ASSOCIATION BETWEEN SHORT INTER PREGNANCY INTERVAL AND PRE-TERM BIRTH

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ABSTRACT

OBJECTIVES: To determine association between short inter pregnancy interval and pre term birth.

METHODOLOGY: A total of 178 patients were included in this case control study. Patients were equally divided into two groups i.e cases and controls (89 patients each group). Cases were defined as patients with alive preterm births, (gestation between 29 and 37 weeks) regardless of mode of delivery. Controls were patients with a live birth at term or more i.e at a gestation of or more than 37 weeks. Detailed history was taken from all these patients and antenatal records were thoroughly reviewed to extract the required information. The presence of short inter pregnancy interval was searched for in the records of all patients.

RESULTS: Mean age of the patients was 33 years with $SD \pm 2.16$. Among cases short inter pregnancy interval was present in 65 (73%) of patients while among controls only 25 (28%) of the patients had short inter pregnancy interval.

CONCLUSION: There is an elevated risk of pre term birth and associated perinatal morbidity and mortality with short inter pregnancy interval.

KEY WORDS: Short inter pregnancy interval, Preterm birth.

INTRODUCTION

Preterm birth (PTB) refers to a birth that occurs before 37 weeks of gestation. PTB and its complications are by far the leading cause of perinatal mortality and morbidity all over the world¹.

Risk factors for PTB are both maternal and fetus related and include maternal stress, low socioeconomic status, depression, life events like (divorce, separation, close relative death), surgery during pregnancy, multiple gestations, polyhydramnios, primigravida, congenital uterine anomaly, fibroid uterus, cervical factors like premature cervical dilatation or effacement, infection like sexually transmitted infections, pyelonephritis, appendicitis, placental pathologies like placenta praevia and abruption, vaginal bleeding, previous preterm delivery, smoking, maternal age (<18 or >40), poor nutrition and low body mass index, anemia (hemoglobin <10 g/dl) and short interpregnancy interval (IPI)^{2,3}.

The short IPI is one of the factors associated with PTB, LBW (low birth weight) (i.e. less than 2500 g), with the highest risk associated with IPI of less than six months. A meta-analysis reported an association between perinatal death and short IPI⁴. Other studies supported the relationship between preeclampsia and short IPI⁵.

Short IPI is associated with adverse maternal and fetal outcome. A woman with short IPI has insufficient time to recover from physiological stress which is imposed by previous pregnancy. This results in depleted nutrient stores, anemia, Infection, Placenta Previa, Placental abruption and preterm labour⁶.

The hypothetical causal mechanisms for explaining the association between short intervals and adverse outcomes identified are: maternal nutritional depletion, folate depletion, cervical insufficiency, vertical transmission of infections, suboptimal lactation related to breast feeding-pregnancy overlap, sibling competition, transmission of infectious diseases among siblings, incomplete healing of uterine scar from

previous cesarean delivery, and abnormal remodeling of endometrial blood vessels^{7,8,9,10}

One study found significant association between short IPI and spontaneous early PTB. Short IPI occurred in 22% of early preterm births, 5.3% in late preterm births and 6.7% of term deliveries with odds ratio of 3.6¹¹. Another study showed that short IPI was significantly associated with increased risks for PTB, SGA (small for gestational age), VSGA (very small for gestational age), early neonatal death and congenital malformations¹².

While a local study has shown a frequency of preterm labor of 7.5%, out of which 69.75% were associated with short IPI¹³.

The results from various parts of the world and various regions are widely varied^{7,8,9,10}. The results of this study will be used to provide emphasis on education of couples to avoid pregnancies within the time interval as defined as short IPI. This will also contribute towards fetal wellbeing, proper protocols to reduce fetal morbidity and mortality due to preterm birth. The results of this study will also be disseminated with other local health professionals and future areas of research will also be identified.

MATERIAL AND METHODS:

The study was conducted after approval from hospitals ethical and research committee. Patients meeting the inclusion criteria were included in the study through the labor ward and were assigned as cases and controls. Cases were those laboring mothers who had preterm birth and controls were those laboring mothers who have normal term birth. Controls and cases were selected from same labor ward. The purpose and benefits of the study were explained to all patients and written informed consent was obtained after explaining them the usefulness of study and maintenance of confidentiality.

