# The Relationship between Maternal Diseases during Pregnancy and Low Birth Weight: a Nested Case-Control Study in Rural Areas of Kurdistan Province (West of Iran)

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## Abstract

*Background:* Low birth weight (LBW) is considered as one of the important health indicators in evaluating prenatal care as well as determining scale of infants' health in the society. The study aimed to investigate maternal diseases during pregnancy and its impact on LBW in rural areas of Kurdistan province, Iran. *Materials and Methods:* This study was conducted in nested case-control study method in rural areas of Kurdistan province- Iran in 2015-2016. In this study, 182 infants less than 2,500gr as case and 364 infants weighing 2,500 g and more as control were entered the study. Information about case and control groups was extracted by investigating records of pregnant women care. Data was analyzed using software Stata-12 with point and interval estimation of odds ratio (OR) using conditional logistic regression. *Results:* The results of single-variable analysis of conditional logistic regression showed that there is a statistical relationship between blood pressure during pregnancy, iron deficiency anemia, mother's thyroid problems, oral and dental problems, and history of bleeding during pregnancy in case and control groups (P<0.05). The results of multivariate analysis in the presence of other factors affecting underweight during pregnancy showed that there was statistically significant relationship between iron deficiency anemia (OR=23.86, 95%CI, 9.31-61.11), blood pressure during pregnancy (OR=13.8, 95%CI, 13.8-60.65), history of bleeding during pregnancy (OR=9.21, 95%CI, 3.39-25.01), and low birth weight (P<0.05). *Conclusion:* The results of this study indicated significant relationship between the diseases of pregnancy (such as blood pressure during pregnancy, iron deficiency anemia, and history of bleeding during pregnancy) and Low birth weight in infants. The birth of a LBW infant can be to a large extent prevented by diagnosing and preventing these diseases and required trainings for pregnant women.

*Key Words:* Diseases of pregnancy, LBW, Iran, Infants, Rural areas.

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## 1- INTRODUCTION

Children are future capital of human society and a vital and fundamental component of the existence and future of every nation (1). Birth weight as one of the important health indicators has a close relationship with the growth- process of evolution and survival of infants in the future, because underweight children are susceptible to mortality and infection with other diseases. Weight less than 2,500 grams at birth are referred to low birth weight (2). The mortality of underweight infants is about 40 times of infants with normal weight (3). Communities and families try to ensure the health of children and having the opportunity to achieve their potential abilities that it is necessary to provide them with all the facilities to achieve this goal (4, 5).

Fetal and Ectopic life together define a path during which growth and development of children influenced by genetic, environmental and social factors will be determined. Prenatal events which are influenced by fetal and maternal factors and delivery events can create an infant at risk. Meanwhile, preterm birth and Low birth weight (LBW) are always considered as important factors of infants' mortality and the major causes of developmental disorders and neonatal complications (6-9).

About 130 million infants are born annually in the world (10). Also, more than 20 million (15.5% of total births) LBW are born annually worldwide that this amount in developing countries constitutes 95.6 live births (11). The noteworthy point is that 99 percent cases of neonatal deaths in the world occurs in poor countries; while, two-thirds of these deaths only occurs in 10 countries of the world and mainly in mainland Asia (12). In 2014, the prevalence rate of LBW has been reported 15% in the world, 13% in developing countries, 9% in Latin America, 6% in East Asia and Pacific

Ocean, 13% in sub-Saharan Africa, 28% in South Asia, and 10% in Iran (13). In Iran, the mortality rate of children under 5 years is 32 per thousand and in children under one year is 26 per thousand that 18 per thousand of them die in the first month and most of them are low birth weight infants (14). In the USA, birth rate of LBW infants has mainly increased during the past two decades due to the increase in preterm deliveries (15). Almost 30% of LBW infants in the USA have intrauterine growth disorder and they have born after week 37. In developing countries, almost 70% of LBW infants have intrauterine growth restriction. Infants with intrauterine growth disorder are exposed to more complications and mortality than infants with sufficient growth and appropriate to gestational age (16, 17).

Therefore, LBW is considered as one of the important health indicators in evaluating prenatal care as well as determining scale of infants' health in the society. Thus, the incidence of LBW infants can be prevented by identifying and controlling risk factors which is dependent on social and biological conditions (18, 19). Studies have shown LBW is caused by maternal factors such as heart and renal failure, respiratory problem, maternal blood pressure, smoking and alcohol during pregnancy, short distance between the recent pregnancy and previous pregnancy, mental and psychological tensions, and depression and the lack of appropriate weight gain (20). LBW not only underlies various diseases (in infancy), but also is closely associated with infection with cardiovascular diseases and stroke in adulthood (21, 22).

