Research Article

Interpregnancy interval and the risk of preterm birth: a case-control study of infants born at Al-sadaqa general teaching hospital, Aden, Yemen

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ABSTRACT

Background: Interpregnancy interval (IPI) is a known risk factor for preterm birth. The aim of this study was to assess the relationship between IPI and spontaneous preterm birth, and to identify the influence of confounding variables such as socioeconomic status, maternal age, and reproductive history.

Methods: This is a hospital-based, case-control study conducted in the department of neonatology, Al-Sadaqa General Teaching Hospital, Aden, during June to September 2011. A case was defined as infant born spontaneously before 37 weeks of gestation and control was a next eligible infant born between 37-42 complete weeks of gestation. Comparison between groups was assessed by statistical analysis and odds ratio were calculated for confounding factors.

Results: A total of 100 preterm (cases) and 100 full-term (controls) infants were evaluated for the effects of IPI. Intervals of both <12 months and 12-<24 months were significantly associated with preterm births compared to control (37% vs 12% and 73% vs 46% respectively, all p<0.05). The risk of preterm birth was higher in association with low number of antenatal care visits (OR=10, 95% CI=1.62-61.46, p=0.018), younger women's age (OR=8, 95% CI= 1.35-8.4, p=0.001), non-educated mother (OR=7.92, 95% CI=2.49-25.22, p=0.002) and gravid 2-3 (OR=6.5, 95% CI= 5.06-53.8, p=0.001). Significant risk was also observed among mother with low socio-economic status and residents of rural areas (all p<0.05).

Conclusions: Short IPI is significant risk factors for preterm birth. This highlights the importance of counseling women in childbearing age to wait at least 24 months between delivery and subsequent conception.

Keywords: Interpregnancy interval, Preterm birth, Birth spacing, Risk factor

INTRODUCTION

Preterm birth (PTB) is defined as a birth occurring before complete 37 weeks of gestation with worldwide estimates of 15 million preterm births each year.[1] The global burden of PTB is varied with higher rate and poor outcomes in low and middle income countries.[2] Prematurity is the leading cause of perinatal mortality, and the second most common cause of death in children under 5 years of age.[3]

Born prematurely are more likely to have several complications soon after birth and lifelong disabilities that impose a significant economic burden on both family, society and the health system.[4] As most preterm births happen spontaneously the exact cause is still unsolved, a search for more predictive and reliable risk factors that may lead to effective intervention strategies are relevant to public health and should be of great interest for both general public and health professionals.[5,6]

Interpregnancy interval (IPI) is a period of time between the end of one pregnancy and the conception of the next pregnancy. Numerous studies have shown relationship between short IPI and spontaneous preterm birth and IPI has been viewed as an important and modifiable risk factor for adverse birth outcomes, including preterm birth.[7-12] Likewise, long interpregnancy intervals might also be important determinant of preterm birth, but fewer studies have analysed the relationship between long intervals and prematurity.[7,13]

The underline mechanism of short IPI on adverse birth outcomes are not well known, but has been attributed to maternal nutritional depletion, of particular interest is folate deficiency.[14,15] This theory assumed that mothers with short birth spacing have insufficient time to replete the nutritional reserve necessary to fetal support. This seems to be important especially for those women with lifelong poverty and inadequate diet which lead to persistent marginalized nutritional status. Other assumption is that with short IPI postpartum stress and uterine inflammatory status have insufficient time for complete resolution and recovery.[5,16]

According to WHO recommendation, waiting at least 24 months after a live birth before attempting subsequent pregnancy is likely to be beneficial for both mother and child health.[11]

Little is known about the effect of IPI on preterm delivery in developing countries particularly those with high fertility rate and low resource settings like Yemen and prior to this no study was conducted in this locality. The aim of the present study is to assess the relationship between interpregnancy interval and spontaneous preterm birth, and to identify the influence of associated variables such as socioeconomic status, maternal age and reproductive history.

METHODS

This is a hospital-based, case control study conducted in the department of neonatology, Al-Sadaqa General Teaching Hospital, Aden during June to September 2011. This hospital is a major referral hospital for women and children in Aden, and the neighbouring governorate and servicing both the urban and the adjacent rural areas.

