Original Article

Risk Factors Associated with Low Birth Weight Among Infants: A Nested Case-Control Study in Southeastern Iran

Abstract

Background: Mortality rate in low-birth-weight infants is almost 30 times more than that in those with normal weight, so the birth of low-birth-weight infants is one of the most serious health problems in the world. Therefore, this nested case-control study was conducted to investigate the risk factors associated with low birth weight among infants in the rural population of Kerman province. **Methods:** This nested case-control study was performed in rural areas of Kerman province, southeastern Iran. Case (n = 155) and control (n = 310) groups were selected using risk set sampling. Data were analyzed through Point and distance estimation (OR, CI) using conditional logistic regression method by Stata-12 software. **Results:** The results of multivariate analysis showed that maternal BMI [OR = 0.3, CI 95% (0.1, 0.9)], gestational age [OR = 3.8, CI 95% (0.9, 6.1)], history of stillbirth [OR = 4.8, CI 95% (1.3, 11)], history of pregnancy bleeding [OR = 3.7, CI 95% (0.7, 9)], pregnancy craving [OR = 3, CI 95% (1.1, 3.8)], and the level of health workers' care [OR = 0.4, CI 95% (0.1, 0.9)] are the risk factors affecting LBW in infants (P < 0.05). **Conclusions:** Low birth weight is a multifactorial phenomenon. Therefore, raising public awareness, providing nutritional counseling to pregnant mothers, regular referral to health homes to receive health care, and identifying risk factors and referral to higher level specialists and health centers can be effective in reducing the risk of birth of LBW infants.

Keywords: *Infant, Iran, low birth weight, nested case-control studies*

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Introduction

Birth weight is one of the determinant factors of a child's physical growth and brain development in the future and is a valid sign of intrauterine growth.[1,2] Birth weight less than 2,500 g is considered low. Weigh is one of the most important health indicators, because low-birth-weight (LBW) infants are at risk of neonatal death and health disorders. In general, the risk of death in LBW infants is 25 to 30 times more than that in those with birth weight less than 2,500 g, therefore, the lower the birth weight, the higher the risk of death.[3] In addition, LBW children who survive often suffer from short- and long-term disabilities 2 to 3 times more than other children.[4]

Every year around the world, 16% of the live births are related to LBW infants, in other words, about 20 million infants are born with a weigh less than 2,500 g. This rate has been reported 7% in developed countries, 16.5% in less developed or developing countries, and 18.6% in the least developed countries.[5] It has also been reported 20% in Asia, 20% in Oceania, 10% in Africa, 7% in North America, 6% in Europe, while it has been reported 10% in Iran, according to the World Health Organization (WHO) report.[6]

In Iran, two-thirds of the neonatal deaths occur within the first 24 hours after birth in LBW infants. In the last two decades, the rate of LBW has increased, so that according to the report of the WHO, 95% of LBW occurs in developing countries.[7]

Many maternal and fetal factors are significantly associated with LBW.[8]

Studies have shown that maternal age, occupation and weigh, gravidity (number of pregnancy), history of smoking, number of deliveries, history of previous deliveries, multiple pregnancy, malnutrition, not paying attention to having a healthy diet and not taking supplements during pregnancy, birth season, the number of care taken during pregnancy, and maternal anemia in mothers who delivered LBW infants have a direct relationship with birth weight.[9]

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Despite the health sector's efforts to manage LBW in newborns, the infant mortality rate in LBW infants is 20 times higher than that in normal-weight infants.[10]

LBW leads to various complications, especially in developing countries and the third World. LBW infants who survive will face with cognitive and neurological disorders, increased risk of high blood pressure, obstructive pulmonary disease, high blood cholesterol, kidney disease, acute watery diarrhea, and immune system disorders.[5] LBW is also one of the determinants of neurodevelopmental disorders, including mental retardation and disability in learning, and physicodevelopmental disorders and chronic diseases in adulthood.[11]

One of the goals of the WHO is to reduce the birth rate of infants weighing less than 2,500 g by 30% by 2030, which means 3% annual reduction in LBW infants from 2012.[12] The first step to achieve this goal is to assess the current situation and determine the risk factors for LBW. Although infant mortality has been significantly reduced in the last two decades in Iran, LBW is still one of the leading risk factors for neonatal mortality. In our country, LBW and its causes are very important in the country's health system. In this nested case-control study, which is an economical alternative compared to cohort studies, the risk factors for LBW in Kerman province were investigated.

