

The Impact of Birth Spacing on Subsequent Feto-Infant Outcomes among Community Enrollees of a Federal Healthy Start Project

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Abstract Numerous studies have shown an association between shorter birth intervals, and several adverse fetal outcomes, including low birth weight (LBW), preterm birth (PTB), and small for gestational age (SGA). However, there is little evidence on the effectiveness of interconception care on fetal outcomes associated with sub-optimal interpregnancy interval (IPI). The purpose of this study is to examine the influence of the Federal Healthy Start's interconception care services on IPI and fetal growth outcomes. This is a retrospective cohort study used records from the Central Hillsborough Healthy Start program in Tampa, Florida linked to Florida vital statistics data covering the period 2002–2009. Only first and second pregnancies were considered, and interpregnancy interval (IPI), the exposure of interest, was categorized in months as 0–5, 6–17, 18–23, and ≥ 24 . The following feto-infant morbidities were considered as primary outcomes: LBW, PTB,

and SGA. A composite variable coding the presence of any of the aforementioned adverse fetal events was also created. Multivariate logistic regression modeling was applied. Overall, mothers with the shortest IPI (0–5 months: AOR = 1.39, 95% CI 1.23–1.56) and longest IPI (≥ 60 months: AOR = 1.13, 95% CI 1.03–1.23) were at a greater risk for adverse fetal growth outcomes, compared to the referent category (18–23 months). Our findings support the need for inter conception care that addresses IPI and delayed childbearing among women.

Keywords Interpregnancy interval · Preterm birth · Low birth weight

Introduction

According to the World Health Organization (WHO), the recommended interval, after a live birth, before attempting a subsequent pregnancy, is at least 24 months to reduce the likelihood of adverse maternal and infant outcomes [1]. This birth-to-pregnancy (BTP) interval refers to the interval between the date of a live birth and the start of the subsequent pregnancy [1]. BTP intervals of 6 months or less have been associated with an increased risk of maternal mortality, whereas BTP intervals of 18 months or less have been associated with elevated risk of feto-infant mortality and morbidities [1]. Furthermore, heightened maternal, perinatal, and infant health risks are related to BTP intervals of 18–27 months [1].

Numerous studies have shown an relationship between shorter birth intervals and a wide array of adverse perinatal outcomes, including preterm birth, [1–9] low birth weight, [1, 2, 5] small size for gestational age, [1, 2, 7] and congenital anomaly, [1, 5, 7] as well as stillbirth [1, 10, 11] and

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neonatal death [1, 6, 7, 10]. The lowest risk for these adverse fetο-infant morbidities is with BTP intervals of 18–23 months [1]. Post-neonatal survival is enhanced with BTP intervals of 15 months or longer, whereas the lowest risk for neonatal mortality is associated with BTP intervals of at least 27 months [1]. Very short BTP intervals of less than 6 months correlate with elevated risk of stillbirths and miscarriages [1, 10, 11].

In this study, we utilize an ecological approach to assess the impact of a Federally-funded Healthy Start program, the Central Hillsborough Healthy Start Project (CHHS), on birth spacing and subsequent birth outcomes among program participants. Specific outcomes of interest include fetal growth parameters, such as preterm birth, low birth weight, and small for gestational age. We also conducted sub-analyses to assess sub-group differences (i.e., racial/ethnic groups) in the level of association between birth spacing and these fetal growth outcomes. The main objectives of the study are: to determine the interpregnancy interval patterns among women in Hillsborough County of Tampa, Florida; and to assess racial/ethnic variances in interpregnancy interval patterns within this population.

Methods

CHHS strives toward the reduction of racial/ethnic disparities in maternal and infant health outcomes among urban populations in Hillsborough County of Tampa, Florida. This project is implemented by REACHUP, a community-based nonprofit organization, and funded through the Maternal and Child Health Bureau's Healthy Start Initiative. CHHS is the primary provider of pre- and post-natal risk reduction services to residents of the central portion of Hillsborough County in Tampa, Florida, which is designated by select zip codes (33602, 33603, 33605, 33607, and 33610). CHHS has been successful in reducing adverse birth outcomes, such as very low birth weight and preterm birth, among program participants by approximately one-third, as compared to other women in the community [12].

