Original Article

Effects of Short Inter-Pregnancy Interval on Maternal and Perinatal Outcomes: A Cohort Study of Pregnant Women in a Low-Income Country

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Abstract

Background: Short inter-pregnancy interval (IPI) is a potential risk factor for adverse pregnancy outcomes. Previous reports from sub-Sahara Africa documented increasing incidence of short IPI but evidence is lacking in its effect on pregnancy outcome. **Aim:** The study aimed to determine the effect of short IPI on pregnancy outcome in Nigeria. **Subjects and Methods:** It was a prospective cohort study of 271 pregnant women receiving antenatal care in a tertiary hospital in Nigeria. For every eligible woman with short IPI (<18 months) recruited; a suitable control with IPI ≥18 months was selected. Statistical analysis was both inferential and descriptive using the statistical package for social sciences version 24 (SPSS Inc. Chicago, Illinois, USA) for windows. A P value of less than 0.05 was considered statistically significant. **Results:** Incidence of maternal anemia was higher in women with short IPI than control (RR: 2.091; 95% CI: 1.4433.031; $P < 0.001$). Other maternal and perinatal outcome measures including premature rupture of membranes, preterm labor/delivery, pregnancy induced hypertension, third trimester bleeding, postpartum hemorrhage, and inadequate gestational weight gain did not show any significant association with short IPI ($P > 0.05$). **Conclusion:** Short IPI is associated with anemia in pregnancy in Nigeria. Public health campaigns for improvement in uptake of family planning services and breastfeeding may help reduce the incidence of short IPI and anemia in low income countries.

Keywords: *Nigeria, pregnancy outcome, short inter-pregnancy interval*

Introduction

Inter-pregnancy interval (IPI), known as period between delivery of one birth and conception of subsequent pregnancy could adversely affect pregnancy outcome. It is said to be short (short IPI) when it is less than 18 months.[1,2] The 'maternal depletion hypothesis' suggests that one or more years between birth of one infant and conception of another are essential to restore depleted maternal resources needed for a successful pregnancy.[3] The theory further postulates that when resources are not replenished, the mother may suffer anemia, premature rupture of membranes (PROM), pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), inadequate gestational weight gain (GWG), etc., while the fetus may develop intrauterine growth restriction (IUGR) or suffer premature delivery, still birth, low birth weight (LBW), etc.[3-7]

Specifically, a study by Lilungulu and co-workers in Tanzania in 2015 observed that pregnant women with short IPI are at higher risk of anemia, preeclampsia, PROM, preterm births, failure of vaginal birth after caesarean section (VBAC), and postpartum hemorrhage, while their neonates are at higher risk of prematurity, birth asphyxia, and LBW.[1]A systematic review by

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Conde-Agudelo *et al*. in 2007 observed that short IPI is associated with increased risk of uterine rupture during VBAC and uteroplacental bleeding disorders.[8] It also observed that the risks of maternal anemia and death are not yet clear, and thus suggested for further studies.[8]

For women with prior Caesarean delivery, an IPI of less than 24 months is associated with adverse maternal outcomes include uterine rupture, postpartum hemorrhage, and increased risk of blood transfusion.[9]

As a short IPI is a potential risk factor for adverse pregnancy outcome,[10] a study on its effect on maternal and perinatal outcome could provide useful information for counseling women, who recently gave birth on the need for appropriate birth spacing.

Previous reports from sub-Sahara Africa documented increasing incidence of short IPI[10-12] but evidence is lacking on its impact on pregnancy outcome. A recent study on birth spacing in the study area, established that mean inter-birth interval among women in Nigeria is short.[10] However, the study did not address possible effects of the observed short birth spacing on pregnancy outcomes. This study therefore aimed at evaluating the effect of short IPI on pregnancy outcome among women in Nigeria.

Subjects and Methods

This was a prospective observational cohort study of 271 eligible pregnant women receiving antenatal care at the University of Nigeria Teaching Hospital (UNTH) Enugu, Nigeria over a 12 months period of March 2015 to March 2016. Enugu State is one of the five states in the South-east geopolitical region of Nigeria and its capital city is Enugu. It lies within the West African rain forest region (latitudes 5° 552 and 7° 102 North and longitudes 6° 502 and 7° 552 East), through a land area of ~ 8000 km^2. The State has 17 Local Government Areas (LGAs) most of which are rural except the three LGAs within the Enugu Metropolis and some part of Oji River and Nsukka urban. According to the 2006 population census, the Enugu state and Enugu Metropolis have a population of 3,257,298 and 722,664 respectively with a female to male ratio of ~1:1. The State has an annual population growth rate of about 2.28% and the population is predominantly Igbos with pockets of other tribes. The religion is predominantly Christianity with pockets of other religions including Islam and traditional religion.

