Preplanned Studies

Effects of Short Interpregnancy Intervals on Adverse Pregnancy Outcomes — Haidian District, Beijing Municipality, China, 2017–2019

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Summary

What is already known about this topic?

Interpregnancy intervals (IPIs) that are either excessively long or short have been linked with an elevated risk of adverse perinatal outcomes. Presently, no pertinent guidelines have been established in China to provide clear direction with regard to optimal IPI.

What is added by this report?

A brief interpregnancy interval may elevate the risk of miscarriage, postpartum hemorrhage, and fetal distress among expectant women.

What are the implications for public health practice?

These results could inform prenatal consultations, guiding pregnant women towards an ideal interpregnancy interval of no less than 24 months.

Research has demonstrated that interpregnancy intervals (IPIs) that are notably short or prolonged could escalate the probability of adverse perinatal outcomes (*1*–*2*). Particularly, short IPIs (SIPIs) may dramatically amplify the risk of negative pregnancy results (*3*) and potentially bring about temporary or enduring complications for the fetus (*4*). This prospective cohort study aimed to examine the pregnancy outcomes amongst various IPI groups of expectant mothers in Beijing's Haidian District, along with the effects of SIPIs on adverse pregnancy outcomes. These include gestational diabetes mellitus, gestational hypertension, preeclampsia, gestational metabolic syndrome, preterm birth, low birth weight, small size for gestational age, miscarriage, postpartum hemorrhage, fetal distress, and premature membrane rupture. Its ultimate goal was to equip clinicians with empirical data for counseling women on optimal pregnancy spacing. The study is comprised of 1,185 women who had registered a file with Beijing Haidian Maternal and Child Health Hospital and volunteered to contribute to a pregnancy cohort. Our findings revealed that a SIPI was a significant predictor for abortion, postpartum hemorrhage, and fetal distress. It is thus advised to enhance health education among women of childbearing ages, to avert excessively brief IPIs and thereby minimize adverse pregnancy outcomes.

With the inauguration of the universal two-child policy in 2016, followed by the introduction of the three-child policy in 2021, China has witnessed a substantial increase in the number of multiparous women. Consequently, an escalating number of couples are having more than one child, drawing attention to the significance of intervals between pregnancies. Recognized as a potentially modifiable risk factor with implications for perinatal and neonatal outcomes, IPI holds immense importance for both maternal and fetal health. To facilitate superior maternal healthcare and mitigate the incidence of undesirable maternal and fetal outcomes during a subsequent pregnancy, it is imperative to provide appropriate recommendations for the optimal duration of interval before a second pregnancy among women of reproductive age.

This prospective cohort study engaged 3,988 pregnant females at or earlier than 20 weeks of gestation. The engagement took place at Beijing Haidian Maternal and Child Health Hospital between October 2017 and November 2019. After excluding participants with first-time pregnancies, twin or multiple pregnancies, and those lacking information on gravidity or IPI, the final subject group consisted of 1,185 individuals (Supplementary Figure S1, available in https://weekly.chinacdc.cn/). Key demographic characteristics, including maternal age, height, and pre-pregnancy weight, along with pregnancy-related details such as education, occupation, gravidity, parity, accidental pregnancy, contraceptive use, and a history of adverse pregnancy, were gathered through in-person administration of questionnaires. Pregnancy outcomes and associated complications were sourced directly

from the hospital case database. All the participants provided consent by signing an informed consent form. The study design was authorized by the pertinent ethics review committee.

In this study, IPI was considered the duration between the conclusion of the preceding delivery — encompassing live births, miscarriages, stillbirths, and abortions — and the start of the subsequent pregnancy. Guidelines from the World Health Organization (WHO) suggest a wait time of at least 24 months from a live birth before embarking on a subsequent pregnancy (*5*). Adhering to these recommendations, subjects were divided into three categories: very short IPI (VSIPI, <12 months) (*6*–*7*), short IPI (SIPI, 12–23.9 months), and normal IPI (NIPI, ≥24 months). The parallel double entry of the survey data was performed using EpiData software (version 3.1, EpiData Association, Odense, Denmark). IBM SPSS (version 26.0; IBM Corp., Armonk, NY, USA) was employed for statistical evaluations. Categorical variables were represented in terms of count (*n*) and percentage (%). A comparison of the risk for negative pregnancy outcomes among different groups was facilitated through Pearson's χ^2 test. Post adjustments for maternal age, education, income, pre-pregnancy body mass index (BMI), adverse maternal history, among other potential confounders, the association between IPI and unfavorable pregnancy outcomes was analyzed via multinomial logistic regression. The results are presented as odds ratios (*OR*s) alongside 95% confidence intervals (*CI*s). A *P*-value less than 0.05 was regarded as indicative of statistical significance.