Methods

Sample

This nested case-control study was conducted in the rural areas of Kerman province from December 16, 2018 to March 16, 2019 during 4 months. In this study, case and control groups were selected using risk set sampling. All infants born weighing less than 2,500 g within the study period were selected as cases, while for each case, two infants were randomly selected from those weighing more than 2,500 g at the same time and geographical location of birth as controls. This study was partly funded by the Endocrinology and Metabolism Research Center, Kerman University of Medical Sciences Kerman, Iran (KUMS) . On March 14, 2018,The Ethic approval Code is IR.KMU. REC.1396.2475.

Due to the nature of the methodology of nested case-control study, which is designed by embedding a control-case study in a prospective cohort study, the follow-up time is the same for cases and controls. The estimated Odds Ratio is straightforward and somewhat the same as Risk Ratio, for this reason, nested case-control study is considered as a risk set sampling, due to the uniform and low estimate and bias of OR to RR.

Data collection

Data were collected using a researcher-made checklist consisted of independent variables and risk factors including maternal age, parental education (illiterate, elementary, middle school, high school, university), parental occupation, and consanguineous marriage, rural (Qamar village) or urban (Kerman) residents, number of pregnancy, number of abortion, history of parental divorce, history of psychological stress, and maternal height, maternal weight, maternal weight gain during pregnancy, maternal BMI, taking supplements during pregnancy, and other variables are listed in Tables in result section.

The required data were extracted from the cases of pregnant women and, if necessary, through interviews with pregnant mothers. In this method, information about exposure was collected and recorded from the beginning of the study period and provided to the researcher. Accordingly, at any time of the study when the desired case (infant weighing less than 2,499 g) was identified, two controls were selected from the same study population (infants weighing 2500 g) at the same time.

Eligibility criteria

Whenever a baby was born with a weigh less than 2,500 g, two babies weighing more than 2,500 g were simultaneously selected as controls.

Exclusion criteria

In this study, the exclusion criteria for assessing the risk factors for LBW were birth weight greater than 4,000 g and congenital anomalies.

Ethics approval and consent to participate

The study aims were completely explained to the participants and it was ensured that all subjects were fully aware of the scope of the study and an informed signed consent form was obtained from them. In this regard, ethical principles on four main issues including harm to participants, deception, invasion of privacy or lack of informed consent were considered. This study was also approved by the ethics committee of Kerman University

of Medical Sciences (*KUMS- Ethical code: IR.KMU. REC.1396.2475*).

Univariate and multivariate analyses were performed using conditional logistic regression. The effects of all variables on LBW in the case and control groups were investigated using univariate analysis. Then, variables with $P < 0.2$ entered the multivariate analysis and their effects on LBW were investigated.

Data were analyzed using point and distance estimation (OR, CI) by conditional logistic regression via Stata-12 software. Statistical significant level was considered at $P < 0.05$.

Results

It was revealed that most mothers in the case (71.7%) and control (81.2%) groups aged 35-35 years and the frequency of high-school education in the case (41.2%) and control (43.5%) groups was high. On the other hand, most of the cases (92.2%) and controls (90.6%) were housewives, but in terms of all these variables, there was no statistically significant difference between case and control groups ($P > 0.05$). Also, 22.6% of the cases and 20.7% of the controls had consanguineous marriage, and only 4.6% of the cases and 2.3% of the controls reported a history of divorce, but this difference in the case and control groups was not significant (P > 0.05) [Table 1].

The results of univariate analysis showed that maternal age, maternal education, history of divorce, maternal BMI, number of pregnancies, number of deliveries, gestational age, inter pregnancy interval, number of abortion, history of stillbirth, history of pregnancy bleeding, pregnancy craving, number of midwives and health workers care ($P < 0.2$) are factors affecting LBW.

The results of multivariate analysis showed that the risk of LBW in mothers with normal weight (18.5≤ BMI <24.9) were about 3 times less than that in underweight mothers (BMI <18.5) [OR = 0.3, CI 95% (0.1, 0.9)], although its risk in overweight mothers (25 ≤ BMI) was less than that in underweight mothers. The risk of LBW in women with a gestational age under 37 weeks was increased by 4 times [OR = 3.8, 95% CI (0.9, 6.1)], while its risk in mothers with a history of stillbirth [OR = 4.8, CI 95% (1.3, 11)], pregnancy craving [OR = 3, CI 95% (1.1, 3.8)], and pregnancy bleeding [OR = 3.7, CI 95% (0.7, 9) was about 3 to 4 times higher than that in other pregnant mothers ($P < 0.05$). The results are shown in Table 2.