For this study, we linked CHHS program data with vital statistics records from the Florida Department of Health for the years 2002 through 2009. Analyses were limited to mothers with records on consecutive singleton first and second pregnancies, and mothers who had both pregnancies in the state of Florida. To ascertain the number of records that met the inclusionary criteria, a multi-step data cleaning and review process was conducted (Fig. 1). During the study period, a total of 36,950 linked records for mothers having both first and second singleton pregnancies were identified in the Florida vital statistics. First, records with an interpregnancy interval of less than 0 were

removed, yielding 36,856 (99.7%). Next, we limited the analysis by considering only viable births (≥ 20 weeks of gestation and ≤ 44 weeks of gestation), resulting in 36,747 (99.5%) records. Finally, those records missing information on small-for-gestational age were excluded, which provided our final sample of 36,718 (99.4%) mother-infant pairs for analysis.

The interpregnancy interval (IPI) is the time period between the first and second pregnancy and was used to assess pregnancy spacing. The IPI was calculated as the length of time that elapsed between the date of the first pregnancy outcome and the date of the second pregnancy, less the gestational age of the second pregnancy. Gestational age was estimated based on the interval between the last menstrual period and the date of delivery of the baby. The IPI was initially calculated in months, and women were then categorized into an exposed group consisting of those with IPI < 24 months and an unexposed group that included women with IPI ≥ 24 . Subgroup analysis was also conducted using the following IPI groupings: 0–5 months; 6–17 months; 18–23 months; and ≥ 24 months (referent category). The IPI was initially calculated in days and were then categorized into interval groupings as follows: 0–5 months; 6–17 months; 18–23 months; and ≥ 24 months. The ≥ 24 months IPI category was used as the referent category for data analyses. Women were categorized as exposed or unexposed based on their interpregnancy interval, with those with IPIs of < 24 months considered

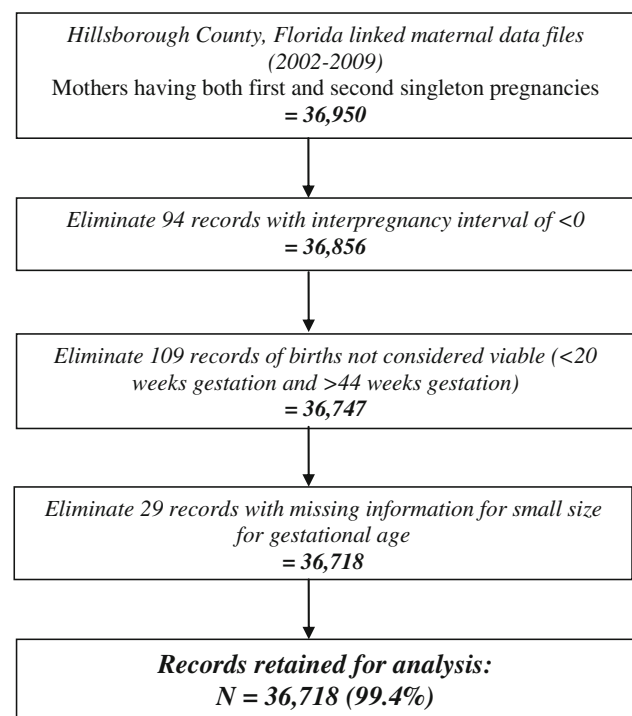


Fig. 1 Flow chart of exclusion criteria for the study

exposed while ≥ 24 months was unexposed. This categorization is based on the WHO's recommendation of 24 months as the optimal interpregnancy interval [1].

Adverse pregnancy outcomes examined in this study included low birth weight (LBW), preterm birth (PTB), and small-for-gestational age (SGA). Low birth weight was defined as a birth weight less than 2,500 g, whereas preterm birth was defined as having a gestational age less than 37 weeks. Small-for-gestational age was defined as birth weight less than the tenth percentile for gestational age based on the US growth curve [13]. Additionally, a composite variable for fetoinfant morbidities was constructed that was defined as the occurrence of at least one of the aforementioned adverse pregnancy outcomes (LBW, PTB, or SGA).