Table 1 outlines the sociodemographic and maternal attributes of the research subjects. The age range of the participants was from 21–47, with an average age of 35.1±4.1, and they were on average at 11.2±2.2 weeks of gestation when included in the study. Of the 1,185 subjects, 188 (15.9%) had a VSIPI, 217 (18.3%) had a SIPI, while the remaining 780 (65.8%) had an NIPI. The educational background of the participants was predominantly high, with the majority employed as educators, healthcare professionals, or government and corporate workers. Hence, they are broadly representative of high knowledge sectors across the country.

Table 2 illustrates that the prevalence of PTB, LBW, SGA, and PROM in the NIPI group was inferior compared to those in the VSIPI and SIPI groups; however, this discrepancy failed to have statistical significance. In contrast, a significant variation was noted in the incidence of complications such as gestational hypertension, miscarriage, postpartum hemorrhage, and fetal distress across the three subgroups of pregnant women.

Table 3 explicates the impact of VSIPI and SIPI on GHTN, miscarriage, postpartum hemorrhage, and fetal distress. Despite SIPI being identified as a risk factor for miscarriage and fetal distress, the difference lacked statistical significance. A marked rise in the risk for all adverse pregnancy outcomes was observed in the VSIPI group compared to the NIPI group, encompassing miscarriage (*OR*: 13.388, 95% *CI*: 4.421–40.537), postpartum hemorrhage (*OR*: 1.653, 95% *CI*: 1.077–2.535), and fetal distress (*OR*: 1.523, 95% *CI*: 1.031–2.250). However, the odds for gestational hypertension were reduced in the VSIPI group (*OR*: 0.310, 95% *CI*: 0.117–0.821) compared to the NIPI group. Thus, it can be concluded that an excessively brief IPI serves as a risk factor for miscarriage, postpartum hemorrhage, and fetal distress.

DISCUSSION

The present study found that 34.18% of pregnant women in Haidian District had an IPI shorter than the WHO recommended two years. This constitutes approximately one-third of the study's participants. These percentages are similar to the 36.2% of the pregnant women with SIPIs in a California birth cohort, yet lower than Ohio's reported 63.49%. The findings indicate that an SIPI may significantly heighten the risk of maternal miscarriage, particularly if the interval is a very short interpregnancy interval (VSIPI ≤ 12 months). Consequently, this can substantially increase the risk for undesirable pregnancy outcomes and complications such as postpartum hemorrhage and fetal distress. These results parallel the findings of a previous study, which reported a heightened risk of premature rupture of membranes (*OR*: 1.69, 95% *CI*: 1.28–2.39) and miscarriage in pregnant women with an IPI less than six months (*8*). A substantial birth cohort study conducted in California showed that pregnant women with a VSIPI (i.e., less than one year after a live birth) have significantly elevated risk for postpartum hemorrhage (*OR*: 1.71, 95% *CI*: 1.65–1.78) (*9*).

The primary strength of this prospective cohort study lies in its accurate depiction of the IPIs and fundamental circumstances of pregnant women in Beijing's Haidian District. Notably, it investigates the impact of various degrees of SIPI on negative

TABLE 1. Sociodemographic and maternal characteristics of pregnant women in Haidian District, 2017–2019.*