Definitions

A case was defined as a singleton neonate who was born spontaneously before 37 week of gestation to a healthy Yemeni woman with no obstetric or medical complications, and whose previous pregnancy outcome was a full term live birth. The gestational age estimation was based on all available evidence at the time of birth, including prenatal record, date of last menstrual period and results of ultrasound evaluation. For each case, a control was selected with same eligibility criteria except a

birth after 37-42 completed weeks of gestation. Twin and post term (≥ 42 weeks) births were excluded.

We defined IPI as the interval between delivery of a live birth of previous pregnancy and the birth of the current child minus the duration of the index pregnancy. Gestational age was estimated as the number of completed weeks of gestation based on last menstrual period or calculated from ultrasound evaluation. IPI was categorized into 4 groups: less than 12, 12 to 23, 24 to 59, and 60 months or longer.

Maternal age was defined as completed years at time of index birth. Gravid was defined as the number of previous pregnancy after completing 28 weeks of gestation including still birth.

Data collection

Detailed medical and obstetric histories were collected for each case from the mother/relatives besides the infant and review of all available documents. Medical records of the patients were also evaluated. Data were extracted using pre-structured questionnaire, which included maternal age, residence, educational level, parity, antenatal care visits, and family income.

There were 42 cases and controls excluded due to inadequate information about gestational age and interpregnancy intervals, primarily because of uncertainty regarding the last menstrual period and/or ultrasound examination was not done.

Agreement of all participants (mother/guardian) to enroll had been asked.

Data analysis

The data were analysed using SPSS 21 program. Cases and controls were assessed for comparability on all the variables collected. Appropriate statistical tests were applied and $p<0.05$ considered significant. The odds ratio with the 95% confidence interval were calculated for lower IPI compared to the assumed ideal IPI (of 24 months and more) as a refer group.

RESULTS

Table 1: Distribution of cases/controls by various interpregnancy intervals.

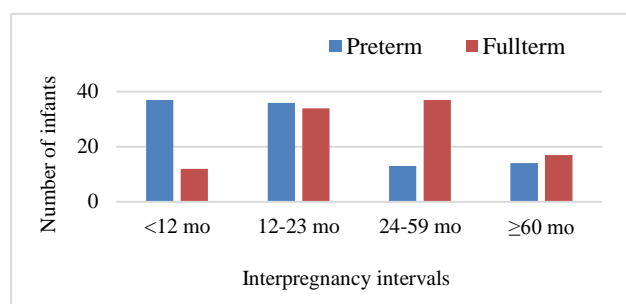| Birth interval	Preterm (cases), n=100	Full term(control), n=100	P value*
<12 mo	37	12	0.001
12-23 mo	36	34	0.81
24-59 mo	13	37	0.001
≥60 mo	14	17	0.6

*Chi square test

A total of 100 preterm neonates were met the eligibility criteria, and consecutive 100 full term act as controls. Less than 12 months IPI was noted among 37% of preterm and 12% of controls (p<0.001).Comparing all those <24 months IPI, there were 73% preterm vs 48% full term infants (p<0.01) (Table 1, Figure 1).

According to WHO reference 24–59 months IPI as optimal birth spacing we considered this band as a referent group, which was identified among 13% and 37% of cases and controls respectively. Our results showed that IPI of ≥ 60 months was not associated with increased proportion of preterm births (p>0.6).

Table 2: Distribution of selected maternal characteristics by interpregnancy interval.

