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Original Article

Risk Factor of Preterm Labor in the West of Iran: A Case-Control Study

***Bahareh DERAKHSHI*[1], **Nader ESMAILNASAB*[2], **Ebrahim GHADERI*[2], *Siroos HEMMATPOUR*[2]**

1. *Student Research Committee, School of Medicine, Kurdistan University of Medical Science, Sanandaj, Iran*
2. *Kurdistan Research Center for Social Determinants of Health, Kurdistan University of Medical Sciences, Sanandaj, Iran*

***Corresponding Author:** Email: esmailnasab@yahoo.com, ebrahimghaderi@yahoo.com

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Abstract

Background: Prematurity is the most common cause of neonatal death. Risk factors of premature birth can be related with ethnicity and genetic. There is no comprehensive high sample size study in Kurdish ethnicity to determine risk factors related to prematurity. This study evaluated risk factors of preterm labor in Kurdish ethnicity.

Methods: This case-control study was conducted in 200 preterm infants (case group) and 400 term infants (control group), in Besat Hospital, Sanandaj, Iran, in the year 2012. Data was analyzed using SPSS software and analysis was performed by Chi-square, Mann-Whitney and logistic regression tests.

Results: In univariate analysis, mother's own prematurity, history of previous preterm labor, prematurity in the first-degree family members, history of dead children, premature rupture of membranes, multiple pregnancies, overt diabetes, chronic hypertension, preeclampsia and eclampsia, infertility and cervical incompetence had significant relationship with preterm labor. However, multivariate analysis results showed that abnormal amniotic fluid, premature rupture of membranes, double and multiple pregnancies, chronic hypertension, family history of premature birth, mothers age over 35 years, and cervical incompetence ($P<0.05$) had significant relationship with the premature birth.

Conclusion: Screening of newborns at risk of preterm labor could be achieved by these risk factors: family history of prematurity, mother's own history of prematurity and previous preterm labor, history of previous neonatal death, decreased amniotic fluid, multiple pregnancies, overt diabetes, hypertension, preeclampsia, infertility and cervical incompetence, however some of these factors are not the direct cause of prematurity. Our study suggests genetic' s role in preterm labor.

Keywords: Prematurity, Risk factor, High risk mothers

Introduction

Premature birth is one of the most common causes of death in newborns. It was defined as delivery before 37 completed weeks of gestation(1). About 28% of early neonatal deaths are related to preterm labor (2). Premature births are the cause of 27% of annual infant mortality worldwide, 70% of prenatal mortality in developing countries, and 50% of neurological disorders (3). Prematurity was the most common reason for death in the following cities with their corresponding prevalence: Tehran (7.2%), Shiraz (5.5%), Arak (8.2%), Khorramabad (8.4%), Yasooj (4.8%). The most common causes related to neonatal mortality were prematurity that accounts for 42.5% of all prenatal deaths (4-6). So, preterm birth is an important prenatal health problem in the world (7) and Iran.

In accordance with the Millennium Development Goals (MDGs), two-thirds of all under-five deaths should be reduced by 2015 (8), thus identification of the reasons associated with premature birth explains the importance of health planning. There is no obvious evidence confirming 45–75% of preterm births, however the known risk factors are exclusive of labor itself. These factors include demographic factors, obstetric history, cervical and uterine factors, bleeding, infection and other factors such as polyhydramnios or oligohydramnios, fetal anomalies especially involving multiple organ systems and central nervous system abnormalities, maternal abdominal surgery in late second or third trimester, maternal medical conditions such as diabetes mellitus and hypertension (essential or pregnancy induced) are associated with a higher rate of preterm delivery; however, these preterm birth are often intentional preterm deliveries because of maternal complications rather than the result of spontaneous preterm labor (9-13).

Other maternal risk factors including multi gravity, short interval between pregnancies and history of abortion have an important role in the risk of preterm labor. However, prevalence of these factors may vary among different communities (13-16). These risk factors can be related with ethnicity and genetic (15). Unfortunately, there have been no comprehensive high sample size studies in Iran and Kurdistan (west part of Iran) which could be extended elsewhere; studying parallel influences of maternal, fetal, and placental factors in preterm labor. So doing study to detect risk factors of preterm labor in the Kurdish ethnicity can be helpful in the prevention and health programming.

