Original Article

The evaluation of risk factors related to the birth of premature infants in a case-control study

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ABSTRACT

Introduction and objectives: Premature birth (less than 37 weeks) is one of the most important reasons of neonatal mortality. 15 million premature infants are born around the world annually that this statistic is different between 5 to 18 percent of all births in different countries of the world. In Iran, one of each 10 infants that is born is a premature one. Even if the premature infants survives, it is more likely to be exposed to various health problems than other babies in the future. Therefore, finding the effective factors in premature birth seems very important. Finding and preventing the risk factors of premature birth can reduce the future costs of the health system of each community. This study was conducted aimed to compare the risk factors for premature births in the city of Eslamabad-e Gharb. Methods: This case-control study was performed on 202 premature infants as the case group as well as 202 neonates as the control group in the infants born in Imam Khomeini Hospital of Eslamabad-e Gharb during the years 2012 to 2016. The case group consisted of neonates born at gestational age less than 37 weeks who had the inclusion criteria and the first neonate with gestational age of 37 to 42 weeks was selected as the control for each premature infant. Data were collected through the study of mothers' health records which had been completed during their pregnancy by the health staff at health centers in the city of Eslamabad-e Gharb and then analyzed using Chi-square, single and multivariable logistic regressions and t-test statistical tests by SPSS software version 20 (α: 0.05). Results: The two case and control groups were matched together in terms of birth date. The results show that 95 (47%) and 107 (53%) of 202 premature infants as well as 103 (51%) and 99 (49%) of 202 normal infants were boys and girls, respectively that no significant difference was seen between two groups (p:0.458). The difference between maternal weight gain more than normal during pregnancy compared with the normal weight gain (p: 0.049, OR: 1.84), mothers' blood type of B compared to the blood type of O (p: 0.03, OR: 0.55), 3 to 5 maternal care during pregnancy against over 6 times (p: 0.0001, OR: 0.28), mother's history in premature birth (p: 0.01, OR: 0.39) and having a husband who is self-employed compared to being a worker (p: 0.016, OR: 2.06) was significant. Conclusion: The number of care during pregnancy, maternal weight gain during pregnancy, blood type of O and spouse's self-employment are the related factors to premature birth that health authorities should take measures to eliminate or reduce these factors in order to decrease the rate of premature births.

Keywords: prematurity, risk factors, odds ratio, premature infant

Introduction

According to the global statistics, 60 to 80 percent of neonatal mortalities which are not associated with congenital anomalies, are due to the premature birth of the babies. After the congenital anomalies, the main cause of the disease and mortality of infants is prematurity [1]. Low birth weight and premature birth are of the effective factors in mortality under one year. Prematurity or gestational age less than 37 weeks is one of the most important health indicators of each community, so that early delivery is a big risk to the baby's health. Average premature babies (32-33 weeks) and late premature babies (34-36 weeks) are 80 percent of premature births [2]. In the conducted studies in Iran, the prevalence of prematurity has been reported 5.5%, 8.21%, 8.7%, 7% and 16.4% in Shiraz, Arak, Tehran, Zanjan and Mashhad, respectively [3, 4]. Although

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Saeed Akbari, Kourosh Sayehmiri, Mir Hadi Musavi, Khairollah Asadollahi. The evaluation of risk factors related to the birth of premature infants in a case-control study. J Adv Pharm Edu Res 2019;9(S2):120-125.
Source of Support: Nil, Conflict of Interest: None declared.

the new methods of caring premature babies have greatly improved the status of these little babies, but there has been no significant and stable reduction in the incidence of early births and the early births are still the reason of 70 percent of mortalities, neurological complications and disability in later years of life in babies without congenital anomalies which impose high costs on the health system [5].

