1.50 – 2.82)	<0.01	1.43 (0.93 – 2.18)	0.28
6–11	1.50 (1.17 – 1.93)	<0.01	1.20 (0.87 – 1.66)	0.51
12–17	1.01 (0.78 – 1.32)	0.99	0.96 (0.69– 1.33)	0.89
24–59	1.00 (0.81 – 1.23)	1.00	0.99 (0.76 – 1.29)	0.94
60–119	1.43 (1.16 – 1.76)	<0.01	1.33 (1.02 – 1.74)	0.17
≥120	2.48 (1.97 – 3.11)	<0.01	1.43 (1.05 – 1.95)	0.16
18–23	1.00 [reference]		1.00 [reference]	
Low parity	Crude		Adjusted[2]	
0–5	1.29 (0.81 – 2.07)	0.43	0.71 (0.36 – 1.37)	0.52
6–11	1.49 (1.09 – 2.05)	0.03	1.21 (0.80 – 1.81)	0.58
12–17	1.10 (0.80 – 1.53)	0.65	0.96 (0.64 – 1.44)	0.89
24–59	0.94 (0.72 – 1.22)	0.72	0.92 (0.66 – 1.27)	0.75
60–119	1.40 (1.08 – 1.82)	0.03	1.30 (0.93 – 1.82)	0.28
≥120	2.46 (1.83 – 3.29)	<0.01	1.43 (0.95 – 2.15)	0.28
18–23	1.00 [reference]		1.00 [reference]	
High parity	Crude		Adjusted[2]	
0–5	2.93 (1.86 – 4.61)	<0.01	2.64 (1.45 – 4.80)	0.03
6–11	1.44 (0.96 – 2.17)	0.13	1.19 (0.69 – 2.02)	0.72
12–17	0.84 (0.53 – 1.33)	0.58	0.91 (0.52 – 1.62)	0.89
24–59	1.18 (0.83 – 1.68)	0.04	1.16 (0.74 – 1.82)	0.72
60–119	1.44 (1.02 – 2.05)	0.07	1.42 (0.90 – 2.22)	0.28
≥120	2.23 (1.54 – 3.22)	<0.01	1.47 (0.90 – 2.41)	0.28
18–23	1.00 [reference]		1.00 [reference]	

[1] adjusted for marital status. Emp & Edu. parity. sex of the child. maternal age. gestational age

[2] adjusted for marital status. Emp & Edu. sex of the child. maternal age. gestational age

[3] results were considered statistically significant when the FDR-adjusted p-value was <0.05

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