Variables	Case (preterm), n=100				Control (full term), n=100			
	<12 mo	12-23 mo	24-59 mo	≥60 mo	<12 mo	12-23 mo	24-59 mo	≥60 mo
	n=37	n=36	n=13	n=14	n=12	n=34	n=37	n=17
% of sample with specified interpregnancy interval								
Maternal age (Years)								
15-19	43.2	22.2	7.7	0.0	16.6	0.0	2.7	0.0
20-29	35.1	44.4	46.1	50.0	58.3	58.8	62.1	5.8
30-39	18.9	25.0	38.4	42.8	25.0	38.2	32.4	94.1
40-50	2.7	8.3	7.7	7.1	0.0	2.9	2.7	0.0
Gravid								
2-3	64.8	69.4	23.0	35.7	50.0	55.8	78.3	23.5
4-5	27.0	11.1	61.5	35.7	41.6	20.5	13.5	29.4
≥5	8.1	19.4	15.4	28.5	8.3	23.5	8.1	47.1
Education Level								
None	59.4	62.1	69.2	42.8	41.6	61.7	54.0	41.1
Up to 9	24.3	24.3	15.3	42.8	33.3	32.3	37.8	17.6
10-12	16.2	11.1	15.3	14.2	25.0	2.9	5.4	29.4
≥ 13	0.0	0.0	0.0	0.0	0.0	2.9	2.7	11.7
Antenatal care visits								
None	72.9	66.6	61.5	64.2	83.3	61.7	70.2	64.7
1-2	21.6	25.0	15.3	28.5	16.6	32.3	24.3	35.2
3-4	5.4	8.3	15.3	7.1	0.0	5.8	5.4	0.0
≥ 5	0.0	0.0	7.7	0.0	0.0	0.0	0.0	0.0
Socio-economic status								
Low	72.9	66.6	61.5	57.1	58.3	50.0	56.7	29.4
Middle	27.0	27.7	30.7	42.8	25.0	38.2	27.0	52.9
High	0.0	5.5	7.7	0.0	16.6	11.7	16.2	17.6
Residence								
Urban	29.7	30.5	30.7	64.2	25.0	44.1	34.2	35.2
Rural	70.2	69.4	69.2	35.7	75.0	55.8	56.7	64.7

Figure 1: Distribution of preterm (Cases)/term (Controls) infants by interpregnancy intervals.

In Table 2, selected maternal characteristics were evaluated in relation to birth spacing. Compared with women who gave birth to full term neonates, women who gave birth of premature infants were less educated (60% vs 53%), more socioeconomically deprived (67% vs 50%), and rural residence (65% vs 60%)irrespective of birth spacing. Seventy three percent of preterm were born to women with less than optimal birth spacing, of them about 2/3 with no antenatal care, low socioeconomic, and were rural residence. Maternal age <20 years was observed in high proportion (43.2%) among cases with IPI <12 months compared to 16.6% in controls.

Table 3 shows the odds ratio associated with selected maternal characteristics for lower IPI groups versus referent group. While IPI of <12 months was found significantly associated with the risk for premature birth. The risk was higher in association with 1-2 visits of antenatal care(OR=10, 95% CI=1.62-61.46, p=0.018), younger women's age (OR=8, 95% CI= 1.35-8.4, p=0.001) in non-educated mother (OR=7.92, 95% CI=2.49-25.22, p=0.002), gravid 2-3 (OR=6.5, 95% CI=5.06-53.8, p=0.001), and significant risk was also observed among rural (OR=6.60, 95% CI=2.46-17.67, p=0.001) more than in urban (OR=6.21, 95% CI= 1.45-26.43, p=0.012) mothers. As well as among low and intermediate socioeconomic status (OR=6.27, 95% CI=2.21-17.7, p=0.004 and OR=6.33, 95% CI=1.41-28.39, p=0.018 respectively).

Table 3: The Odds ratio of selected maternal characteristics for preterm birth in relation to pregnancy interval.

Variables	<12 months			12-23 months		
	OR	95% CI	P	OR	95% CI	P
Maternal age (years)						
15-19	8.0	(1.35-8.4)	0.001	-	-	-
20-29	3.43	(1.09-10.72)	0.029	1.47	(0.57-3.79)	0.48
30-39	5.94	(1.29-27.2)	0.025	1.76	(0.58-5.29)	0.397
40-50	-	-	-	1.5	(0.05-40.63)	0.714
Gravid						
2-3	6.5	(5.06-53.8)	0.001	5.43	(2.05-14.4)	0.007
4-5	1.54	(0.39-5.95)	0.735	0.43	(0.10-1.93)	0.465
>5	5.5	(0.46-65.1)	0.272	1.6	(0.38-6.64)	0.719
Education level						
None	7.92	(2.49-25.22)	0.002	1.97	(0.83-4.68)	0.091
Up to9	4.78	(1.12-20.32)	0.040	1.74	(0.51-5.87)	0.537
≥ 10	5.0	(0.82-30.4)	0.102	5.0	(0.64-39.1)	0.161
Antenatal care visits						
None	5.87	(2.32-14.82)	0.001	2.48	(1.09-5.65)	0.04
1-2	10.0	(1.62-61.46)	0.018	2.05	(0.56-7.45)	0.34
≥ 3	-	-	-	0.75	(0.06-8.83)	0.65
Socio-economic status						
Low	6.27	(2.21-17.7)	0.004	2.29	(0.95-5.53)	0.08
Middle	6.33	(1.41-28.39)	0.018	1.46	(0.47-4.50)	0.57
High	-	-		4.5	(0.31-65.2)	0.517
Residence						
Urban	6.21	(1.45-26.43)	0.012	1.24	(0.43-3.50)	0.790
Rural	6.60	(2.46-17.67)	0.001	3.01	(1.26-7.15)	0.018