Of maternal factors which lead to premature birth; mother's disease, chorioamnionitis, multiple births, smoking, placental abruption, placenta Previa, uterine problems and etc can be mentioned [6]. Some risk factors such as multiple pregnancies, Preterm Rupture Of Membeans (PROM) (responsible for one third of premature birth cases), uterine and placental problems, preeclampsia, history of abruption and stillbirth, young age mothers, occupational factors, psychological stress, genetic factors, inadequate weight gain during pregnancy, maternal hypertension, vaginal infection have been known as the factors which involved in premature birth in various countries of the world including Iran [7, 8]. Two factors of low socioeconomic status and the history of previous premature birth are the main risk factors for premature birth but unfortunately, despite the introduction of multiple risk factors, the cause is unknown in 50% of cases [9].

Eslamabad-e Gharb with a total area of 2100 km^2 is located in west of Iran and 65 km from the city of Kermanshah and has a population of 148638 people including 24572 urban households with a total population of 92117 people and 14240 rural households with a total population of 56154 people [10].

Considering the importance of premature birth and its extent throughout the world as well as Iran, this study evaluates the epidemiologic factors related to the birth of premature infants between the years 2012 to 2016.

Methods

In this case-control study, all premature babies that were born between the year 2012 to 2016 in Imam Khomeini Hospital of Eslamabad-e Gharb and were living there, were extracted from the hospital records and selected in case of having the inclusion criteria. Then, a normal baby born at gestational age of 37 to 42 weeks that was immediately born after the premature infant was selected as the control for each premature infant born at gestational age under 37 weeks. The classification criteria of infants' age were based on Last Menstrual Period (LMP) and the ultrasound criteria. The premature cases that were due to congenital or chromosomal anomalies and diagnosed by the pediatrician as well as Intrauterine Growth Restriction (IUGR) cases were excluded from the study. The two groups were matched together in terms of date of birth. The checklist was used to collect data. Using the mothers' national cards, the health care centers where the mothers had received care during their pregnancy were identified. Then, the checklist was completed by studying the mother's health record at the health center. It should be noted that mother had received the care by a midwife during the pregnancy. The collected data were entered to SPSS software version 20 and the statistical tests of chi-square, single and multivariable logistic regressions and t-test were used to compare the risk factors in the two groups (α: 0.05). The sample size of the cases and the controls was obtained based on census and selecting the first baby born after the premature infant which was included 202 cases and 202 controls.

Results

Using the chi-square test, 95 (47%) and 107 (53%) of 202 premature infants as well as 103 (51%) and 99 (49%) of 202 normal infants were boys and girls, respectively that no significant difference was seen between two groups (p:0.458). 145 (82%) and 57 (28%) infants of 202 premature babies were living in the city and village as well as 127 (63%) and 75 (37%) of the normal babies were living in the city and village, respectively that no significant difference was observed (p: 0.056). In terms of mother's occupation, 185 (91.5%) of 202 premature infants and 186 (92%) of 202 normal babies were housewives and 17 (8.5%) of 202 premature infants and 16 (8%) of 202 normal babies were employed that no significant difference was seen (p: 0.152).

Using the t-test, the mean age of mothers in the case and control groups were 29.6±5.9 and 29.8±5.9 years old (p: 0.69). The average BMIs of the mothers before pregnancy were 25.3±4.1 and 25.6±4.5 in case and control groups, respectively (p: 0.516). The hemoglobin mean during pregnancy was 11.5±0.8 in the case group and 11.5±0.9 in the control one (p: 0.434). The birth rate in the case and control groups were 1.8±0.8 and 2±0.9, respectively (p: 0.120). The average number of care during pregnancy was 7.5±1.7 in the case group and 5.7±1.4 in the control group (p: 0.0003).

Using the single-variable logistic regression, the variable of maternal weight gain during pregnancy, the odds ratio of the birth of premature infants was 1.84 more than normal babies in mothers whom their weights were more than normal (p: 0.049, OR: 1.84). Also, the odds ratio of premature birth in the mothers with blood type of B compared to O blood type was 0.55 less than normal birth (p: 0.03, OR: 0.55). In the variable of the number of care during pregnancy, the mothers with 3 to 5 times of care during pregnancy had 0.28 lower chance to give the birth to a premature infant compared to the mothers who had received 6 times and more care (p: 0.0001, OR: 0.28). Regarding the variable of premature birth history, the odds ratio of premature birth in mothers without this history was 0.39 less than the mothers with this history (p: 0.01, OR: 0.39) and about the spouse's job variable, the odds ratio of premature birth in the mothers whom their husbands are self-employed was 2.06 higher than the mothers whom their husbands are worker (p: 0.016, OR: 2.06).