On the other hand, the UNTH Enugu is the pioneer teaching hospital in Southeastern Nigeria. The hospital offers tertiary health services to patients from Enugu state and adjourning states, and it is a major referral tertiary health care center in south-east region of Nigeria. The ante-natal clinic holds daily on weekdays from Monday to Friday and it is run by a team of doctors and midwives headed by consultants. It practices the traditional model of antenatal care whereby women are generally seen monthly until 28 weeks of gestation, fortnightly until 36 weeks, and then weekly until delivery. There are 40 consultants and 32 residents in the Department of Obstetrics and Gynecology. The department records average of 1,500 deliveries annually with a caesarean section rate of 27.6%.[13] The newborn special care units (NBSCU) have incubators and are located very close to the labor wards. Further details of Enugu state and UNTH have been clearly described in previous studies.[10,14]

Written informed consents were obtained from all eligible women before recruitment. Ethical clearance for the study was obtained from the Institutional Review Board of the UNTH, Enugu.

The minimum sample size (n) for this study was calculated using the formula for comparison of proportions.[15]Assuming a 30% increase in incidence of anemia in the study population (40.4%)[16] with an attrition rate of 10% for possible drop outs or loses to follow up; the n was 146, corresponding to 80% statistical power, and 5% level of significance.

The eligible women were consecutively recruited at booking at gestational age of <14 weeks. For every eligible pregnant woman with short IPI (IPI <18 months) recruited into the study; a suitable control (matched for age group, parity group, and social class) with IPI ≥18 months was also recruited. The inclusion criteria were women with singleton fetuses and normal (uncomplicated) pregnancy at gestational age of <14 weeks. The exclusion criteria included previous preterm birth, smoking, intake of alcoholic beverages, and early pregnancy complications such as threatened miscarriage and severe nausea and vomiting. Following recruitment, both groups of women were followed-up throughout pregnancy and labor (routinely) to observe for development of any adverse maternal and/or perinatal outcomes.

The hospital protocol recommends routine iron supplementation in pregnancy using once daily oral preparations that contains 60 mg of elemental iron per tablet. This prescription is in accordance with World Health Organization (WHO) guidelines for iron supplementation in pregnancy.[17] Participants were not queried regarding identification of iron formulation, as the primary preparation currently dispensed in the hospital contains 60 mg of elemental iron and 350 µg of folic acid per tablet. Both groups of participants received iron supplementation from recruitment to delivery.

Data collected included the socio-demographic characteristics, IPI, current pregnancy history, gestational age, and any adverse pregnancy or perinatal outcomes. The primary outcome measure was incidence of anemia in pregnancy. The secondary outcome measures included: incidence of inadequate GWG, PROM, preterm labor, PIH, PPH, third trimester bleeding, preterm births, birth asphyxia, still birth, and LBW.

The hemoglobin concentration of each participant was obtained at booking using Hemocue Hb 301, a B-hemoglobin photometer.[18] The mean hemoglobin concentration for each group was calculated at booking. Thereafter, the hemoglobin concentration was recorded at every antenatal visit. A participant was said to have anemia in pregnancy if her mean hemoglobin concentration after booking to 3839 weeks was <11g/dl while mean hemoglobin concentration of ≥11g/dl was considered as normal.

Total GWG was calculated as participant's weight at 3839 weeks gestation minus her weight at booking.[19] This calculation was based on assumption that maternal weight and body mass index (BMI) remain unchanged in first trimester of pregnancy and before 14 weeks gestation (Fattah *et al*. 2010),[20] and that weight gain within this period has no significant relationship with birth weight.[21-23]

The weighing took place in the clinics with the participants barefooted and wearing light clothing to the nearest 0.5 kg. All the "weighing" was done using the same weighing scale (RGZ-160). The RGZ-160 was gauged at onset of the study, and thereafter regularly during data collection, with a known weighted mass, as described in a recent study.[19] It was also checked regularly for zero error. Total GWG <10 kg was considered as inadequate, 1015kg as normal, and >15 kg as excessive GWG.[19,24]

The weights of the newborns were recorded in a warm room without clothing or diapers, within 1 h of birth. Infant weighing scale ("Way master") was used to record the weight of the newborns to the nearest 0.05 kg, as described in a recent study.[19] The weighing scale was also standardized as above. Normal birthweight was defined as birthweight between 2.5 and 3.9 kg, LBW as <2.5 kg, and macrosomia as ≥ 4.0 kg.[19,25] Birth asphyxia was defined as fifth minute APGAR score <7.[25]

The blood pressure was measured in the clinic at each visit using sphygmomanometer with the patient sitting down and relaxed. PIH was defined as blood pressure greater than 140/90mmHg after 20 weeks gestation with or without proteinuria.