Characteristics	VSIPI *n* (%)	SIPI *n* (%)	NIPI *n* (%)	χ^2	*P*†
n	188	217	780		
Age group (years)				28.786	<0.001
<30	26 (13.9)	18 (8.4)	50 (6.4)		
30–34	95 (50.5)	110 (51.1)	317 (40.8)		
≥35	67 (35.6)	87 (40.5)	410 (52.8)		
Education§				9.965	0.041
Primary	59 (31.6)	57 (26.3)	272 (34.9)		
Secondary	88 (47.0)	94 (43.3)	336 (43.1)		
Higher	40 (21.4)	66 (30.4)	172 (22.0)		
Ethnic				1.114	0.573
Han ethnicity	174 (92.6)	202 (93.1)	736 (94.4)		
Ethnic minority	14 (7.4)	15 (6.9)	44 (5.6)		
Occupation				4.497	0.343
Farmer, worker and server	44 (23.8)	48 (22.3)	220 (28.6)		
Institution staff	99 (53.5)	120 (55.8)	389 (50.7)		
Other	42 (22.7)	47 (21.9)	159 (20.7)		
Per capita household income in Chinese Yuan (CNY)				15.378	0.018
<50,000	31 (18.2)	26 (13.6)	164 (24.2)		
50,000–99,999	51 (30.1)	65 (34.0)	229 (33.7)		
100,000–149,999	48 (28.2)	61 (31.9)	163 (24.0)		
≥150,000	40 (23.5)	39 (20.5)	123 (18.1)		
Prepregnancy BMI (kg/m^2)				1.711	0.789
Underweight (<18.5)	22 (12.2)	25 (12.0)	80 (10.7)		
Normal (18.5–23.9)	124 (68.9)	135 (64.6)	505 (67.4)		
Overweight (≥24)	34 (18.9)	49 (23.4)	164 (21.9)		
Gravidity				0.834	0.659
2	104 (55.3)	120 (55.3)	453 (58.1)		
≥3	84 (44.7)	97 (44.7)	327 (41.9)		
Parity				104.410	<0.001
Primipara	144 (76.6)	134 (61.8)	302 (38.7)		
Multipara	44 (23.4)	83 (38.2)	478 (61.3)		
Accidental pregnancy				10.016	0.007
No	131 (70.1)	151 (71.2)	470 (61.4)		
Yes	56 (29.9)	61 (28.8)	296 (38.6)		
Maternal contraceptive use				5.664	0.059
No	174 (93.0)	209 (96.3)	753 (96.8)		
Yes	13 (7.0)	8 (3.7)	25 (3.2)		
Gestational weight gain >18 kg				0.557	0.757
No	155 (83.8)	177 (83.9)	654 (85.5)		
Yes	30 (16.2)	34 (16.1)	111 (14.5)		
Adverse pregnancy history				10.346	0.006
No	149 (79.3)	175 (80.6)	679 (87.1)		
Yes	39 (20.7)	42 (19.4)	101 (12.9)		
Last pregnancy outcome				169.996	<0.001
Vaginal delivery	11 (6.0)	28 (13.0)	260 (33.7)		
Cesarean section	9 (4.9)	12 (5.5)	158 (20.5)		
Spontaneous or induced abortion	163 (89.1)	176 (81.5)	353 (45.8)		

Abbreviation: VSIPI=very short interpregnancy interval (<12 months); SIPI=short IPI (12–23.9 months); NIPI=normal IPI (≥24 months); BMI=body mass index.

* Owing to unavailable information, the sum of demographic characteristics at each level may deviate from the number of cases within each category.

† Pearson's chi-square test.

§ Education: Primary (college degree or below), secondary (undergraduate degree), or higher (master's degree or above).

TABLE 2. Univariate analysis of the interpregnancy interval and adverse pregnancy outcomes* among pregnant women in Haidian District, 2017–2019.