Discussion

The results of this study showed that maternal BMI, gestational age, history of pregnancy bleeding, pregnancy craving, and the level of health workers' care can be factors affecting the birth of LBW infants ($P < 0.05$).

According to the results of this study, maternal BMI can be one of the factors affecting LBW in infants, which is consistent with the results of a study conducted by Nahar *et al*. (1998) in Bangladesh, indicating that maternal weight and height can be the risk factor for birth of LBW infants.[11] The results of studies by Safari *et al*.[12] and Yodav *et al*.[7] are consistent with the results of this study. Another study conducted in India showed that the prevalence of birth of LBW infants by mothers with a BMI lower than the normal BMI is higher than that by those with a normal BMI.[13] Maternal anthropometric characteristics such as maternal weight and BMI, which indicate adequate energy intake affecting the size of the placenta, can directly affect infants weight.[14-16]

Maternal weight loss (BMI <18.5) affects pregnancy outcomes. Infants of underweight women are more likely to be born preterm and have low birth weight. Socioeconomic status, lifestyle, and the presence of chronic diseases in mothers may lead to maternal weight loss before and during pregnancy, and as a result, the birth of LBW infants.[17]

Lee Tang *et al*. ported that maternal nutritional deficiencies lead to preterm delivery (less than 37 weeks), and as a results, the birth of LBW infants.[18]

Table 1: Maternal demographic variables in the case and control groups

Variable		Case (*n*=155)	Control (*n*=310)	Chi-2	*P*
Maternal age	19<	14 (9.1)	11 (3.6)	1.6	0.1
	20-35	111 (71.7)	252 (81.2)		
	35≤	30 (19.2)	47 (15.2)		
Maternal education	College education	29 (18.7)	37 (11.9)	5.5	0.23
	Diploma	64 (41.2)	135 (43.5)		
	Middle school	36 (23.2)	88 (28.4)		
	Elementary	22 (14.1)	46 (14.8)		
	Illiterate	4 (2.5)	4 (1.2)		
Maternal occupation	Housewife	144 (92.9)	281 (90.6)	0.67	0.41
	Employee	11 (7.1)	29 (9.4)		
Parental relationship ratio	Yes	35 (22.6)	64 (20.7)	0.23	0.63
	No	120 (77.4)	246 (79.3)		
History of parents' separation	Yes	7 (4.6)	7 (2.3)	1.8	0.1
	No	148 (95.4)	303 (97.7)		

Table 2: Univariate and multivariate analysis of risk factors affecting LBW in the case and control group