As described in a previous study,[26] social class of participants was defined using a scoring system based on educational level of the woman and her husband's occupation. Thus, high social class was defined as belonging to class I or II, whereas low social class was defined as belonging to class III, IV, or V.

Data analysis was both descriptive and inferential at the 95% confidence level, using SPSS Software version 24 (IBM Inc: Chicago, Illinois, USA). Hypotheses were tested using relative risk as applicable. All tests were two sided, and statistical significance was considered to be at probability value of < 0.05.

Results

A total of 292 eligible participants were recruited for the study; however, 271 concluded the study. Of the 271 participants, 134 had normal IPI while 137 had short IPI. The baseline characteristics of the two groups including age, marital status, tribe, religion, parity, educational level, social class, and hemoglobin concentration at booking were similar [Table 1].

Table 1: The socio-demographic characteristics of the participants*

Variables	Short IPI No. (%)	Normal IPI No. (%)	*P*
Age group			
<25	9 (6.6)	9 (6.7)	0.920
26-30	40 (29.2)	37(27.6)	
31-35	67 (48.9)	63(47.0)	
36-40	16 (11.7)	17(12.7)	
>40	5(3.6)	8(6.0)	
Marital status			
Married	137 (100.0)	134 (100.0)	NA
Religion			
Christian	137 (100.0)	134 (100.0)	NA
Parity			
1-4	128 (93.4)	124 (92.5)	0.773
≥5	9 (6.6)	10 (7.5)	
Tribe			
Igbo	133 (97.0)	134 (100.0)	0.122
Others	4 (3.0)	0 (0.0)	
Educational level			
No formal education	1 (0.7)	2 (1.5)	0.946
Primary	4 (2.9)	4 (3.0)	
Secondary	56 (40.9)	55 (41.0)	
Tertiary	76 (55.5)	73 (54.5)	
Social class			
I	34 (24.8)	30 (22.4)	0.962
II	41 (29.9)	38 (28.4)	
III	33 (24.1)	33 (24.6)	
IV	27 (19.7)	31 (23.1)	
V	2 (1.5)	2 (1.5)	
Hemoglobin conc.	11.54±2.3	11.97±2.5	0.142

IPI=Inter-pregnancy interval; NA=Not applicable; * χ^2 for categorical variable, *t*-test for continuous variable

Table 2: Association between adverse maternal outcome and short inter-pregnancy interval (IPI)

Variables	Short IPI No. (%)	Normal IPI No. (%)	*P*	RR	95% CI for RR
Anemia in pregnancy					
Yes	62 (45.3)	29 (21.6)	<0.001	2.091	1.443-3.031
No	75 (54.7)	105 (78.4)			
Premature rupture of membranes					
Yes	10 (7.3)	11 (8.2)	0.780	0.889	0.391-2.024
No	127 (92.7)	123 (91.8)			
Preterm labor/delivery					
Yes	11 (8.0)	6 (4.5)	0.236	1.793	0.683-7.102
No	126 (92.0)	128 (95.5)			
Pregnancy induced hypertension					
Yes	10 (7.3)	8 (6.0)	0.661	1.223	0.498-3.003
No	127 (92.7)	126 (94.0)			
Third trimester bleeding					
Yes	4 (2.9)	1 (0.7)	0.220	3.912	0.443-34.554
No	133 (97.1)	133 (99.3)			
Primary postpartum haemorrhage					
Yes	8 (5.8)	5 (3.7)	0.421	1.565	0.525-4.663
No	129 (94.2)	129 (96.3)			
Inadequate GWG					
Yes	92 (67.2)	88 (65.7)	0.796	1.023	0.863-1.211
No	45 (32.8)	46 (34.3)			

GWG=Inadequate gestational weight gain; RR=Relative risk; CI=Confidence interval

Table 3: Association between adverse short IPI and perinatal outcome

Variables	Short IPI No (%)	Normal IPI No (%)	*P*	RR	95% CI for RR
Low birth weight					
Yes	10 (7.3)	3 (2.2)	0.065	3.260	0.917-11.587
No	127 (92.7)	131 (97.8)			
Birth asphyxia					
Yes	12 (8.8)	13 (9.7)	0.789	0.903	0.428-1.907
No	125 (91.2)	121 (90.3)			
Still birth					
Yes	6 (4.4)	1 (0.7)	0.099	5.869	0.716-48.097
No	131 (95.6)	133 (99.3)			
Preterm births					
Yes	11 (8.0)	6 (4.5)	0.236	1.793	0.683-4.711
No	126 (92.0)	128 (95.5)			

RR=Relative risk; CI=Confidence interval

The mean gestational age at delivery was 38.7 (2.3) (95% CI: 36.339.5; range: 2541) weeks. The mean total GWG of the participants was 7.5 (6.3) (95% CI: 5.49.1; range: 117) kg, while the mean birth weight of the neonates was 3.3 (0.6) (95% CI: 2.85.1; range: 15.4) kg.

