Risk Factors for Spontaneous Preterm Delivery Before 34 Weeks of Gestation Among Taiwanese Women

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SUMMARY

Objective: To identify the risk factors for spontaneous preterm delivery before 34 weeks of gestation among Taiwanese women.

Materials and Methods: This retrospective cohort study involved 36,453 Taiwanese women who delivered between July 1990 and December 2003. Pregnancies complicated by multiple gestation, fetal anomalies, and iatrogenic preterm births due to maternal or fetal indications were excluded.

Results: Five hundred and five spontaneous preterm deliveries (1.4%) were identified. Risk factors for early preterm delivery included a prior preterm delivery (odds ratio [OR], 16.5; 95% confidence interval [CI], 11.1–24.6), placental abruption (OR, 13.4; 95% CI, 9.4–19.2), history of fetal demise (OR, 11.8; 95% CI, 7.7–18.0), chorioamnionitis (OR, 10.5; 95% CI, 7.4–14.9), oligohydramnios (OR, 10.1; 95% CI, 6.7–15.3), history of abruption (OR, 7.9; 95% CI, 2.4–26.0), unmarried (OR, 6.2; 95% CI, 2.9–13.2), conception by reproductive technology (OR, 2.7; 95% CI, 1.4–5.5), maternal age less than 20 years (OR, 3.5; 95% CI, 1.8–6.7), maternal age greater than 34 years (OR, 1.6; 95% CI, 1.2–2.1), three or more abortions (OR, 1.6; 95% CI, 1.9–2.3), and premature rupture of membranes (OR, 1.6; 95% CI, 1.3–2.0).

Conclusion: Some of the risk factors for early preterm delivery among Taiwanese women were the same as those of other ethnic groups, whereas some of the other risk factors were different. [*Taiwan J Obstet Gynecol* 2007; 46(4):389–394]

Key Words: early preterm delivery, risk factors, Taiwanese women

Introduction

Preterm delivery (before 37 completed weeks of gestation) is one of the leading causes of perinatal morbidity and mortality. With advances in perinatal care, infants born after 34 weeks are not at increased risk for short- or long-term morbidities when compared with those born after 37 weeks [1]. In contrast, infants born before 34 weeks have an increased frequency of permanent neurologic handicaps and mortality [1,2].

The cause of early preterm delivery (defined as less than 34 weeks of gestation) remains elusive. Risk factors for early preterm delivery include hypertension, fetal growth restriction, infection, spontaneous rupture of membranes, multiple pregnancy, cervical dysfunction, antepartum hemorrhage, stress, and malnutrition [3–8]. Most previous studies used birth registries and data collected over a number of decades. Accordingly, such data may suffer from misclassification and the shortcoming of excluding cases of iatrogenic preterm deliveries, which have been reported with a frequency of up to 30% of all preterm deliveries [3,9]. More importantly, the studies did not take into account the possibility of including a woman for analysis if she had delivered more than one time during the study period; inclusion of repeat preterm deliveries may skew certain factors

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or characteristics of the same woman who had been included in the analysis more than once.

Furthermore, most prior studies were carried out on the American and European populations. It has been suggested that there is racial variation in the frequency and risk factor profiles for preterm delivery [3,10]. Some studies have focused on Asian populations; however, the studies were based on small sample sizes and did not consider the potential confounding factors [11–13]. Most Taiwanese are the descendants of early settlers from the southeast coast of China and are genetically related to other south Asian populations [14]. We, therefore, sought to examine whether there was a similar risk factor profile for early preterm delivery within a large homogeneous Taiwanese population.

Materials and Methods

Data were obtained from the Chang Gung Memorial Hospital computerized obstetric database, which included demographics, medical and obstetric histories, the course of the current pregnancy, and perinatal outcomes. Data in this database were collected by trained personnel through daily abstraction of medical and delivery records with a postpartum interview, if necessary, to collect supplemental information. Audits of these data were routinely performed at weekly departmental meetings. Details of the database have been reported previously [15–17]. We included all deliveries after 20 weeks of gestation between July 1990 and December 2003 (n = 51,266) for analysis.