Maternal socio-demographic variables were abstracted from vital statistics data and included race/ethnicity, marital status, age at first pregnancy, and educational level at first pregnancy. Race/ethnicity was categorized into four different categories: white, black, Hispanic, and other. Marital status was dichotomized into married or single, with all persons divorced, widowed, or of unknown marital status classified as single. We categorized maternal age into two groups: < 35 years and ≥ 35 years. Educational level was classified as either < 12 years of education or ≥ 12 years of education. Maternal prenatal smoking was dichotomized as either a yes or no response.

Adequacy of prenatal care was assessed using the Revised Graduated Index algorithm (R-GINDEX), which assesses the adequacy of care based on the trimester when prenatal care began, the number of visits, and the gestational age of the infant at birth [14]. This variable was dichotomized as either adequate or inadequate, with inadequate prenatal care utilization referring to women who either had missing prenatal care information, had prenatal care but the level was considered sub-optimal (i.e., fewer prenatal care visits as compared to the length of pregnancy), or had no prenatal care at all.

Crude frequency comparison for the presence of common obstetric and medical complications was performed. These variables included: anemia (defined as < 30 c/l hematocrit and/or < 12 g/dl hemoglobin); insulin dependent diabetes mellitus (defined as absolute deficiency of insulin secretion); other types of diabetes mellitus (defined as either gestational diabetes or adult-onset diabetes); chronic hypertension (defined as an increase in systolic or diastolic pre-existing blood pressure to a level of $\geq 140/90$ mm Hg, respectively, prior to 20th week of gestation); preeclampsia (defined as pregnancy-induced high blood pressure at $\geq 140/90$ mm Hg and excess protein in the urine after 20 weeks of pregnancy); eclampsia (defined as pregnancy-induced hypertension associated with convulsions); abruptio placenta (defined as premature separation from the uterus of normally implanted placenta); placenta previa (defined as attachment of the

placenta to the uterine wall close to or covering the cervix); and renal disease. We also constructed a composite variable indicating the presence of at least one of these conditions during the second pregnancy.

Statistical Analysis

Within this study, we used chi-square tests to compare baseline characteristics of mothers in the exposed group (IPI < 24 months) and unexposed group (IPI ≥ 24 months), categorized by whether women resided within the CHHS service area or in the rest of Hillsborough County, outside of the area serviced by CHHS. Multivariate logistic regression was used to generate adjusted odds ratios and 95% confidence intervals to assess the association between IPI and each of the adverse pregnancy outcomes, including overall fetoinfant morbidity. Stratification of the association between IPI and adverse pregnancy outcomes by geographic region was also conducted. Additionally, we calculated rate ratios for the fetoinfant growth outcomes by race/ethnicity. Variables included in the logistic regression analysis were based on a review of the literature and biologic plausibility.

All tests were two-tailed with a type 1 error rate fixed at 5%, and SAS version 9.2 (SAS Institute, Cary, NC, USA) was used to perform all analyses. This study was approved by the Institutional Review Board at the University of South Florida.

Results

Overall, we analyzed 36,718 mother-infant pairs from Hillsborough County during the study period of 2002–2009. Among the entire study sample, 263 mother-infant pairs were within the CHHS service area, while the remaining 36,455 occurred in the rest of Hillsborough County. Of these pairs, 20,672 (42.5%) had an IPI that was < 24 months, whereas 16,046 had an IPI of ≥ 24 months. Table 1 shows that there were no significant differences in race, age, marital status, educational level, adequacy of prenatal care, smoking status, or maternal morbidities among mothers within the CHHS service area. However, mothers with shorter interpregnancy intervals (IPI ≤ 24 months) in the rest of Hillsborough County were significantly more likely to be black, younger (< 35 years), to have < 12 years of education, to be married, and to smoke, as compared to women with longer IPIs (IPI ≥ 24 months) ($P < 0.01$). Additionally, these women were less likely to experience any maternal morbidity, which includes anemia, insulin dependent diabetes mellitus, other types of diabetes mellitus, chronic hypertension, preeclampsia, eclampsia, abruptio placenta, placenta previa, and renal disease.