Therefore this study intended to identify risk factors that could play an important role in preterm labor in Kurdish ethnicity.

Materials and Methods

This case-control study has been conducted on 600 (200 cases and 400 controls) neonate born in Besat Hospital, Sanandaj, Iran in the year 2012. The study was approved by Ethics Committee of Kurdistan university of Medical Sciences. Case and control groups were selected from Besat Hospital (main Hospital for pregnant delivery in Sanandaj). Cases included newborns who were born before 37 weeks and after 20 weeks of gestational age. Prematurity was approved by their medical care records and ultrasounds. The control group was newborns, born between 37 to 42 weeks of pregnancy.

Sample size of 196 cases were calculated, considering type I error of 5%, power of 85%, acceptable Odd Ratio equal to 2 (OR=2) and control group prevalence of risk factors about 20%. To increase the accuracy of the study, two controls were selected for each case.

For data collection, a trained midwife checked mothers in the postpartum ward (where mothers are transferred to shortly after delivery) as well as the medical records of the newborns (including ultrasound and medical reports).

Then in case of encountering preterm infant, those cases were enrolled in the study. After that two other newborns, closest in time to the birth of the preterm, were selected as controls. Furthermore maternal or newborn deaths during labor were recorded each day for identifying bias in the study.

Data were analyzed using SPSS.11.5 software. Then quantitative and qualitative data were compared between the two groups using independent T-test, Mann–Whitney U test (for ordinal variables) and Chi-square test respectively. For multivariate analysis, variables with *P*-value less than 0.2 in univariate analysis were entered in the logistic regression model. Prematurity was considered as dependent variable and mother's own prematurity, previous delivery, vaginal damages, neonatal death, abnormal amniotic fluid, premature rupture of membranes, twin, previous preterm labor, overt diabetes mellitus, hypertension, family history of preterm labor and age group were independent variables. After preparing the model, variables with high *P*-value were excluded from the model for better maximum likelihood estimation of variances. Significant *P*-value was considered less than 0.05.

Results

From a total of 600 cases, 10 infants (1.66%) died, 9 were preterm and 1 was term but had cardiac anomaly. Median birth rate in preterm and full-term mothers were 3 (P=0.824) and pregnancy rate was 1 (P=0.75). No statistically significant difference was seen between the maternal weight gain during pregnancy (P=0.16) and total family income (P=0.104) in the two groups of preterm and full-term newborns (Table 1).

Given the following string variables; prematurity in the mother herself (OR=3.09; P=0.027), history of previous premature babies (OR=4.8; P<0.001), history of preterm labor in mothers and sisters of the expecting women (OR=3.2; P<0.001), number of dead children (OR=2.58; P=0.011), Oligohydramnios (OR=3.3; P<0.001), premature rupture of membranes (PROM) (OR=3.5; P<0.001); double and multiple pregnancies (OR=10.8; P<0.001), overt diabetes mellitus (OR=3.5; P=0.03), chronic hypertension (OR=2.6; P<0.001), preeclampsia and eclampsia (OR=3.5; P<0.001), Infertility (OR=3.9; P<0.001) and cervical incompetence (OR=3.09; P=0.027); univariate analysis showed statistically significant relation with preterm labor. However, mother's age, occupation and education, history of smoking, history of abortion and stillbirth, urinary tract infection (UTI), anemia, and uterine related pathologies and abnormalities (uterine myoma, unicornuate and bicornuate) in mother showed no statistically significant relation with preterm labor (Table 2).

Based on multivariate analysis; abnormal amniotic fluid (P=0.001), PROM (P=0.002), double and multiple pregnancies (P=0.001), chronic hypertension (P=0.007), family history of preterm labor (P=0.045), maternal age of more than 35years (P=0.035), and cervical incompetence (P=0.032); were all significantly associated with the incidence of preterm labor (Table 3).