Pregnancies complicated by multiple gestation (n = 1,738) and known fetal anomalies (chromosomal or structural; n = 683) were excluded. Furthermore, iatrogenic preterm births due to maternal or fetal indications were excluded, such as preeclampsia (including HELLP syndrome and eclampsia; n = 656) and placenta previa (n = 457). During the study period, 8,903 women had two pregnancies, 971 had three pregnancies, 38 had four pregnancies, and one had five pregnancies. For these women, only one pregnancy was randomly selected for analysis, as previously described [16]. Briefly, a computer-generated random number was assigned to each pregnancy, and the pregnancy with the largest number was selected for analysis. A total of 36,453 pregnancies were included in this study.

Gestational age was estimated based on the first day of the last normal menstrual period or assigned by ultrasound dating if the information was missing or questionable. In our hospital, women are routinely offered an ultrasound scan between the eighth and 12th gestational week for pregnancy dating, and two anatomic and biophysical scans between the 18th and 22nd gestational week and 32nd to 34th gestational week, respectively, in which fetal anatomy, fetal growth, amniotic fluid volume, and placental location were assessed. Moreover, women delivered at this hospital are mainly from the urban Taipei metropolitan area and are from the upper or middle class. The population of this study was, therefore, considered homogenous in terms of socioeconomic status.

The following variables were evaluated as potential confounders: maternal age at the time of conception, parity, years of education, pre-pregnancy body mass index, urinary tract infection, placental abruption, prior placental abruption, uterine fibroids, chorioamnionitis, premature rupture of membranes, marital status, working during pregnancy (defined as work other than housework of more than 30 hours per week), method of conception (natural or with assisted reproductive technology), fetal gender, having undergone amniocentesis, prior fetal demise, prior preterm delivery, previous cesarean delivery, previous induced abortion, overt diabetes, gestational diabetes in the pregnancy, uterine malformations (including didelphys, bicornuate or septate uterus), polyhydramnios (defined as an amniotic fluid index [AFI] of more than 24 cm), and oligohydramnios (AFI of less than 5 cm).

For statistical analysis, SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) was used. The Fisher's exact test was used to characterize the patients with early preterm delivery and the control cohort. Multiple logistic regression analysis with a backward elimination stepwise regression approach was used to evaluate the association between early preterm delivery and potential risk factors. Adjusted odds ratios with their associated confidence intervals were used to describe the relative risk of the potential risk factors.

Results

Early preterm delivery affected 505 of the 36,453 (1.4%) singleton pregnancies analyzed. The characteristics of the study population are shown in Table 1. The early preterm delivery cohort was characterized by a significantly higher prevalence of women who were ≥ 34 years or < 20 years of age, of low educational level, unmarried, and with a parity of three or more. In addition, women, who had worked during pregnancy, had induced abortion of three times or more, a history of fetal demise or preterm delivery, a history of placental abruption, or conception with reproductive technology were also at an increased risk for early preterm delivery. Furthermore, pregnancies complicated by

Table 1. Characteristics of women with early preterm delivery and control cohort*

