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Role of Family History in the Prediction of Preterm Labor- A Case Control Study in a Tertiary Care Centre

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ABSTRACT

A case control study was conducted on maternal determinants of preterm labor at Department of Obstetrics and Gynecology, in Sree Avitom Thirunal (SAT) Hospital, Medical College, Thiruvananthapuram among 460 women (230 cases and 230 controls). All cases delivered between gestational age of 24-37 weeks were taken as cases and next term delivery (gestational age beyond 37 weeks but below 42 completed weeks) happened in labor room as controls from November 1st, 2012 to November 30th, 2013. All consecutive cases as per the case definition and satisfying the inclusion exclusion-criteria are included in the study till the sample size of 460 is attained. The association of family history of preterm birth with preterm birth was found using univariate analysis by chi square test and multivariable analysis by logistic regression method. Primary objective of the study was to identify various risk factors for mothers undergoing preterm delivery and the secondary objective was the role of family history in the prediction of preterm labor. The family history of preterm birth (OR-9.693 and 95% CI of 2.037-46.128, p value=0.004) and preterm labor has significant association with the study. The role of maternal genetic study in foetal health and pregnancy outcome is not clear. Williams et al. carried a study to investigate familial recurrence of preterm labour, and analyse the relative contributions of maternal and foetal genotypes and the risk of preterm delivery. From the study, more than 90% of cases and controls had no family history of preterm birth. When comparing between cases and controls, the percentage of cases with a family history of preterm birth was higher than that of control group. Preterm birth is a complex trait with a significant familial component. So it is essential to anticipate preterm labor and give appropriate counselling to the mother regarding the factors which may contribute to preterm labor and regarding preventable etiological factors and to conduct frequent antenatal checkups.

Keywords: Preterm labor, Genetics, Family history, Preterm delivery

INTRODUCTION

Preterm birth is also the most important of short and long term morbidities in infants and children and can have long term health consequences such as cerebral palsy, blindness, developmental deficiencies including cognitive, learning and language deficits.

Prematurity affects 1 in 10 births or 11% world wide and 40-75% of neonatal deaths. The incidence of preterm delivery is rising worldwide because of increased frequency of multiple births due to artificial methods of reproduction, more working mothers, increased stress and medically induced prematurity. The precise aetiologies of preterm labour remain elusive, limiting the development of preventive and therapeutic strategies. Despite decades of research much of the aetiology remains unknown and hence, the rate of premature births has not decreased and existing data suggest that it is on the rise.

Family history of preterm labour

A more recent and extensive study of this hypothesis suggested that fathers contributed little to the preterm delivery risk. Genetic researchers have instead concentrated on both maternal and foetal genes, as poor perinatal outcomes can, in principle, be affected by both the maternal genotype and the foetal genotype. It is obvious that foetal genes can affect foetal wellbeing. However, the role of maternal genetic study in fetal health and pregnancy outcome is not clear and carried a study to investigate

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familial recurrence of preterm labour and analyse the relative contributions of maternal and fetal genotypes and the risk of preterm delivery.

They concluded as the recurrence risk of preterm birth was transmitted through the mother and a higher risk if the mother was born preterm herself. There was no added risk with the father's previous history or genetic input. Other studies shows a significant increase in risk children, whose siblings were affectedby preterm birth, because of maternal and/or foetal genetic influences. This added risk still persists even after adjustment for non-genetic environmental risk factors in families.

Study design

A case control design was followed for the conduct of study in order to study the role of multiple risk factors on a single outcome.

Study setting

The study was conducted at the Department of Obstetrics and Gynaecology, Sree Avittom Thirunal (SAT) Hospital, Medical College Thiruvananthapuram, a tertiary care referral teaching hospital in Kerala.

Study population

Study population included 460 women admitted in SAT Hospital, Thiruvananthapuram (230 women as cases and 230 women as controls).

Period of study

The study period was from November 1st, 2012 to November 30th, 2013 at Sree Avittom Thirunal Hospital, Government Medical College, Thiruvananthapuram.