OR: Odds Ratio, CI: Confidence Interval

DISCUSSION

There is well documented evidence to link short IPI to adverse perinatal outcomes, including in particular the increased risk of preterm births, therefore appropriate birth spacing has been recommend to achieve favourable outcomes.[7,17] To our knowledge this is the first study of its type investigating the association of short IPI with preterm births in Yemen. The study showed that women who conceived after a short IPI of less than 24 months after a live birth had a high risk of preterm birth and the highest risk was seen among those with < 12 months birth interval. Short birth spacing was shown to be significantly confounded by younger maternal age, lack of antenatal care, low education level and 2-3 gravid. The result of this study is in corresponding with data reported from other countries in the region such as UAE, Sudan and Qatar.[18-20]

In Yemen, approximately 54% of population live under the poverty line and survive on fewer than 2 dollars per day, with about two thirds of the population live in rural areas where health care are limited and of poor quality.[21] The importance of maternal education as one of the key determinants for maternal and child health is well recognized.[22] In our population illiteracy rate is high among females in rural (62%) as well as urban (54%) settings.[23] Available antenatal care was poorly utilized and a single visit for this purpose was noted among 47% and only 13.9% of women had four visits in approximate.

Therefore, it is obviously that the effect of these confounding factors cannot be marginalized, and their influence is interrelated and interdependent.

In our study, 43% of women were adolescent and gave birth to premature babies in their 2nd or 3rd pregnancy within< 12 moths IPI, but whether adolescent pregnancy or the short IPI is the sole factors contributing to premature birth, is a question remains to be answered in this setting. However, numerous studies from developed as well as developing countries have consistently reported that teenage pregnancy were at increased risk for preterm birth, Yemen, like other developing countries, most women begin their childbearing life early during adolescence, before reaching their full biologic and social maturity.[24-26]

Antenatal care plays an important role in the women's reproductive health, primarily through caring for pregnant women and monitoring pregnancy course facilitating early detection of obstetric complications. It is also addressing other reproductive health needs, such as family planning and provides contraceptive aids. In Yemen the primary health care centers in rural areas are scarce and remote from women's household, and the available centers are inadequately equipped and are running by under qualified persons, which could explain the underutilization of antenatal care by mothers in the current report.[26]

Strict optimal IPI has not been agreed upon universally, but 18-59 months interval was a period found to be associated with lowest risk of preterm birth and our result of 24-59 months IPI is within the same reported limit and in consistent with other studies.[7,8,13,27]

Some studies found that longer IPI ($\geq$ 60 months) was also a risk factor for preterm birth but we did not identify such relationship and our finding is similar to that reported by other researchers.[13,18,28,29] However, in current study a small number of participants in this age band could be a potential explanation.

Some limitations of this study worth to be mentioned. Although our results are in corresponding with other similar studies based on population surveys, comparison should be taken cautiously, as our sample size is relatively small, the study is a hospital based and preterm births were not phenotypically subdivided to early and late as adverse effect is increase with decrease of gestational age.[30] Some other confounding factors were not included in the current analysis such as smoking, Qat chewing habit, uses of contraception and lactation practice.

A strength of this study is the inclusion only of mother with former healthy full term infant as women with history of prior preterm birth have a higher tendency to deliver prematurely in a subsequent pregnancies, in addition primigravida women have a higher risk of preterm birth and other adverse outcomes, therefore they were exclude.[9,28]

CONCLUSION

Our findings, in conjunction with those of other studies on the relationship between IPI and preterm birth, strongly suggest that a short IPI is an important risk factor, and this can be used to support actions targeting improvement of primary health care for pregnant women and addressing the importance of spacing between births.

The rate of preterm birth can be partly reduced by increase birth spacing and delay a second pregnancy through better access to female counselling, contraceptive care and promotion of breast feeding. Women, particularly those who are in adolescent age, are not educated, and from low income families; should be advised about the potential risk and consequences of having premature infant after a short IPI and the benefits of ideal birth interval.

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