Variables	Early preterm delivery ($n=505$)	Control cohort ($n=35,948$)	$p^{\dagger}$
Maternal age (yr)			
<20	11 (2.2)	239 (0.7)	<0.01
20–33 (reference)	398 (78.8)	30,704 (85.4)	1.00
≥34	96 (19.0)	5,005 (13.9)	<0.01
Education (yr)			
<9	45 (8.9)	2,146 (6.0)	<0.01
9–12 (reference)	435 (86.1)	31,157 (86.9)	1
>12	25 (5.0)	2,645 (7.1)	<0.01
Prepregnancy BMI‡ (kg/m^2)			
<19.8	167 (33.1)	12,220 (34.0)	0.70
19.8–24.2 (reference)	294 (58.2)	20,835 (58.0)	1
>24.2	44 (8.7)	2,893 (8.0)	0.57
Prior cesarean section			
0	476 (94.7)	33,489 (92.7)	1
1	19 (3.8)	1,915 (5.3)	0.19
≥2	10 (1.5)	544 (2.0)	0.36
Abortion			
0	296 (58.6)	20,986 (58.4)	1
1–2	170 (33.7)	13,319 (37.1)	0.13
≥3	39 (7.7)	1,643 (4.5)	<0.01
Parity			
1	246 (48.7)	18,204 (50.6)	0.40
2	174 (34.5)	13,570 (37.7)	0.14
≥3	65 (12.9)	3,628 (10.1)	0.04
Amniocentesis	58 (11.5)	4,873 (13.0)	0.35
Work during pregnancy	435 (86.1)	26,415 (73.5)	<0.01
Unmarried	9 (1.8)	94 (0.3)	<0.01
Placental abruption	50 (9.9)	245 (0.7)	<0.01
Prior history of abruption	4 (0.8)	36 (0.1)	<0.01
Chorioamnionitis	51 (10.1)	319 (0.9)	<0.01
Urinary tract infection	2 (0.4)	52 (0.1)	0.17
Uterine anomaly	1 (0.2)	52 (0.1)	0.53
Fibroids	3 (0.6)	255 (0.7)	1
Premature rupture of membranes	118 (23.4)	6,162 (17.1)	<0.01
Gestational diabetes mellitus	26 (5.2)	2,275 (6.3)	0.31
Overt diabetes mellitus	2 (0.4)	71 (0.2)	0.27
Prior history of fetal demise	48 (9.5)	205 (0.6)	<0.01
Prior history of preterm delivery	57 (11.3)	160 (0.4)	<0.01
Conception by reproduction technology	10 (2.0)	290 (0.8)	<0.01
Male fetus	284 (56.2)	19,048 (53.0)	0.15
Polyhydramnios	7 (1.4)	181 (0.5)	0.02
Oligohydramnios	41 (8.1)	196 (0.5)	<0.01

**Data are presented as n (%); †Fisher's exact test or binary logistic regression; ‡body mass index (BMI) calculated as weight in kilograms divided by the square of height in meters.*

placental abruption, chorioamnionitis, premature rupture of membranes, and oligohydramnios were also significantly associated with early preterm delivery.

The results of multiple logistic regression analysis are presented in Table 2. Significant risk factors for early preterm delivery included a history of fetal demise or preterm delivery, placental abruption, and maternal age of <20 years or ≥34 years. Moreover, women who were unmarried, had worked during pregnancy, were conceived by reproductive technology, had induced

Table 2. Results of multiple logistic regression analysis on risk factors for early preterm labor*

Variable	Adjusted OR	95% CI
Prior history of preterm delivery	16.5	11.1–24.6
Placental abruption	13.4	9.4–19.2
Prior history of fetal death	11.8	7.7–18.0
Chorioamnionitis	10.5	7.4–14.9
Oligohydramnios	10.1	6.7–15.3
Prior history of abruption	7.9	2.4–26.0
Unmarried	6.2	2.9–13.2
Conception by reproductive technology	2.7	1.4–5.5
Work during pregnancy	2.2	1.7–2.9
Maternal age < 20 years	3.5	1.8–6.7
Maternal age ≥ 34 years	1.6	1.2–2.1
Abortion ≥ 3 times	1.6	1.9–2.3
Premature rupture of membranes	1.6	1.3–2.0

**Adjusted for all the variables listed in Table 1. OR = odds ratio; CI = confidence interval.*

abortion three times or more, or had pregnancy complications, such as oligohydramnios, premature rupture of membranes, placental abruption and chorioamnionitis, were at a 1.5- to 10-fold increased risk for early preterm delivery.

Discussion

Estimates generated by logistic regression analysis of data in this retrospective cohort study should be interpreted with caution, especially because the numbers for risk factors were small and the confidence intervals were wide. Nevertheless, the strength of our study lies in its ability to adjust for as many confounding factors as possible and in the use of patient interview and medical record data rather than vital statistics or birth certificate data. Thus, the association between each potential risk factor and the presence of early preterm delivery was objectively investigated. Moreover, only one pregnancy was randomly selected for the women who delivered more than once during the study period.