The mean hemoglobin concentration of participants with short IPI was 10.03 (2.3) (95% CI: 9.311.2) gm/dl, while that of the control was 11.4 (2.6) (95% CI: 9.712.3) gm/dl. The observed difference was statistically significant (mean difference: 1.4, 95% CI 0.791.97; $P < 0.001$).The incidence of maternal anemia was significantly higher in women with short IPI than control (RR: 2.091; 95% CI: 1.4433.031; $P < 0.001$). Other maternal outcome measures including PROM, preterm labor/delivery, PIH, third trimester bleeding, PPH, and inadequate GWG did not show any significant association with short IPI ($P > 0.05$). Details are as shown in Table 2.

With respect to neonatal outcome measures, none of the factors including preterm birth, stillbirth, birth asphyxia, and LBW had significant association with short IPI ($P > 0.05$). Details are as shown in Table 3.

Discussion

This study found that short IP1 is associated with anemia in pregnancy. In fact pregnant women with short

IPI are three times more likely to develop anemia than their counterparts with normal IPI. The reason for this observation is unclear but may be related to the already described "maternal depletion hypothesis."[3] There appears to be insufficient time to restore nutritional reserves needed to support fetal growth and development in subsequent pregnancy. This is because repletion of stores often takes several months.[27] In Nigeria, the incidence of anemia in pregnancy is very high, ranging from 32.5 to 64.1%.[16,28-32] As this condition constitutes a significant cause of maternal and perinatal morbidity, efforts should be intensified at its primary prevention and control. Interestingly, observation from this study suggests that preventing short IPI could significantly reduce the incidence of anemia in pregnancy. There is therefore need for improvement in public enlightenment campaigns on adequate birth spacing, as well as adverse effects of short IPI. This campaign should be aggressive in Nigeria where IPI is not only short but the incidence showing a progressive upward trend.[10] Strategies for addressing the unmet needs for contraception and improving contraceptive uptake must be urgently and aggressively addressed. Improved campaign for adequate duration of breastfeeding (>10 months) should also be strongly considered since a recent study from Nigeria observed that adequate IPI could be achieved through adequate breast-feeding duration.[10] The observed association between short IPI and anemia in pregnancy is similar to report from a previous study.[1,2] Other adverse maternal and perinatal outcome measures including PIH, third trimester bleeding, PROM, preterm labor/birth, PPH, still birth, birth asphyxia, and LBW did not show any significant association with short IPI, unlike in a previous study.[1] The observed difference is difficult to explain and thus suggests a need for further researches with larger sample sizes on impact of short IPI on pregnancy outcome in low income countries.

The limitations of this study include the use of weight obtained at recruitment as prepregnancy weight, on assumption that maternal weight remains unchanged in first trimester and before 14 weeks gestation, and that weight gain within this period has no relationship with birth weight.[20,33] The GWG at the end of pregnancy was based on weights obtained at 3839 weeks gestation[19]which may be lower when compared with weights at higher gestation (4042 weeks) in cases where the pregnancy progressed beyond 3839 weeks gestation. Although the traditional cut off for short IPI is <18 months (as used in this study), a cut off <6 or <12 months might have given more significant outcomes as seen in a previous study.[2]The very small frequencies and wide confidence intervals obtained in some of the outcome measures of interest in the study suggest that a larger sample size would have improved the study's precision. Furthermore, this study is hospital based and as such limits its generalization to the entire population.

The major strength of this study lies in its prospective design and the robust sampling technique for determination of incidence of anemia. Using mean hemoglobin concentration (as done in present study) seems to be a better measure of anemia in pregnancy than using any single values (as reported in previous studies).[9] This sampling variation may explain why the incidence of anemia recorded in short IPI group (45.3%) was within the 32.564.1% previously reported at booking.[16,28-32]Also, the routine use of iron supplementation from recruitment (at booking) to 3839 week gestation might have contributed to the relatively similar incidence with previous studies done where anemia was estimated for at booking.

In conclusion, short IPI is associated with anemia in pregnancy in Enugu, Nigeria. Public health campaigns for improvement in uptake of family planning services and breastfeeding may help reduce the incidence of short IPI and maternal anemia. A well-designed multi-centre prospective cohort study with large sample size is required to confirm the findings of this study since most previous studies are low powered or retrospective in design.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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