Pregnancy outcome/complication	VSIPI *n* (%)	SIPI *n* (%)	NIPI *n* (%)	χ^2	*P*
GDM				1.493	0.474
No	126 (73.7)	153 (78.9)	543 (77.4)		
Yes	45 (26.3)	41 (21.1)	159 (22.6)		
GHTN				7.475	0.024
No	163 (96.4)	187 (94.0)	639 (90.6)		
Yes	6 (3.6)	12 (6.0)	66 (9.4)		
PE				1.435	0.488
No	181 (96.3)	210 (96.8)	762 (97.7)		
Yes	7 (3.7)	7 (3.2)	18 (2.3)		
GMS				1.238	0.538
No	158 (84.0)	190 (87.6)	677 (86.8)		
Yes	30 (16.0)	27 (12.4)	103 (13.2)		
Gestational metabolic disorders				1.845	0.397
No	89 (47.3)	112 (51.6)	362 (46.4)		
Yes	99 (52.7)	105 (48.4)	418 (53.6)		
PTB				0.610	0.737
No	180 (95.7)	206 (94.9)	736 (94.4)		
Yes	8 (4.3)	11 (5.1)	44 (5.6)		
LBW				0.123	0.941
No	182 (96.8)	209 (96.3)	751 (96.3)		
Yes	6 (3.2)	8 (3.7)	29 (3.7)		
SGA				1.615	0.446
No	180 (95.7)	211 (97.2)	743 (95.3)		
Yes	8 (4.3)	6 (2.8)	37 (4.7)		
Miscarriage				60.534	<0.001*
No	167 (88.8)	211 (97.2)	774 (99.2)		
Yes	21 (11.2)	6 (2.8)	6 (0.8)		
Postpartum hemorrhage				7.126	0.028
No	145 (77.1)	185 (85.3)	662 (84.9)		
Yes	43 (22.9)	32 (14.7)	118 (15.1)		
Fetal distress				10.571	0.005
No	126 (67.0)	153 (70.5)	603 (77.3)		
Yes	62 (33.0)	64 (29.5)	177 (22.7)		
PROM				1.639	0.441
No	138 (73.4)	171 (78.8)	597 (76.5)		
Yes	50 (26.6)	46 (21.2)	185 (23.5)		

Abbreviation: VSIPI=very short interpregnancy interval (<12 months); SIPI=short IPI (12–23.9 months); NIPI=normal IPI (≥24 months); GDM=gestational diabetes mellitus; GHTN=gestational hypertension; PE=preeclampsia; GMS=gestational metabolic syndrome; PTB=preterm birth; LBW=low birth weight; SGA=small for gestational age; PROM=premature rupture of membranes.

* The research encompasses various adverse pregnancy outcomes including GDM, GHTN, PE, GMS, PTB, LBW, SGA, miscarriage, postpartum hemorrhage, fetal distress, and PROM.

pregnancy outcomes. This diverges from earlier IPI-related studies, where the focus was largely on maternal pregnancy complications and postpartum issues. Conversely, prior research chiefly centered on poor infant birth outcomes such as low birth weight, premature birth, and small size for gestational age,

TABLE 3. Association between adverse pregnancy outcomes* and interpregnancy intervals among pregnant women in Haidian District, 2017–2019.

Adverse pregnancy outcomes	SIPI			VSIPI		
	aOR†	95% *CI*	*P*	*aOR*†	95% *CI*	*P*
GHTN	0.618	0.286–1.335	0.221	0.310	0.117–0.821	0.018
Miscarriage	2.481	0.663–9.280	0.177	13.388	4.421–40.537	<0.001
Postpartum hemorrhage	0.988	0.624–1.564	0.959	1.653	1.077–2.535	0.021
Fetal distress	1.446	0.993–2.106	0.055	1.523	1.031–2.250	0.035

Abbreviation: VSIPI=very short interpregnancy interval (<12 months); SIPI=short IPI (12–23.9 months); a*OR*=adjusted odds ratio; *CI*=confidence interval; GHTN=gestational hypertension.

* Adverse outcomes of pregnancy include GHTN, miscarriage, postpartum hemorrhage, and fetal distress.

† This analysis has been adjusted for factors including maternal age, education level, per capita income of the household, pre-pregnancy BMI, parity, occurrences of accidental pregnancy, history of maternal adversity, and outcomes of the most recent pregnancy.

among others. According to a previous study (*10*), older women with an SIPI were more prone to very preterm births and bearing babies with extremely low birth weights. Another study (*11*) echoed these results, highlighting a significantly increased risk for preterm birth among women with an SIPI. Our study did identify variations in low birth weight (LBW), preterm birth (PTB), and small for gestational age (SGA) incidence among the IPI groups. However, these findings were not statistically significant, suggesting that further research may be necessary to understand this association.