No significant difference was observed between case and control groups in terms of some variables such as sex of the baby, place of residence, mother's occupation, hypertension, diabetes and other mother's diseases (congenital hypothyroidism), family marriage, care before pregnancy,

smoker's spouse, mother's age, nutritional consulting during pregnancy, mother's education, mother's BMI before pregnancy, hemoglobin mean during pregnancy and birth rate in the analysis by single-variable logistic regression.

The variables of place of residence, other diseases, premature birth history, smoker's spouse, nutritional consulting during pregnancy, mother's blood type, maternal weight gain during pregnancy, the number of care during pregnancy, spouse's occupation and birth rate which their p-value was less than 0.2 in single-variable logistic regression, were entered to multivariable logistic regression and were analyzed using the Forward: LR method. The variables of place of residence, number of care during pregnancy, blood type and premature birth history were remained in the model (table 2).

Table 1. Frequency distribution of the studied variables in the case and control groups

Independent variables		Case group	Control group
		Number (%)	Number (%)
Sex of baby	Boy	95 (47%)	103 (51%)
	Girl	107 (53%)	99 (49%)
Place of residence	City	145 (72%)	127 (63%)
	Village	57 (28%)	75 (37%)
Mother's occupation	Housewife	185 (91.5%)	186 (92%)
	Employed	17 (8.5%)	16 (8%)
Mother's blood pressure	Hypertension	4 (2%)	7 (3.5%)
	Normal	198 (98%)	195 (96.5%)
Mother's diabetes	has	9 (4.5%)	15 (7%)
	Does not have	193 (95.5%)	187 (93%)
Other diseases (hypothyroidism)	has	8 (4%)	14 (7%)
	Does not have	194 (96%)	188 (93%)
Family marriage	Does not have	42 (21%)	32 (16%)
	has	160 (79%)	170 (84%)
History of premature birth	have	12 (6%)	28 (14%)
	Does not have	190 (94%)	174 (86%)
Care before pregnancy	Yes	89 (44%)	89 (44%)
	No	113 (56%)	113 (56%)
Smoker's spouse	Yes	71 (35%)	84 (42%)
	No	131 (65%)	118 (58%)
Nutritional consulting during pregnancy	Yes	23 (11%)	32 (16%)
	No	179 (89%)	170 (84%)
Mother's age	<18	3 (1.5%)	1 (0.5%)
	18-35	164 (81.2%)	169 (83.7%)
	>35	35 (17.3%)	32 (15.8%)
Mother's education	Illiterate	10 (5%)	12 (5.9%)
	Under diploma	96 (47.5%)	105 (52%)
	Diploma	56 (27.6%)	47 (23.3%)
	Associate degree	10 (5%)	11 (5.4%)
	Bachelor and higher	30 (14.9%)	27 (13.4%)
Mother's BMI (kg/m^2)	<18.5	6 (3%)	6 (3%)
	18.5-24.9	95 (47%)	94 (46.5%)
	25-29.9	76 (37.6%)	70 (34.6%)
	≥30	25 (12.4%)	32 (15.9%)
Mother's blood type	A	75 (37.1%)	66 (32.7%)
	B	36 (17.8%)	52 (25.7%)
	AB	13 (6.4%)	22 (10.9%)
	O	78 (38.7%)	62 (30.7%)
Mother's weight gain	Less than normal	84 (41.6%)	98 (48.5)
	More than normal	39 (19.3%)	22 (10.9%)
	Normal	79 (39.1%)	82 (40.6%)
Number of care during pregnancy	2 times	2 (1%)	7 (3.5%)
	3-5	22 (10.9%)	60 (29.6%)
	6 and more	178 (88.1%)	135 (66.9%)
Hemoglobin mean (mg/dl)	≤7	0	0
	7.1-9.99	7 (3.5%)	10 (5%)
	10-10.99	38 (18.8%)	40 (19.8%)
	≥11	157 (77.7%)	152 (75.2%)
Spouse's occupation	Unemployed	9 (4.5%)	6 (3%)
	Employee	25 (12.3%)	31 (15.3%)
	Teacher	3 (1.5%)	8 (4%)
	Driver	19 (9.4%)	20 (9.9%)
	Farmer	14 (6.9%)	15 (7.4%)
	Animal husbandry	5 (2.5%)	5 (2.5%)
	Self-employed	103 (51%)	79 (39.1%)
	worker	24 (11.9%)	38 (18.8%)
Infant birth rate	1	78 (38.6%)	71 (35.2%)
	2-3	114 (56.4%)	115 (56.9%)
	≥4	10 (5%)	16 (7.9%)