Table 1: Comparison of quantitative variables between case and control groups

Variable	Group	Mean	Standard deviation	Significant level
Maternal weight gain	Preterm	8.99	5.267	0.160
	Term	9.63	5.188	
Total family income	Preterm	520.16	284.796	0.104
	Term	480.85	257.226	

Discussion

In univariate analysis; history of prematurity in the mother herself, history of previous preterm labor, family history of preterm labor in mother and sisters of the pregnant women, number of dead children, PROM, oligohydramnios, double and multiple pregnancies, overt diabetes mellitus, chronic hypertension, preeclampsia and eclampsia, infertility and cervical incompetence; had statistically significant relation with the occurrence of preterm labor. But mother's age, mother occupation and education, smoking, history of abortion, stillbirth, UTI, mother's anemia, and uterine pathologies and abnormalities had no statistically significant relation with the occurrence of preterm labor.

However, after logistic regression analysis; abnormal amniotic fluid, PROM, double and multiple pregnancy, hypertension, family history of prematurity, maternal age of over 35 years, and cervical incompetence; were significantly associated with the incidence of preterm labor. In univariate analysis, variables that were statistically significant and were associated with prematurity could be considered as risk factors for screening high risk women who should receive more attention during pregnancy. But these factors could be correlated; hence some of them were not significant in multivariate analysis.

Table 2: Comparison of maternal variables between case and control groups

Variable	Situation	Groups		Total n (%)	OR (CI 95%)	Significant level
		Preterm n (%)	Term n (%)			
Mother's own prematurity	No	191 (32.6)	394 (67.4)	585 (100)	3.094	0.027†
	Yes	9 (60)	6 (40)	15 (100)	(1.08-8.819)	
Previous delivery	NVD	77 (34.1)	149 (65.9)	266 (100)	0.665	0.096
	C/S	33 (25.6)	96 (74.1)	129 (100)	(0.411-1.077)	
Episiotomy in previous birth	No	101(31)	234 (69)	339 (100)	1.642	0.178
	Yes	14(42.4)	19 (57.6)	33 (100)	(0.793-3.400)	
Damage to the vaginal canal	No	92 (29.9)	216 (70.1)	308 (100)	1.713	0.055
	Yes	27 (42.2)	37 (57.8)	64 (100)	(0.986-2.978)	
previous child death	No	184 (32.2)	387 (67.8)	571 (100)	2.58	0.011†
	Yes	16 (55.2)	13 (44.8)	29 (100)	(1.22-5.49)	
Amniotic fluid status	Normal	152 (29.3)	366 (70.7)	518 (100)	3.325	<0.001†
	Abnormal	47 (58)	34 (42)	81 (100)	(2.059-5.380)	
Premature rupture of membranes	No	97 (23.9)	309 (76.1)	406 (100)	3.571	<0.001†
	Yes	102 (52.8)	91 (47.2)	193 (100)	(2.483-5.134)	
Twin	Single	146 (27.4)	387 (72.6)	533 (100)	10.807	<0.001†
	Twin and more	53 (80.3)	13 (19.7)	66 (100)	(5.822-20.408)	
Infant Gender	Girl	75 (29.8)	177 (70.2)	252 (100)	1.329	0.109
	Boy	125 (36)	222 (64)	347 (100)	(0.938-1.882)	
History of prematurity	No	182 (31.7)	392 (68.3)	574 (100)	4.846	<0.001†
	Yes	18 (69.2)	8 (30.8)	26 (100)	(2.069-11.352)	
family history of prematurity	No	179 (31.7)	386 (68.3)	565 (100)	3.236	0.001†
	Yes	21 (60)	14 (40)	35 (100)	(1.608-6.508)	
History of overt Diabetes mellitus	No	193 (32.8)	395 (67.2)	588 (100)	3.582	0.032†
	Yes	7 (63.7)	4 (36.4)	11 (100)	(1.036-12.383)	
Gestational diabetes mellitus	No	166 (33)	337 (67)	503 (100)	1.096	0.695
	Yes	34 (35.1)	63(64.9)	97 (100)	(0.694-1.730)	
Chronic Hypertension	No	156 (30.2)	361 (69.8)	517 (100)	2.611	<0.001†
	Yes	44 (53)	39 (47)	83 (100)	(1.631-4.176)	
Preeclampsia/ eclampsia	No	166 (30.5)	378 (69.5)	544 (100)	3.519	<0.001†
	Yes	34 (60.7)	22 (39.3)	56 (100)	(1.997-6.201)	
Infertility	No	175 (31.2)	386 (68.8)	561 (100)	3.939	<0.001†
	Yes	25 (64.1)	14 (35.9)	39 (100)	(1.999-7.761)	
Place of residence	City	115 (31.2)	254 (68.8)	369 (100)	1.280	0.164
	Village	84 (36.7)	145 (63.3)	229 (100)	(0.904-1.811)	
Mother's job	Housekeeper	194 (33.3)	388 (66.7)	582 (100)	0.833	0.735
	Employed	5 (29.4)	12 (70.6)	17 (100)	(0.289-2.399)	
Parent's satisfaction about newborn gender	No	13 (33.3)	26 (66.7)	39 (100)	1	1
	Yes	187 (33.3)	374 (66.7)	561 (100)	(0.502-1.991)	
Parent's family relationship	No	167 (32.2)	352 (67.8)	519 (100)	1.480	0.109
	Yes	33 (41.3)	47 (58.7)	80 (100)	(0.914-2.396)	
Mother's Anemia	No	140 (32.3)	294 (67.7)	519 (100)	1.2	0.341
	Yes	60 (32.3)	105 (67.7)	165 (100)	(0.824-1.747)	
Mother's prenatal care level	Health Center	152 (32.9)	310 (67.1)	462 (100)	1.1	0.642
	Gynecologist	48 (35)	89 (65)	137 (100)	(0.737-1.643)	
Mother's reference to the Pregnancy Care Center	Regular	175 (33.4)	349 (66.6)	524 (100)	0.997	0.991
	Irregular	25 (33.3)	50 (66.7)	75 (100)	(0.597-1.666)	
Mother's trauma during labor	No	194 (32.9)	395 (67.1)	589 (100)	3.054	0.072
	Yes	6 (60)	4 (40)	10 (100)	(0.852-10.949)	
History of cervical insufficiency	No	174 (30.8)	391 (69.2)	565 (100)	7.303	<0.001†
	Yes	26 (76.5)	8 (233.5)	34 (100)	(3.241-16.455)	
Age groups	18-35 years old	175 (33.8)	343 (66.2)	518 (100)	-	-
	Less than 18 years old	7 (50)	7 (50)	14 (100)	1.96 (0.677-5.676)	0.215
	>35 years old	18 (25.5)	50 (73.5)	68 (100)	0.706 (0.4-1.246)	0.229