The prevalence of early preterm delivery was about 1.4% in our study population, which is less than the prevalence reported by others [4,18]. A reason for this difference may be that we excluded iatrogenic preterm deliveries, such as pregnancies complicated by placenta previa with antepartum hemorrhage and gestational hypertensive diseases (including severe preeclampsia and eclampsia). Indeed, the rate of preterm deliveries due to maternal or fetal indications has been estimated to be as high as 30% [3]. Another possible cause for the difference between our finding and the reported prevalence is that our study was a single-hospital study rather than a nationwide study based on birth certificate data.

Our analysis confirmed most prior studies that women with a history of fetal demise or preterm delivery, increased number of induced abortions, and pregnancies complicated by oligohydramnios and chorioamnionitis were significantly associated with early preterm deliveries [4,7,12,19]. In this study, being unmarried was significantly associated with early preterm delivery. This is contradictory to a previous study involving the Chinese population [12]. The reason for this discrepancy is unclear; however, the previous report had a smaller sample size and did not control for as many confounding factors as in the current study. In support of our findings, a recent study from Finland reported that marital status was protective against preterm labor and low birth weight despite maternal care [20]. Compared with that report, unmarried women in our population carried a 5-fold increased risk of having an early preterm delivery once they were pregnant [20]. Free maternity care and a wide acceptance by virtually the entire pregnancy population probably contribute to the lower magnitude of risk in Finland.

In our study, maternal age of ≥ 34 years or < 20 years was significantly associated with early preterm delivery, which is compatible with previous studies [12,19,21,22]. The increased risks of preterm labor and preterm delivery appear to be particularly strong for those young adolescents who are biologically immature; such adolescents appear prone to preterm labor, possibly reflecting the irritability and immaturity of the adolescent uterus [21]. In contrast, women aged 34 years and older are associated with other risk factors, such as fetal demise, preterm delivery and very low birth weight [23–25]. Uteroplacental insufficiency is considered to be associated with an adverse obstetric outcome, and a recent study indicated that uterine flow impedance by Doppler ultrasonography was increased in the maternal group older than 35 years of age as compared with the younger cohort [26]. A notable feature of the placental bed in pregnancies complicated by preeclampsia or fetal growth restriction is the absence of physiologic vascular change, thought to be the result of a failure of trophoblast invasion and interaction with the spiral arteries in early pregnancy [27]. Moreover, vascular abnormalities, including acute atherosis and thrombosis in maternal vessels, are correlated with a reduction in uteroplacental blood flow [27,28]. The real cause of the higher rate of fetal demise

and other adverse obstetric outcomes remains elusive. Nevertheless, antepartum fetal surveillance in women of the advanced maternal age group is a worthwhile addition to routine prenatal care, particularly after 37 weeks of gestation [23].

In our study, conception by reproductive technology is associated with early preterm delivery after excluding multiple pregnancies. The prevailing hypotheses concern underlying causes of infertility that may be associated with preterm birth, including uteroplacental insufficiency or other female infertility factors [29,30]. Others have suggested that increased medical intervention in this group of pregnancies is causal [6]. A recent large study showed an increased incidence of abnormal placentation with *in vitro* fertilization (IVF), including a 2.4-fold increased risk of placental abruption and a 6.0-fold increased risk of placenta previa noted in IVF pregnancies compared with controls. A 2.7-fold increased risk of preeclampsia in IVF pregnancies was also revealed [31]. Preeclampsia, placental abruption, and placenta previa are all related to abnormalities of location and function of the chorion. Therefore, when pregnancy and formation of the chorion are initiated *in vitro*, an inherent difference in the nature of the placenta itself may predispose the patient to these conditions during pregnancy.

There are several limitations to this study. First, it had a limitation of a hospital study in which there was the risk of bias due to both overdiagnosis and underdiagnosis by the attendent. Second, markers used by some clinicians in predicting preterm labor, such as cervical length, fetal fibronectin and Bishop's scores [10], were not used in this study. Our results suggest that among this very homogenous Asian population, some of the risk factors for early preterm delivery among Taiwanese women were the same as those of other ethnic groups, whereas some of the other risk factors were different. Lastly, there were no non-Asians controls in this study; the comparison of our findings with other ethnicities is therefore limited.

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