Variable		Groups		Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
		Case (*n*=155)	Control (*n*=310)				
Maternal age (Year)	19<	14 (9.1)	11 (3.6)	1	---	1	---
	20-35	111 (71.7)	252 (81.2)	0.3 (0.1, 0.8)	0.04	0.6 (0.2, 1.9)	0.2
	35≤	30 (19.2)	47 (15.2)	0.5 (0.2, 1.3)	0.1	1.5 (0.4, 5.5)	0.4
Maternal education	College education	29 (18.7)	37 (11.9)	1		1	
	Diploma	64 (41.2)	135 (43.5)	0.4 (0.1, 1.9)	0.2	0.5 (0.09, 2.9)	0.4
	Guidance	36 (23.2)	88 (28.4)	3 (0.08, 1.5)	0.1	0.3 (0.06, 1.7)	0.1
	Elementary	22 (14.1)	46 (14.8)	0.4 (0.1, 1.8)	0.2	0.4 (0.09, 2.2)	0.3
	Illiterate	4 (2.5)	4 (1.2)	0.7 (0.1, 3.3)	0.2	0.9 (0.1, 4.9)	0.9
Maternal occupation	Housewife	144 (92.9)	281 (90.6)	1		---	---
	Employee	11 (7.1)	29 (9.4)	1.3 (0.6, 2.7)	0.4	---	---
Consanguineous marriage	Yes	35 (22.6)	64 (20.7)	1		---	---
	No	120 (77.4)	246 (79.3)	0.8 (0.5, 1.4)	0.6	---	---
Divorced	Yes	7 (4.6)	7 (2.3)	1		1	---
	No	148 (95.4)	303 (97.7)	0.5 (0.1, 1.4)	0.1	0.5 (0.1, 2.2)	0.4
BMI Maternal	18.5<	24 (15.5)	21 (6.8)	1		1	---
	18.5-24.9	89 (57.4)	143 (46.1)	0.5 (0.2, 1.05)	0.07	0.3 (0.1, 0.9)	0.02
	25≤	42 (27.1)	146 (47.1)	0.2 (0.1, 0.4)	0.001	0.1 (0.05, 0.3)	0.001
Gravidity (Number of pregnancies)	The first	104 (67.1)	51 (32.9)	1		1	---
	2≤	180 (58.06)	130 (41.94)	1.4 (0.9, 2.2)	0.05	1.2 (0.3, 4.1)	0.3
Number of deliveries	The first	117 (75.4)	206 (66.4)	1		1	---
	2≤	38 (24.6)	104 (33.6)	1.5 (1.01, 2.4)	0.04	1.1 (0.1, 3.2)	0.3
Gestational age	≤37	111 (71.7)	297 (95.8)	1		1	---
	>37	44 (28.3)	13 (4.2)	7.7 (3.9, 10.4)	0.000	3.8 (1.7, 6.1)	0.001
Interpregnancy interval	2<	68 (43.9)	182 (58.7)	1		1	---
	≤2	87 (56.1)	128 (41.3)	1.7 (1.2, 2.6)	0.003	1.4 (0.8, 2.4)	0.2
Number of abortion	0	123 (79.3)	258 (83.2)	1		1	---
	1≤	32 (20.7)	52 (16.8)	1.3 (0.7, 2.1)	0.2	1.8 (0.8, 7.2)	0.2
History of stillbirth	No	145 (93.6)	303 (97.7)	1		1	---
	Yes	10 (6.4)	7 (2.3)	2.3 (0.9, 6.9)	0.03	4.8 (1.3, 11)	0.03
History of bleeding	No	146 (94.2)	304 (98)	1		1	---
	Yes	9 (5.8)	6 (2)	3.8 (1.1, 12.6)	0.02	3.7 (1.7, 9)	0.03
Pregnancy craving	No	84 (54.2)	203 (65.5)	1		1	---
	Yes	71 (45.8)	107 (34.5)	1.9 (1.2, 3.1)	0.006	2 (1.1, 3.8)	0.01
IVF	No	152 (98)	307 (99)	1	---	---	---
	Yes	3 (2)	3 (1)	2 (0.4, 9.9)	0.3	---	---
Smoking	No	97 (98.7)	307 (99.03)	1		---	---
	Yes	2 (1.3)	3 (0.97)	1.3 (0.2, 7.9)	0.7	---	---
Secondhand smoke	No	147 (94.8)	298 (96.1)	1		---	---
	Yes	8 (5.2)	12 (3.9)	1.3 (0.5, 3.5)	0.5	---	---
Psychological tension	No	150 (96.8)	294 (94.8)	1		---	---
	Yes	5 (3.2)	16 (5.2)	1.63 (0.5, 4.5)	0.3	---	---
Self-medication or arbitrary use of drugs	No	151 (97.4)	303 (99)	1		1	
	Yes	4 (2.6)	3 (1)	2.6 (0.5, 11.9)	0.1	4.2 (0.5, 15)	0.2
Baby's sex	Female	84 (54.2)	171 (55.2)	1		---	---
	Male	71 (45.8)	139 (44.8)	1.7 (0.3, 8)	0.4	---	---
Birth season	Spring	33 (21.3)	71 (22.9)	1		---	---
	Summer	38 (24.5)	71 (22.9)	2.9 (0.5, 17)	0.3	---	---
	Fall	43 (27.7)	81 (26.1)	3 (0.3, 25.8)	0.3	---	---
	Winter	41 (26.5)	87 (28.1)	1.5 (0.1, 12.5)	0.4	---	---
Physician care	≤5	113 (72.9)	227 (73.2)	1		---	---
	6-9	28 (18.1)	56 (18)	1 (0.5, 1.8)	0.9	---	---
	10≤	14 (9)	27 (8.8)	1.1 (0.3, 3.3)	0.8	---	---

Contd...

Table 2: Contd...