Table 2. Multivariable logistic regression for the risk factors related to premature birth

Variables		Confidence interval	Odds ratio	p-value
Place of residence	City	3.470-1.386	2.193	0.001
	village	Reference population		
Number of care	2 times	1.534-0.053	0.285	0.144
	3-5 times	0.365-0.116	0.206	0.0001
	6 times and more	Reference population		
Premature birth history	Yes	0.744-0.164	0.350	0.006
	No	Reference population		
Blood type	A	1.487-0.164	0.901	0.684
	B	0.93-0.293	0.522	0.027
	AB	0.898-0.181	0.403	0.026
	O	Reference population		

Discussion

Infant premature birth is one of the main causes of neonatal mortalities and a high cost on health care systems of the countries, so it is necessary to reduce its incidence. This case-control study was conducted to determine the effective factors on infant premature birth among 404 infants born between the years 2102-2016 in the hospital of Eslamabad-e Gharb using the statistical tests of chi-square, single and multivariable logistic regression and t-test (α: 0.05).

Various studies have shown that inadequate care during pregnancy can be an effective factor in early delivery and mothers who receive inadequate care are at risk. So that, not using the prenatal care leads to increase the risk of premature birth for two-times [11]. In the United States, prenatal care is associated with a decline in preterm delivery [12]. However, in the present study, the odds ratio of premature birth in mothers who received care in 3 to 5 times was significantly lower than mothers with 6 times of care and more. It seems that the mothers who are at risk more than other mothers, visit the health care centers, more. So mothers with high levels of care should choose the high quality and suitable care of health. On the other hand, this significant increase can be explained by low quality care during pregnancy because the quality and content of pregnancy care is very important in preventing the birth of a

premature infant. As Scholl and Krueger in 2000 showed that the mothers with inadequate care were at risk of early delivery twice more than the mothers with adequate or moderate care [13].

In addition, the results of the research conducted in 2008 by Vahidinia et al as well as Howard et al confirmed that the percent of early delivery in high risk pregnant mothers with inadequate care has been higher [14, 15]. On the other hand, it cannot be said that there is a direct or even indirect relationship between the care during pregnancy and the birth of premature infant due to according to Walker et al findings, low-risk pregnant women whose number of visits had been decreased, there was no harmful effect related to maternal and neonatal outcomes [16].

Different factors affect the mother and fetus health that mother's proper nutrition is one of them. Maternal weight gain during pregnancy is of valid criteria for assessing nutritional status [17]. Mother's weight during pregnancy and the assessment of weight gain are the very effective factors in a safe and normal delivery which are used to control health during pregnancy. Pre-pregnancy weight is an important factor in predicting complications and mortality of neonates and mothers [18]. Weight gain during pregnancy less than the recommended weight is the reason of many congenital defects, preterm labor and low birth weight and it was suggested that low weight gain during pregnancy is considered as an important predictor for early delivery [19]. In the current study, mothers with weight gain higher than normal during pregnancy had a higher chance for the birth of premature infant compared to the mothers with normal weight gain. Several studies show that there is a significant relationship between the reduction in gestational weight gain (GWG) and the increase in risk of early delivery especially among lean women [20]. Another meta-analysis study showed that low gestational weight gain increases that risk of preterm labor and low birthweight [21]. In another study, the relationship between weight gain (in kg) per week of pregnancy and the increase in the net maternal weight per week of pregnancy and preterm labor was evaluated in a population of 266172 people of women with low income and it was shown that low and high maternal weight gain as well as the net maternal weight gain per week are associated with an increased risk of early delivery [22]. Therefore, it can be said that mothers who do not have normal weight gain during pregnancy have a higher chance for the birth of a premature neonate.