† Statistically Significant

Table 3: Multivariate analysis of factors influencing prematurity

Variables	Beta	S.E.	Wald	Df	Significant level	Odds Ratio	95% C.I. for Odds Ratio	
							Lower	Upper
Amniotic Fluid	1.476	0.376	15.430	1	<0.001†	4.376	2.095	9.141
Premature rupture of membranes	0.973	0.309	9.924	1	0.002†	2.646	1.444	4.846
Twin	2.891	0.645	20.112	1	<0.001†	18.004	5.090	63.684
Hypertension	0.902	0.342	6.944	1	0.008†	2.466	1.260	4.825
Family history of preterm labor	1.250	0.617	4.101	1	0.043†	3.490	1.041	11.700

† Statistically Significant.
Mother's own Prematurity, Previous delivery, Vaginal damages, Neonatal death, Previous preterm labor, Overt Diabetes mellitus and Age group were removed from the model.

Age over 35 years was inversely associated with the incidence of prematurity and these women were not at risk of premature birth. However, in a study (17), the mean age of mothers with preterm infants were higher compared with mothers with term infants. In two studies (4,13) the incidence of prematurity was greater in older mothers; however, there was no statistically significant relation. In two other studies (18,19) maternal age was not a direct cause of prematurity. In another study (20), mothers over the age of 35 years had direct relation with increased prematurity. However it was showed that significant association of preterm birth was found with low maternal age (21). Different results could be due to complications associated with multiple age groups. In our study we tried to control confounding factors by logistic regression to obtain a more accurate result.