Underweight infants are more exposed to risks such as cerebral palsy, mental retardation, the incidence of neurological and physical disabilities, respiratory diseases, sudden death syndrome, complications caused by being hospitalized in the intensive care unit than

infants with normal weight (23, 24). In addition to physical-mental problems, the cost of care and treatment of these infants is 6 times more than other infants (3). Birth of LBW infant will encounter public health system with a risky person at birth and even after birth. On the other hand, its frequency is indirectly the chart of state of maternal health and socio-economic welfare of society due to being related to various factors such as maternal health during pregnancy, education, health literacy and socio-economic condition of the family (13, 19).

Given this issue, investigation of the risk factors associated with that is a key guidance in choosing appropriate strategies to prevent and reduce risk factors on the one hand and on the other hand will help improve the health status of children and ultimately the community. The aim of this study is to investigate maternal diseases durring pregnancy and its impact on LBW in alive born infants in rural areas of Kurdistan province.

## 2- MATERIALS AND METHODS

### 2-1. Study Design and Population

This study was conducted in nested case-control study method in rural areas of Kurdistan province and in time interval from December 2015 until the end of June 2016 for 6 months**.**

### 2-2. Methods

In this study, the selection of case and control groups was conducted based on nested design that is the approach of Risk set sampling. All infants born weighted less than 2,500 grams in mentioned interval time were selected as case and for each case that occurs, two people were selected as control randomly from infants who have weight more than 2,500 grams and have born in the same interval time and geographic location.

### 2-3. Measuring tools

Data collection tools in this study included a researcher made checklist of family health record which was included independent variables and risk factors were investigated. The variables used in this research are mother's age during pregnancy, diseases of pregnancy including gestational diabetes, gestational hypertension, iron deficiency anemia, urinary tract infection (UTI), thyroid problems, oral and dental problems, a history of bleeding during pregnancy, and other demographic variables. This data was extracted from prenatal care records and if necessary, by referring to them.

### 2-4. Eligibility criteria

At any time of the study when infants under 2,500 grams were born were selected as case and simultaneously two infants weighted more than 2,500 grams were selected as control.

### 2-5. Ethical considerations

The informed consent to participate in the study was taken from all participants in the study and individuals were entered the study consciously and with written consent. The questionnaires were filled without mentioning the name of participants and data was analyzed and reported as a group.

### 2-6. Data analyses

Data was analyzed using software Stata-12 with point and interval estimation (OR [odds ratio], CI [Confidence Interval]) using conditional logistic regression and the level of error was considered less than 5%.

## 3-RESULTS

In this study, 182 cases and 364 controls were selected and entered the study. The results of this study in the initial analysis showed that in the case group 15 mothers (7.48%) were under 19 years, and 33 mothers (18.3%) were over the age of 35 years, and in the control

group 29 mothers (8.11%) were under 19 years, and 62 mothers (17.3%) were over the age of 35 years, that no statistically significant relationship was observed between mother's age and LBW in the case and control groups (P>0.05) as well as no statistically significant relationship was observed between parents' occupation, parents' education, kinship, and a history of parents' separation from each other and stillbirth in the case and control groups (P>0.05) (**Table.1**).

The results of study showed that there was no significant relationship between Mother diseases and neonatal gender in both case and control groups. (P>0.05) **(Table2)**. The results of study showed thst 51.65% of infants in the case group and 52.75% of infants in the control group were male and there was not significant relationship between the gender of infants and Their placement in the case and control groups (P>0.05) **(Figure.1)**.

The results of this study in the univariate conditional logistic regression analysis showed that there was statistical relationship between gestational hypertension, iron deficiency anemia,

mother's thyroid problems, oral and dental problems, and a history of bleeding during pregnancy in the case and control groups (P<0.05), but no statistical relationship was observed between gestational diabetes and urinary tract infection (UTI) in the case and control groups (P>0.05) (**Table.3**).

In the next step, it was entered into the multivariate model in order to investigate the impact of factors affecting LBW in the presence of other important variables with P> 0.2 which multiple regression analysis (multivariate conditional logistic regression) was used.

The results of multivariate analysis in the presence of other factors affecting LBW (P <0.2), showed that there is statistically significant relationship between iron deficiency anemia, gestational hypertension, and a history of bleeding during pregnancy in the case and control groups (P<0.05), but no statistically significant relationship was observed between thyroid problems, and oral and dental problems during pregnancy in the case and control groups (P>0.05) (**Table.4**).