Among both cases and controls, detailed history was taken and required information was

extracted from antenatal records to detect the presence of short inter-pregnancy interval.

All the observations, diagnosis and clinical assessment were conducted under supervision of an expert gynecologist. All the above mentioned information including name, age address was recorded in a pre designed proforma. Extreme care was exercised in the selection of cases and controls to avoid selection bias, similarly extreme care was taken in extraction of information and scrutiny of medical records to avoid responder bias. Additionally, exclusion criteria had been strictly followed to control confounders and bias in the study results.

RESULTS:

Age distribution among 178 patients was analyzed as 45(25%) patients were in age range 25-30 years, 71(40%) patients were in age range 31-35 years, and 62 (35%) patients were in age range 36-40 years. Mean age was 33 years with standard deviation ± 2.16 . (Table No 1).

Status of parity among 178 patients was analyzed as 36(20%) patients were multi para, 53(30%) patients were grand multi para and 89(50%) patients were great grand multi para. (Table No 1).

TABLE NO 1. AGE DISTRIBUTION and STATUS OF PARITY (N= 178)

	Age(years)				Parity			
	25-30	31-35	36-40	Total	Multi para	Grand multipara	Grang grand multi para	Total
Freq uency	45	71	62	178	36	53	89	178
Perce ntage	25%	40%	35%	100%	20%	30%	50%	100%

Mean age was 33 years with standard deviation ± 2.16

Frequency of short inter pregnancy interval among cases and control was analyzed as in cases (patients with preterm birth), 65(73%) patients had short inter pregnancy interval (interval less than 6 months), while 24(27%) patients had long inter pregnancy interval whereas in control group (patients with normal term birth), 25(28%) patients had short inter

pregnancy interval while 64(72%) patients had long inter pregnancy interval. (Table 2).

TABLE NO 2. FREQUENCY OF SHORT INTERPREGNANCY INTERVAL IN CASES AND CONTROL (N=178)

PARITY	Cases (preterm birth) (n=89)	Control (normal term birth) (n=89)
Short inter pregnancy interval	65(73%)	25(28%)
Long inter pregnancy interval	24(27%)	64(72%)
Total	89	89

Chi square test was applied in which p value was 0.631

Association of short inter pregnancy interval with age distribution was analyzed as in preterm birth group (cases) 65 had short inter pregnancy interval in which 14 patients were in age range 25-30 years, 27 patients were in age range 31-35 years and 24 patients were in age range 36-40 years, whereas in normal term birth (control group) 25 patients had short inter pregnancy interval in which 7 patients were in age range 25-30 years, 8 patients were in age range 31-35 years and 9 patients were in age range 36-40 years. (Table No 3)

TABLE NO 3. ASSOCIATION OF SHORT INTERPREGNANCY INTERVAL IN AGE DISTRIBUTION (N=178)

PARITY	Cases (preterm birth)			Control (normal term birth)		
	25-30 years	31-35 years	36-40 years	25-30 years	31-35 years	36-40 years
Short inter pregnancy interval	14	27	24	7	8	9
Long inter pregnancy interval	8	9	7	16	27	22
Total	22	36	31	23	35	31
P Value	0.571			0.601		

Association of short intra pregnancy interval with parity was analyzed as in preterm birth group (cases), 65 had short inter pregnancy interval in which 14 patients were multi para, 18 patients were grand multi para and 33 patients were great grand mutipara whereas in normal term birth (control) group, 25 patients had short inter pregnancy interval in which 6 patients were multi para, 9 patients were grand multi para and 10 patients were great grand mutipara. (Table No 4)

TABLE No 4 ASSOCIATION OF SHORT INTERPREGNANCY INTERVAL IN AGE DISTRIBUTION (N=178)

PARITY	Cases (preterm birth)			Control (normal term birth)		
	Multi Para	Grand Multi Para	Great grand Multi Para	Multi Para	Grand Multi Para	Great grand Multi Para
Short inter pregnancy interval	14	18	33	6	9	10
Long inter pregnancy interval	4	8	12	12	18	34
Total	18	26	45	18	27	44
P Value	0.433			0.521		