In the present study, the birth rate of premature infants in the families who are self-employed is more than the worker families. It has been proven in many studies that work-related stresses and physical activities can cause more premature birth in mothers [23, 24]. The risk of premature birth has a direct relationship with socioeconomic status. On the other hand, self-employment mentioned on the checklist includes a wide range of jobs that it is even possible that unemployed people have mentioned self-employment as their job during answering. Thus, it can be said that mothers with special stresses due to lack of job security, lack of health insurance and lack of fixed and specified monthly income have a higher rate of premature birth.

In this study, the birth rate of premature infants in mothers with B blood type was less than those with blood type of O. Also in an another study which was conducted between the years 2005 and 2011, the rate of premature birth for blood types of mothers to babies in blood types of A, B and B, AB was more than others [25]. But in the other study in Iran, the blood type of A in mothers was significant among the cases of recurrent premature birth under the study [26]. In addition, in the first study conducted among Asian women in Thailand to evaluate the relationship between the blood type and its effects on mother and baby, no relationship was found between the mother's blood type and premature birth and even low birth weight, but there was a relationship with preeclampsia [27]. It seems that there is still a controversy between the birth of premature infant and blood types.

The research show that women with the history of premature birth have a high risk for the next premature birth are at risk. So that, the risk of premature birth in women who their first baby had been premature is triple compared with women who gave birth to their firstborn in natural time [28]. On the other hand, research has shown that paternal genes have a very small share in preterm labor, as against women with congenital phenotypes of premature birth have a high risk of premature birth [29]. But in this study, women with the history of premature birth have a lower chance for the birth of premature infant. It seems that this result may be due to the inaccuracy in completion of health records by the health staff and even mothers' misconduct.

In the present study, there is no significant relationship between maternal hypertension and premature birth which is consistent with J. Kang's study [30], but a significant relationship between maternal hypertension and premature birth was observed in another study which was conducted in Iran [31]. In addition, there was no difference in the rate of premature birth between the employed women and housewives in the present study which is consistent with another research that showed women's employment do not affect the rate of premature birth [32] but in the study of Ismael Nasab et al, it was indicated that mother's employment increases the birth of premature infant [33]. Also, no significant relationship was found between the smoker's spouse and premature birth in this study while it is shown that mothers who are exposed to smoke during pregnancy are more likely to develop premature births [34]. On the other hand, it has been proven in the research of Del Pisheh et al that exposure to cigarette smoking affects the growth of embryo of pregnant mothers [35].

In general, there was no significant relationship between two case and control groups in the variable of hemoglobin mean, sex of baby [36], mother's age, mother's occupation [37], mother's education [38], maternal BMI before pregnancy, maternal diseases such as hypertension [31], diabetes, hypothyroidism, smoker's spouse [33], nutritional consulting during pregnancy and baby's birth rate [39] in the present study which is consistent with a number of studies that have been done before. Small studied population and even the cultural and social

characteristics of the area under study can be mentioned as the reasons of making these variables insignificant that had been effective in obtaining these results.

Conclusion

The number of prenatal care, gestational weight gain, O blood type and spouse's self-employment are the factors related to the birth of premature infant and the health authorities should take measures to eliminate or reduce these factors in order to decrease the birth of premature infants. On the other hand, by a better training of health care staff and more activating the health care centers, the quality of services offered at these centers can be increased to high risks.

Acknowledgment

All of the personnel of Imam Khomeini Hospital and Health Center of Eslamabad-e Gharb who helped us with this research are sincerely appreciated.

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