Variable		Groups		Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
		Case (*n*=155)	Control (*n*=310)				
Midwife caring	≤5	94 (60.6)	156 (50.3)	1		1	---
	6-9	48 (31)	134 (43.2)	0.5 (0.3, 0.8)	0.007	0.7 (0.4, 1.4)	0.4
	10≤	13 (8.4)	20 (6.4)	0.8 (0.2, 0.9)	0.02	2.3 (0.8, 7)	0.1
Health care worker's care	≤5	134 (86.4)	241 (77.7)	1		1	---
	6-9	19 (12.3)	64 (20.6)	0.4 (0.2, 0.8)	0.01	0.4 (0.1, 0.9)	0.03
	10≤	2 (1.3)	5 (1.7)	0.6 (0.1, 0.9)	0.2	0.7 (0.09, 5.5)	0.7

*Variables with *P*<0.2 in the univariate analysis that entered the multivariate analysis. **OR: Odds Ratio, CI: Confidence Interval

This study showed that gestational age is one of the risk factors associated with LBW, which is consistent with the results of other studies.[3,4,13,19-21] A study by Mosayebi *et al*. (2004) also showed that more than 50% of the LBW infants were premature.[3] The lower the number of weeks of pregnancy, the lower the birth weight of the infants due to the poor fetal growth.[22,23] Momeni *et al*.[15] also found that in 75% of the cases, preterm birth alone is effective in LBW. In the United States and developing countries, 30% and 70% of LBW infants were respectively born preterm.[24]

The results of this study showed that there is a relationship between the history of bleeding in mothers during pregnancy and LBW, which is consistent with the results of some studies.[20-22,25-28] Bleeding or spotting in the second and third trimesters of pregnancy, can be a sign of dangerous conditions such as sudden separation of the placenta from the uterus (placental abruption), miscarriage or premature labor, and subsequently, preterm birth,[29,30] which can be a cause of LBW.

The history of bleeding in pregnant mothers may lead to premature birth, which in turn can lead to the birth of LBW infants due to young gestational age. On the other hand, mothers' lifestyle can affect the activities of mothers during pregnancy. In mothers who have heavy activities during pregnancy, it may cause bleeding and as a result, the birth of a premature baby with low birth weight.[10]

The results of this study showed that health workers care during pregnancy reduces the risk of LBW, which is consistent with the results of some other studies,[16,31] indicating that health care provided by the health system may have a protective effect on LBW, as well as an effective role in reducing the birth rate of LBW infants. One of the most important reasons for prenatal care is the dominance of the health system, regular monitoring of weight, as well as increased awareness of the complications of pregnancy such as diabetes, high blood pressure and so on.

Access to health care centers and health professionals and prenatal care training by the specialists and prenatal care for pregnant mothers, recommendation of micronutrient supplements (iron and folic acid) for pregnant women, family planning method for preventing unwanted and unplanned pregnancies can be effective in reducing the birth rate of LBW babies.[32]

The results of this study showed that pregnancy craving can be one of the underlying risk factors for the birth of LBW infants. A study by Taheri *et al*. (2007) in Iran also showed that the history of pregnancy craving is associated with an increased risk of LBW infants, which is consistent with the results of this study.[30] Calorie restriction caused by pregnancy craving has a detrimental effect on fetal growth and reduces the average weight of infants.[33]

LBW in both developed and developing countries imposes a tremendous pressure on the health care system and family members.[18] Newborns care for more than one-third of the costs of health care. The cost of saving the lives of LBW infants with special care often exceeds a few thousand dollars. Besides, another important issue for LBW infants is the quality of their future life.[7]

Conclusions

According to the results, LBW is related to several factors, therefore, it is a multifactorial phenomenon. Maternal BMI, gestational age, history of pregnancy bleeding, pregnancy craving, and level of health workers care are the factors associated with LBW. Therefore, raising public awareness, counseling pregnant mothers, and providing nutritional counseling to increase maternal BMI in those with low BMI, regular referral to health homes to receive health care in order to prevent preterm births can be effective in reducing the risk of birth of LBW infants. By improving the quality of maternal care and training and their referrals to higher level specialists and health centers, the risk of birth of LBW infants can be decreased. In addition, other prenatal risk factors identified should be considered and planned to reduce the risk of birth of LBW infants.

Limitations of the study

Since this study was conducted in the rural areas of Kerman province, Iran, and this province is different from other provinces in terms of cultural and socio-economic conditions, so, the results of this study may not be illustrative example of the country's population; thus,

different studies with more examples and larger sample size are recommended to solve this problem.

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Conflicts of interest

There are no conflicts of interest.

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