DISCUSSION:

The main finding of this study is that in women having a second birth a short preceding interpregnancy interval was an independent risk factor for extremely preterm birth, moderately preterm birth, and neonatal death not due to congenital abnormality. The association occurred even among women whose first pregnancy was a term live birth and persisted after adjustment for maternal age, marital status, height, socioeconomic deprivation category, smoking, previous birth weight vigesimal, and previous

caesarean section. These findings are consistent with other study¹¹. The association was specific to preterm birth and neonatal death, as no association existed between a short interpregnancy interval and the risk of delivering a growth restricted infant and the confidence intervals were sufficiently narrow to exclude even a weak association which is not the case in the study conducted by agustin et al¹². the reasons can be that the study is not an original study but a systemic review and the great majority of the studies included in this review calculated the interpregnancy interval using mother's recall of her previous child's date of birth and last menstrual period instead of birth record and gestational age recorded by ultrasonography. In the review in most studies the intervals were calculated using two consecutive live births ignoring spontaneous and induced abortion between them which can produce even longer intervals between live births. And also that study did not address properly the potential confounding factors other than socioeconomic status and maternal age like marital status, height, smoking, previous birth weight vigesimal, and previous caesarean section which is not the case in our study.

When we examined the outcome of all first births in relation to the subsequent interpregnancy interval, women with a short interpregnancy interval had a significant excess of intrauterine growth restriction, preterm birth, and perinatal deaths in their first births. Indeed, approximately 10% of women with an interval of less than six months had a first birth that had ended in perinatal death, compared with less than 1% of women with an interval of 18-23 months. These observations are consistent with previous studies and underline the importance of excluding women with complications in their first birth when examining associations between interpregnancy interval and the outcome of the second birth¹⁴. An association has previously been shown between maternal age less than 20 years at the time of the second birth and adverse obstetric outcome¹⁵. In the some studies we found that this association was independent of

interpregnancy interval and complications of the first pregnancy. However, the association between maternal age less than 20 years and adverse outcome was attenuated by adjustment for marital status, socioeconomic deprivation category, smoking status, height, previous birth weight vigesimal, and previous caesarean section, although a statistically significant association persisted in multivariate analysis. We cannot exclude the possibility that maternal age less than 20 years is a marker for some other environmental factor. However, it is unlikely that the associations with a short interpregnancy interval were due to unmeasured or residual confounding. Firstly, after adjustment for maternal age, adjustment for other maternal factors had very little effect. Secondly, the strength of the association was virtually unchanged when we confined the analysis to married, non-smoking women aged 25 and above. Thirdly, no statistically significant first order interactions occurred between a short interpregnancy interval and other maternal factors. Finally, the association was specific for preterm birth and neonatal death. No association existed between a short interpregnancy interval and delivering a small for gestational age baby. In contrast, a high socioeconomic deprivation category (that is, more deprived) was significantly associated with delivering a small for gestational age baby in multivariate analysis¹⁶.

The lack of association between interpregnancy interval and growth restriction also suggests that the relation between a short interpregnancy interval and other adverse outcomes is unlikely to be due to depletion of maternal nutritional reserves. A specific association between a short interpregnancy interval and preterm birth is biologically plausible. The control of parturition is thought to be mediated by a two step process of activation and stimulation¹⁷. Activation is defined as the up regulation of expression of a range of contraction associated proteins, such as Gprotein coupled receptors, in the weeks leading up to term. Stimulation is defined as the process by which synthesis and release of natural

agonists for these receptors, such as prostaglandins, initiates uterine contraction. We hypothesise that failure to allow expression of contraction associated proteins to return to prepregnancy levels may be the mechanism by which a short interpregnancy interval predisposes to preterm birth¹⁸.

CONCLUSION

We conclude that women should be informed of a small but significantly elevated risk of preterm birth and perinatal death when they conceive shortly after a birth. Contraceptive advice should be targeted towards women who are most likely to have a subsequent short interpregnancy interval—namely, teenagers and women who have just experienced a perinatal loss.

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