Definition of case

Women in the age group of 18-35 who delivered in SAT hospital at a gestational age of 24-37 weeks, gestational age estimated by the patients' last menstrual period (LMP). It was determined on the basis of whether menstruation was regular or by ultrasonography detecting gestational age of less than 12 weeks.

Definition of controls

Women whose delivery occurred in SAT hospital at or beyond a gestation age of 37 but below 42 completed weeks, gestational age estimated by the patients' last menstrual period (LMP), additionally confirmed by first and second trimester ultrasound.

Exclusion criteria

1. IUDs and still births.
2. Women not willing to participate in the study.

Sample size

Based on a pilot study conducted at SAT Hospital, Thiruvananthapuram.

Sample size was calculated using the formula

$$n = \frac{\left\{Z_{1-\frac{\alpha}{2}}\sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right\}^2}{(P_1-P_2)^2}$$

$$P1 = \frac{OR \times P_2}{1+P_2(OR-1)}$$

$$\bar{P} = \frac{P_1+P_2}{2}$$

P_2= Proportion of exposure in control group

P_1= Proportion of exposure in cases

OR= Odds ratio

α = Significance level

1-β= Power

Taking a case control ratio of 1:1, 230 cases and 230 controls were recruited for the present study **(Table 1)**.

Table 1. Determination of sample size (from the literature).

Proportion of exposure in control group (Vaginal infections)- P_2	0.08
Anticipated odds ratio (OR)	2.4
Proportion of exposure in case group – P_1	0.17
Power (1- beta) %	80
Alpha error (%)	5
1 or 2 sided	2
Required sample size in each of the case & control groups	201

Selection of cases and controls

All consecutive cases as per the case definition and satisfying the inclusion - exclusion criteria were included in the study till the sample size was attained. Women as per the definition criteria for controls and those coming next to every case was selected as controls.

ASSOCIATION OF PRETERM BIRTH AND FAMILY HISTORY OF PRETERM LABOUR

Family history of preterm birth

The study examined the association between family history of preterm birth and present preterm birth. More than 90% of cases and controls had no family history of preterm birth. When comparing between cases and controls, the percentage of cases with a family history of preterm birth was higher than that of control group and this difference in percentage was found to be statistically significant by using the chi-square test. Odds ratio of 3.9 (p value 0.010 and 95% CI=1.3-12.1) indicates that the chance of preterm birth was nearly 4 times more among mothers who had a family history of preterm birth **(Table 2 and Figure 1)**.

Table 2. Association between family history of preterm birth and present preterm birth.

	Cases N=230		Control N=230		x^2 value	OR (95% CI)
Family history	N	%	N	%	p-value	
Yes	15	6.5	4	1.7	6.643	3.9
No	215	93.5	226	98.3	0.01	(1.3-12.1)

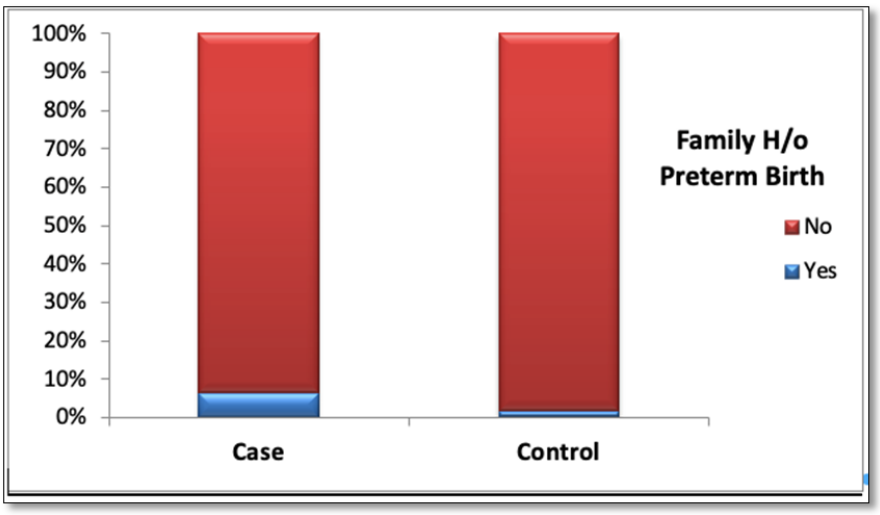

Figure 1. Family history of preterm birth.