Table 1 Crude frequencies of maternal socio-demographic characteristics and pregnancy complications of women in Tampa, Florida (1998–2007)

Characteristics	Mothers within CHHS service area ^a <i>N</i> = 263		Rest of Hillsborough County <i>N</i> = 36,455			
	Interpregnancy intervals		Interpregnancy intervals		<i>P</i> -value ^b	
	<24 month <i>N</i> = 215 <i>n</i> (%)	≥24 months <i>N</i> = 48 <i>n</i> (%)	<24 months <i>N</i> = 20,457 <i>n</i> (%)	≥24 months <i>N</i> = 15,998 <i>n</i> (%)		
Race					0.01	
White	19 (8.84)	4 (8.33)	12,857 (62.86)	8,927 (55.79)		
Black	157 (73.02)	36 (75.00)	4,092 (20.01)	3,337 (20.85)		
Hispanic	22 (10.23)	6 (12.50)	1,441 (7.05)	1,701 (10.63)		
Other	17 (7.91)	2 (4.17)	2,064 (10.09)	2,036 (12.72)		
Advanced age (≥35 years old)	13 (6.05)	3 (6.25)	2,737 (13.38)	2,961 (18.51)	0.01	
Education (≥12 years)	115 (53.49)	21 (43.75)	16,266 (79.52)	13,219 (82.61)	0.01	
Smokers	9 (4.19)	5 (10.42)	1,330 (6.50)	1,022 (6.39)	0.01	
Adequate prenatal care	100 (46.51)	28 (58.33)	12,914 (63.14)	10,189 (63.68)	0.29	
Married	34(15.81)	9 (18.75)	13,310 (65.07)	10,120 (63.25)	0.01	
Any maternal morbidity ^c	19(8.84)	5 (10.42)	1,702 (8.32)	1,697 (10.61)	0.01	

^a CHHS Central Hillsborough Healthy Start in Hillsborough County of Tampa, Florida; consists of five zip codes: 33602, 33603, 33605, 33607 and 33610

^b Significant values in bold font. *P*-values of 0.05 or less are considered significant

^c Any maternal morbidity includes: anemia; insulin dependent diabetes mellitus; other types of diabetes mellitus; chronic hypertension; preeclampsia; eclampsia; abruptio placenta; placenta previa; and renal disease

In Table 2, the adjusted odds ratios for fetoinfant morbidities by interpregnancy interval are presented. The fetoinfant morbidities included low birth weight, preterm birth, and small size for gestational age. Additionally, overall fetoinfant morbidity was assessed through a composite variable. When comparing women with IPIs of <24 months to those with IPIs of ≥24 months, no difference in risk for fetoinfant morbidities was observed, regardless of whether a mother resided within the CHHS service area or the rest of Hillsborough County.

Table 3 summarizes the adjusted estimates for the association between varying IPIs and each of the observed fetal growth parameters, including overall fetoinfant morbidity, stratified based on whether the mother resides within the CHHS service area. The IPI of 18–23 months was the referent category in this analysis. None of the sub-categories of IPI was significant in mothers in the CHHS service area for all of the fetoinfant morbidity outcomes considered in this study. Among mothers in Hillsborough County (not including those in the CHHS service area), an IPI of 0–5 months was found to be associated with a 43% increase in risk for LBW (AOR = 1.43, 95% CI 1.20–1.69). An increased risk was also seen for PTB among mothers in Hillsborough County with IPIs of 0–5 months (AOR = 1.58, 95% CI 1.37–1.83), 6–17 months (AOR = 1.18, 95% CI 1.05–1.33), and ≥24 months (AOR = 1.17, 95% CI

Table 2 Adjusted odds ratios (AOR) and 95% confidence intervals (CI) of fetoinfant morbidities between longer interpregnancy interval (≥24 months) and shorter interpregnancy interval (<24 months) in Tampa, Florida (1998–2007)