The precise mechanism that explains the role of IPI length in the emergence of adverse perinatal outcomes remains undetermined. Numerous researchers have put forth hypotheses to elucidate this phenomenon (*12*). The nutritional deficiency hypothesis is widely recognized and suggests that nutrients in a pregnant woman facing depletion are predominantly distributed to the mother, thereby compromising the fetus (*13*). An excessively short IPI means the mother has inadequate recovery time after enduring the stress of the initial pregnancy and subsequent postpartum lactation. Her nutritional reserves might not have fully replenished to the optimum level, resulting in a deficiency of critical nutrients potentially leading to unfavorable pregnancy outcomes. Additionally, a plausible explanation for prolonged intervals leading to negative outcomes is the physiological regression hypothesis, suggesting that pregnancy enhances a mother's capacities that support growth (including numerous changes in the physiological and anatomical reproductive system). If another child is not conceived for an extended duration, these capacities might gradually regress post birth, leading to a woman's physiological characteristics becoming similar to those of first-time mothers. Past investigations have identified an excessively long IPI as a risk factor for gestational hypertension (GHTN) among other adverse pregnancy outcomes. This may elucidate our findings indicating that an excessively short IPI may act as a protective factor against GHTN.

This study has several limitations that stem primarily from the numerous and intricate confounding factors that influence the interval of pregnancy, such as gestational weight gain. Some confounding factors result from reproductive behaviors and histories, while others are impacted by incalculable cultural and societal norms that offer challenges for precise control measures during research; these factors were not effectively controlled in our study. Moreover, the use of self-reported questionnaires could lead to information bias.

Furthermore, given the adjustments to China's birth policy, a substantial number of women giving birth multiple times might have an IPI exceeding ten years, equating to an IPI of 60 months or more in our definition. However, the longest interval range our questionnaire provided was an IPI of greater than two years, thereby lumping these women with all those whose pregnancy intervals were over two years. This methodology may inadvertently fold women with longer intervals into the NIPI population, potentially downplaying the negative effects of significant SIPI and VSIPI on GDM, PTB, SGA, LBW, and other outcomes.

This limitation may have resulted in an underestimation of the harm associated with an SIPI and a VSIPI, further emphasizing the necessity for meticulous control of IPI. A larger sample size and more precise grouping of IPIs could potentially reveal statistically significant differences.

In conclusion, SIPIs are positively correlated with multiple adverse pregnancy outcomes and maternal and infant complications. Therefore, it is imperative to strengthen health education regarding optimal IPIs

within the target population. By promoting the use of postpartum contraception, we can significantly mitigate potential maternal and fetal health issues caused by SIPI.

Conflicts of interest: No conflicts of interest.

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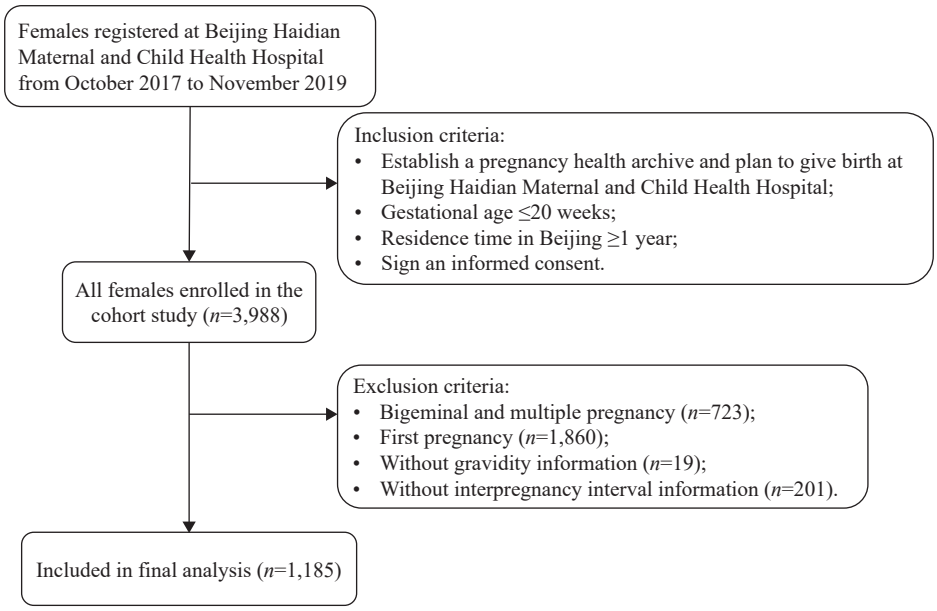
REFERENCES