Data Analysis

The data was analysed using descriptive and inferential statistics. The distribution of variables were looked into and appropriate statistical significance test were undertaken. Collected data was entered in MS EXCEL. Completeness was checked and analysis was done using downloaded version of statistical software SPSS version 20. Qualitative variables were expressed using proportions and quantitative variables in mean and standard deviation**.** Quantitative variables were categorized using suitable cut offs and analysed appropriately.

Test of association was done using Chi square test and Fisher's exact test. Odds ratio and 95% confidence interval was computed as the estimate of strength of risk. Logistic regression (Backward stepwise method) was done as multivariable analysis to find out the significant determinants after finding the collinearity of the variables.

RESULTS

A case control study was undertaken to identify the various determinants of preterm delivery, during the period 1st November 2012 to 30th November 2013 at SAT hospital, Thiruvananthapuram. A total of 460 subjects were studied; 230 cases, women delivered between 24-37 weeks of

gestation and 230 controls, women who delivered after 37 weeks but before 42 weeks. Distribution of study variables in relation to case-control status were analysed. Chi-square test was used for finding the association between the variables in the present study. Strength of association of significant variables were presented using odds ratios with 95% confidence interval after dichotomously categorizing them. This was followed by the presentation of logistic regression analysis to find out the significant determinants

DISCUSSION

The role of maternal genetic study in foetal health and pregnancy outcome is not clear [1]. Carried a study to investigate familial recurrence of preterm labor and analyse the relative contributions of maternal and foetal genotypes and the risk of preterm delivery. From the study, more than 90% of cases and controls had no family history of preterm birth. When comparing between cases and controls, the percentage of cases with a family history of preterm birth was higher than that of control group and this difference in percentage was found to be statistically significant by using the chi-square test. Odds ratio of 3.9 indicates that the chance of preterm birth was nearly 4 times more among mothers who had a family history of preterm birth. In a study from 1974, the sisters of women who delivered preterm appeared to be almost twice as likely as sisters-in-law to themselves deliver prematurely [2]. Mother's family history could pose risk for preterm birth, according to a study by researchers from Ben-Gurion university of the Negev and Soroka University Medical Centre. The study published in American Journal of Perinatology followed 2300 mothers and daughters over 22 years and found that the risk of preterm delivery was significantly higher among 34 percent women whose mothers had a history of preterm birth. In the present study, family history of preterm birth came out to be a significant determinant with an adjusted Odds ratio of 9.693 with (95% CI of 2.037- 46.128, p value=0.004). The strongest established risk factor for PTD is a previous PTD (7), but women who themselves were born preterm or whose sisters delivered prematurely have also been shown to be at increased risk of delivering preterm (8-11). Despite recognition of a familial component to PTD, the strongest established risk factor for PTD is a previous PTD (7), but women who themselves were born preterm or whose sisters delivered prematurely have also been shown to be at increased risk of delivering preterm (8-11). Despite recognition of a familial component to PTD, the strongest established risk factor for PTD is a previous PTD (7), but women who themselves were born preterm or whose sisters delivered prematurely have also been shown to be at in-creased risk of delivering preterm (8–11). Despite recognition of a familial component to PTD, n the strongest risk factor for preterm labour is previous preterm labour but the women who are themselves born preterm or whose sisters delivered prematurely have also been shown to be at increased risk of delivering preterm [3-6].

CONCLUSION

Preterm birth is a complex trait with a significant familial component. So from the study it is established that if a pregnant women has a family history of preterm labor, she is at significant risk for preterm birth of her baby. So, it is essential to anticipate preterm labor and give appropriate counselling to the mother regarding the factors which may contribute to preterm labor and regarding preventable etiological factors and to conduct frequent antenatal checkups. Thus, reducing the personal expenditure and government expenditure in government hospitals by preventing preterm births.

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