Fetoinfant morbidities	Mothers within CHHS service area ^a		Rest of Hillsborough County	
	<i>n</i> ^b	AOR (95% CI)	<i>n</i> ^b	AOR (95% CI)
Low birth weight	35	1.75 (0.57–5.34)	2,544	1.06 (0.98–1.15)
Preterm birth	43	1.71 (0.65–4.54)	3,816	1.02 (0.96–1.10)
Small for gestational age	39	0.73 (0.29–1.80)	2,621	0.95 (0.87–1.03)
Any fetoinfant morbidity	74	1.18 (0.55–2.54)	5,923	0.99 (0.93–1.05)

Referent = IPI ≥ 24 months

Estimates were adjusted for by the following variables: maternal age, parity, race, smoking, education, marital status, adequacy of prenatal care, and a composite variable that included any of the following (anemia, gestational diabetes, diabetes mellitus, chronic hypertension and renal disease)

^a CHHS Central Hillsborough Healthy Start in Tampa, Florida; consists of five zip codes: 33602, 33603, 33605, 33607 and 33610

^b *n* number of fetoinfant morbidity outcomes

1.05–1.31). Overall, the shortest IPI, 0–5 months, was associated with a 39% increase in risk for any of the fetoinfant morbidities studied (AOR = 1.39, 95% CI 1.23–1.56), while the longest IPI (≥24 months) was

Table 3 Adjusted odds ratios (AOR) and 95% confidence intervals (CI) of fetoinfant morbidities by interpregnancy interval in Tampa, Florida (1998–2007)

Fetoinfant morbidities	Mothers within CHHS service area ^a		Rest of Hillsborough County	
	n ^b	AOR (95% CI)	n ^b	AOR (95% CI)
Low birth weight	35	1.75 (0.57–5.34)	2,544	1.06 (0.98–1.15)
<6 months	9	1.33 (0.31–5.69)	314	1.43 (1.20–1.69)
6 to <18 months	18	1.48 (0.37–5.94)	812	1.07 (0.93–1.23)
18 to <24 months	3	1	304	1
≥24 months	5	0.79 (0.15–4.08)	1,114	1.05 (0.92–1.20)
Preterm	43	1.71 (0.65–4.54)	3,816	1.02 (0.96–1.10)
<6 months	12	1.98 (0.50–7.85)	443	1.58 (1.37–1.83)
6 to <18 months	22	2.00 (0.53–7.57)	1,237	1.18 (1.05–1.33)
18 to <24 months	3	1	438	1
≥24 months	6	1.09 (0.23–5.05)	1,698	1.17 (1.05–1.31)
SGA	39	0.73 (0.29–1.80)	2,621	0.95 (0.87–1.03)
<6 months	9	0.81 (0.21–3.07)	281	1.11 (0.93–1.31)
6 to <18 months	17	0.95 (0.27–3.33)	817	0.98 (0.86–1.12)
18 to <24 months	4	1	325	1
≥24 months	9	1.25 (0.31–5.02)	1,198	1.06 (0.93–1.21)
Any fetoinfant morbidity	74	1.18 (0.55–2.54)	5,923	0.99 (0.93–1.05)
<6 months	19	1.20 (0.42–3.44)	663	1.39 (1.23–1.56)
6 to <18 months	35	1.30 (0.48–3.55)	1,885	1.09 (0.99–1.19)
18 to <24 months	7	1	708	1
≥24 months	13	1.04 (0.33–3.27)	2,667	1.13 (1.03–1.23)

Estimates were adjusted for by the following variables: maternal age, parity, race, smoking, education, marital status, adequacy of prenatal care, and a composite variable that included any of the following (anemia, gestational diabetes, diabetes mellitus, chronic hypertension and renal disease)

Significant values in bold font, but since these are AORs, they are estimates where the confidence interval ranges exclude 1

^a CHHS Central Hillsborough Healthy Start in Tampa, Florida; consists of five zip codes: 33602, 33603, 33605, 33607 and 33610

^b n number of fetoinfant morbidity outcomes

associated with a 13% increase in risk for any fetoinfant morbidity (AOR = 1.13, 95% CI 1.03–1.23). SGA was not found to be significantly associated with any of the IPI categories among mothers in Hillsborough County.

Discussion

We found that very short (IPI < 6 months) and long (≥24 months) interpregnancy intervals result in an increased risk for fetoinfant morbidities, including low birth weight and preterm birth. For the outcome of small size for gestational age, we did not observe an increase in risk for any of the IPI categories.