Based on this study, a significant relationship was seen between mothers' own history of prematurity and their premature births. This parameter has not been investigated in other studies. Although it is not significant in multivariate analysis, but due to the presence of another variable, named family history of prematurity, they may be related. Therefore prematurity of the mother is likely an independent risk factor for premature newborn; however it is not evaluated in the other studies. History of preterm labor in pregnant women's family members (sisters and mother) was also a risk factor. This finding suggests genetic effect on premature labor. However such result is not mentioned as an independent risk factor in reliable references which shows the importance of designing and implementation of extended studies for accepting or rejecting the role of genetic in preterm labor.

There was no statistically significant difference in the number of previous pregnancies, previous obstetric history and perineal trauma after vaginal delivery between the two groups which is consistent with some other studies (5, 22), however in several studies (13, 19, 23) multiparity has a significant association with preterm labor, which may be due to a range of side effects associated with the number of previous pregnancies. Unfortunately, some parameters have not been investigated in many studies; however one study shows that previous cesarean section had a significant relationship with the following preterm labor (17).

Abnormal amniotic fluid (almost all oligohydramnios) and twin or multiple pregnancies were the risk factors for prematurity. These results are consistent with Afrakhteh et al study (6) that oligohydramnios accounted for 9.6% of prematurity. In a study (5), PROM was a common causes of preterm labor (35.5%), which is consistent with a number of other studies that have shown the correlation between PROM and premature birth (16, 17, 24).

In a study (25), 19.2% of preterm newborns and 4.2% term newborns were related to the multiple pregnancies. In another study (5) 19.7% of premature newborns were due to multiple pregnancies which are consistent with our study.

In multivariate analysis, preeclampsia and eclampsia were excluded from the model due to their col-

linearity with hypertension, thus just hypertension was entered in the model. However, these two variables were risk factors for prematurity. In a study (5), preeclampsia with a rate of 21.9% has been mentioned as the third cause of prematurity. Additionally, in a study (17), numbers of preterm neonates in preeclamptic mothers were 7.7 times more than that of term infants. In another study (6), preeclampsia was the cause of 17.7% of preterm labors also another case control study confirmed a significant association of preeclampsia-proteinuria with preterm birth (21).

Diabetes mellitus and gestational diabetes mellitus (GDM) didn't have relation with prematurity however, diabetes can directly or indirectly (e.g. by increasing risk of infection, polyhydramnios, hypertensive disorders and severe diabetic nephropathy) triggers a preterm delivery (19, 26). Overall rates of preterm delivery were significantly higher among women with diabetes mellitus (38%) than control group in another study (27). Also, those with chronic hypertension had higher rates of indicated preterm delivery but there were no differences in rates of spontaneous preterm delivery. Further analysis of chronic diseases associated with preterm labour has been published and discussed elsewhere (28).

Univariate analysis showed statistically significant relation between mothers' infertility and prematurity; however, this relationship was not seen in multivariate analysis due to the likelihood of multiple pregnancies after infertility treatment, which has reduced the strength of infertility effect in our model. In a study (24), the incidence of prematurity in women treated for infertility was 1.7 times higher than others. In another study (29) infertility has been an important cause of prematurity. All these findings show that increase in the use of assisted reproductive technology resulted in multiple pregnancies and preterm labor.

Place of residence, mother's job and income are not recognized as independent risk factors for premature birth. Other studies did not find any relation between place of residence and prematurity (19, 30). In some studies, prevalence of prematurity was increased in people with lower socioeconomic level (especially lower family's income) than other groups, which could be due to inadequate prenatal care program(13, 15, 31, 32). In our country, access to free health services for all pregnant women could be a reason for this finding.

Conclusion

Screening of newborns at risk of preterm labor could be achieved by these risk factors: family history of prematurity, mother's own history of prematurity and previous preterm labor, history of previous neonatal death, decreased amniotic fluid, multiple pregnancies, overt diabetes, hypertension, preeclampsia, infertility and cervical incompetence, however some of these factors are not the direct cause of prematurity. In addition, our study suggests genetic' s role in preterm labor.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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