1. Yaya S, Uthman OA, Ekholuenetale M, Bishwajit G, Adjiwanou V. Effects of birth spacing on adverse childhood health outcomes: evidence from 34 countries in sub-Saharan Africa. J Matern Fetal Neonatal Med 2020;33(20):3501 – 8. http://dx.doi.org/10.1080/14767058.2019.1576623.
2. Shree R, Caughey AB, Chandrasekaran S. Short interpregnancy interval increases the risk of preterm premature rupture of membranes and early delivery. J Matern Fetal Neonatal Med 2018;31(22):3014 – 20. http://dx.doi.org/10.1080/14767058.2017.1362384.
3. Ahrens KA, Nelson H, Stidd RL, Moskosky S, Hutcheon JA. Short interpregnancy intervals and adverse perinatal outcomes in high-resource settings: An updated systematic review. Paediatr Perinat Epidemiol 2019;33(1):O25 – 47. http://dx.doi.org/10.1111/ppe.12503.
4. Liauw J, Jacobsen GW, Larose TL, Hutcheon JA. Short interpregnancy interval and poor fetal growth: Evaluating the role of pregnancy intention. Paediatr Perinat Epidemiol 2019;33(1):O73 – 85. http://dx.doi.org/10.1111/ppe.12506.
5. World Health Organization. Report of a WHO technical consultation on birth spacing: Geneva, Switzerland 13–15 June 2005. Geneva: World Health Organization; 2007. https://apps.who.int/iris/handle/10665/69855.
6. Mahfouz EM, El-Sherbiny NA, Wahed WYA, Hamed NS. Effect of inter-pregnancy interval on pregnancy outcome: a prospective study at Fayoum, Egypt. International Journal of Medicine in Developing Countries 2018;2(2):38 – 44. http://dx.doi.org/10.24911/IJMDC.51-1520268317.
7. Defranco EA, Ehrlich S, Muglia LJ. Influence of interpregnancy interval on birth timing. BJOG 2014;121(13):1633 – 40. http://dx.doi.org/10.1111/1471-0528.12891.
8. Hegelund ER, Urhoj SK, Andersen AMN, Mortensen LH. Interpregnancy interval and risk of adverse pregnancy outcomes: a register-based study of 328, 577 pregnancies in Denmark 1994-2010. Matern Child Health J 2018;22(7):1008 – 15. http://dx.doi.org/10.1007/s10995-018-2480-7.
9. Shachar B, Mayo J, Lyell D, Baer R, Jeliffe-Pawlowski L, Stevenson D, et al. Interpregnancy interval after live birth or pregnancy termination and estimated risk of preterm birth: a retrospective cohort study. BJOG 2016;123(12):2009 – 17. http://dx.doi.org/10.1111/1471-0528.14165.
10. Ihongbe TO, Wallenborn JT, Rozario S, Masho SW. Short interpregnancy interval and adverse birth outcomes in women of advanced age: a population-based study. Ann Epidemiol 2018;28(9):605 – 11. http://dx.doi.org/10.1016/j.annepidem.2018.06.007.
11. Coo H, Brownell MD, Ruth C, Flavin M, Au W, Day AG. Interpregnancy interval and adverse perinatal outcomes: a record-linkage study using the Manitoba population research data repository. J Obstet Gynaecol Can 2017;39(6):420 – 33. http://dx.doi.org/10.1016/j.jogc.2017.01.010.
12. Conde-Agudelo A, Belizán JM, Breman R, Brockman SC, Rosas-Bermudez A. Effect of the interpregnancy interval after an abortion on maternal and perinatal health in Latin America. Int J Gynecol Obstet 2005;89(S1):S34 – 40. http://dx.doi.org/10.1016/j.ijgo.2004.08.003.
13. Petersen JM, Yazdy MM, Getz KD, Anderka MT, Werler MM, National Birth Defects Prevention Study. Short interpregnancy intervals and risks for birth defects: support for the nutritional depletion hypothesis. Am J Clin Nutr 2021;113(6):1688 – 99. http://dx.doi.org/10.1093/ajcn/nqaa436.

SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Flowchart representing the participation of individuals in the study.