Our findings are consistent with those of previous studies. Nabukera and colleagues conducted a population-based, retrospective cohort study using maternally linked files from Missouri over a 20 year period from 1978–1997 [15]. In their study, a similar design was employed and women with an IPI of <6 months had an elevated risk for low birth weight (AOR = 1.22, 95% CI 1.12–1.32), preterm birth (AOR = 1.12, 95% CI 1.05–1.20), and small for gestational age (AOR = 1.14, 95% CI 1.06–1.22) [15]. However, the referent IPI category in their analysis was ≥6 months. Our findings demonstrate that an IPI of 6–17 months still confers an increase in risk for fetoinfant morbidities, which could not be observed in Nabukera’s study. Therefore, it is possible that the odds ratios presented underestimate the risk of fetoinfant morbidities within the study population. A meta-analysis by Conde-Agudelo et al. [2] also assesses the association between IPIs and fetoinfant morbidities. When compared to an IPI of 18–23 months, IPIs of <6 months, 6–11 months, and 12–17 months were found to be significantly associated with low birth weight, preterm birth, and small for gestational age. This is consistent with our findings for preterm birth and low birth weight.

While the reasons for the observed associations between short IPI and fetoinfant morbidities remain unclear, some explanations have been proffered, prominent among them is “maternal depletion syndrome” [16]. This explanation posits that the rapid succession of pregnancies does not afford the mother’s body time to recover from the stresses of the preceding pregnancy, thus leading to a worsened nutritional status. This depletion then places the mother and fetus at an increased risk for adverse outcomes [16]. Similar to this idea of a worsened nutritional status is the folate depletion hypothesis, [17] which postulates that concentrations of folate begin to decrease in the pregnant mother during the fifth month of pregnancy. This decline then continues during subsequent months and folate reserves remain relatively low for a few months following birth. Consequently, for women who conceive soon after a pregnancy, it is likely that they have not restored their folate reserves, and as a result, the developing fetus has an elevated risk for folate-insufficiency-associated adverse outcomes, including neural tube defects, preterm birth, and low birth weight [2, 17].

There are some limitations within our study. As a result of low numbers of mothers with an IPI of ≥60 months, our analysis could not include this IPI category. Previous research has indicated that this there is a dose–response relation, and that an IPI of ≥60 months is associated with the investigated outcomes of preterm birth, low birth weight, and small for gestational age [2, 15, 18]. Inclusion of women that were in this IPI category (≥60 months) into the shorter IPI category of ≥24 months might have led to

an overestimation of the risk for fetoinfant morbidities in this category. However, the number of mothers with an IPI of ≥ 60 months was so small that we considered this impact to have been negligible. Furthermore, the number of mothers from within the CHHS service area available for analysis was much smaller than the number available from the rest of Hillsborough County. This smaller number would have yielded a reduced level of power to be able to detect significant differences in risk. Therefore, although no associations were detected between IPI and fetoinfant morbidities, it cannot be ruled out that an association would have been found with a larger sample of mothers. Finally, due to the fact that the data used are from only one county, there is limited generalizability.

Despite these shortcomings, this study has certain noteworthy strengths. We had data for births throughout Hillsborough County, Florida from 2002 to 2009, resulting in sufficient sample size, which minimizes selection bias and bolsters the power for the study to detect differences in risk. In our analysis, we controlled for several potential confounders, although we cannot rule out residual confounding due to unmeasured variables.

In conclusion, this study offers further evidence of the association between IPI and fetoinfant morbidities. While the direct mechanism that results in the observed association remains unclear, these findings have significant public health implications. Interconception care is a recommended public health strategy to reduce fetoinfant morbidities [19, 20]. A component of interconception care is the provision of education and counseling services to aid women in determining appropriate pregnancy spacing for optimal birth outcomes [19]. Our findings support the need for prioritization of such activities with women prior to subsequent pregnancy. While our study results were inconclusive regarding the role of Healthy Start in the association between interpregnancy intervals and fetoinfant morbidities, further research is required to elucidate the role of community service organizations, such as Healthy Start, in interconception activities designed to address pregnancy spacing.

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