**Table-1**: Distribution of parents' demographic variables in the case and control groups in the rural areas of western Iran

| Variables | Cases N (%) | Controls N (%) | Chi-square | P-value |
|---|---|---|---|---|
| **Mother's age** | | | | |
| 20-35 years | 134(74.1) | 273(74.16) | | |
| <19 | 15(7.48) | 29(8.11) | 0.12 | 0.93 |
| 35> | 33(18.03) | 62(17.3) | | |
| **Mother's education** | | | | |
| College education | 3(1.64) | 12(3.31) | | |
| Diploma | 34(18.58) | 53(14.6) | | |
| Guidance | 30(15.92) | 70(19.16) | 3.18 | 0.52 |
| Elementary | 88(49.87) | 180(49.77) | | |
| Illiterate | 27(14.75) | 49(13.50) | | |

| | | | | | |
|---|---|---|---|---|---|
| **Mother's occupation** | | | | | |
| Housewife | 164(90.01) | 322(88.39) | | | |
| Employee | 1(0.55) | 10(2.75) | | 3.52 | 0.31 |
| Laborer | 16(8.74) | 28(7.71) | | | |
| Other | 1(0.55) | 4(1.10) | | | |
| **Father's education** | | | | | |
| College education | 5(2.73) | 17(4.68) | | | |
| Diploma | 34(19.26) | 85(23.34) | | 3.16 | 0.48 |
| Guidance | 46(25.14) | 93(25.63) | | | |
| Elementary | 86(46.99) | 147(40.50) | | | |
| Illiterate | 11(6.01) | 22(6.06) | | | |
| **Father's occupation** | | | | | |
| Employee | 8(4.37) | 19(5.22) | | | |
| Laborer | 51(27.87) | 111(30.58) | | | |
| Self-employment | 94(51.01) | 190(52.02) | | 2.83 | 0.29 |
| Unemployed | 6(3.28) | 9(2.48) | | | |
| Other | 23(13.37) | 35(9.86) | | | |
| **History of parents' separation (Separation of living place)** | | | | | |
| Yes | 170(93.44) | 346(95.04) | | | |
| No | 12(6.56) | 18(4.96) | | 2.74 | 0.43 |
| **History of stillbirth** | | | | | |
| Yes | 174(95.63) | 353(96.97) | | | |
| No | 8(4.37) | 11(3.03) | | 3.1 | 0.54 |

**Table-2:** The relationship between maternal diseases and neonatal gender

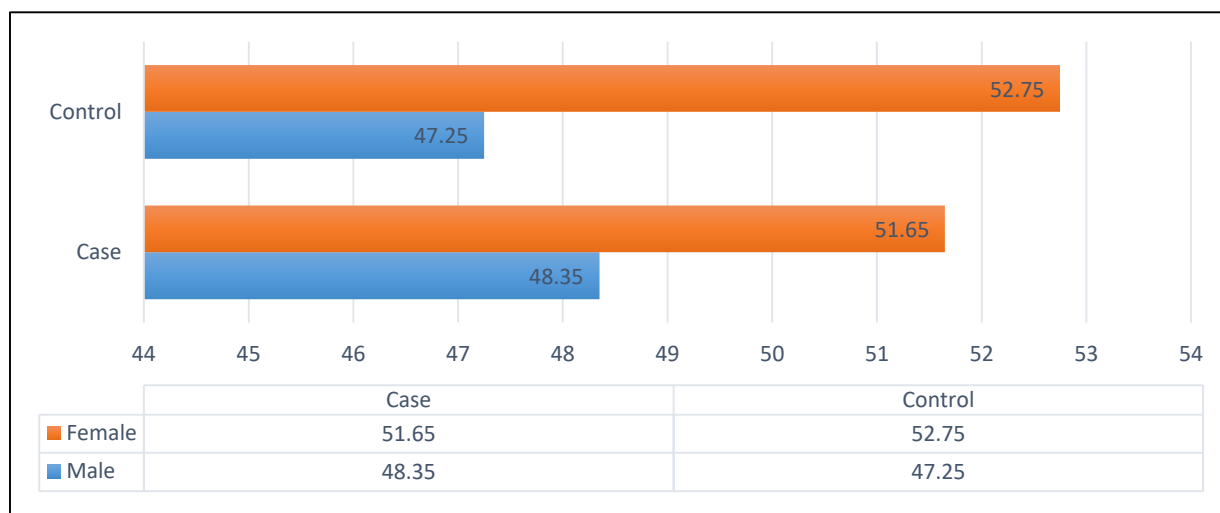| Mother disease | | Case | | P-value | Control | | P-value |
|---|---|---|---|---|---|---|---|
| | | Male | Female | | Male | Female | |
| Gestational Diabetes | Yes | 3(30) | 7(70) | | 7(38.89) | 11(61.11) | |
| | No | 85(49.42) | 87(50.58) | 0.23 | 165(47.69) | 181(53.31) | 0.46 |
| Gestational hypertension | Yes | 12(80) | 3(20) | | 3(75) | 1(25) | |
| | No | 76(45.51) | 91(54.49) | 0.12 | 169(46.94) | 191(53.06) | 0.26 |
| Iron deficiency anemia | Yes | 41(57.75) | 30(42.45) | | 5(33.33) | 10(66.67) | |
| | No | 58(52.25) | 53(47.75) | 0.18 | 167(47.85) | 182(52.15) | 0.27 |
| Urogenital infection | Yes | 3(37.5) | 5(62.5) | | 4(30.77) | 9(69.23) | |
| | No | 85(48.85) | 89(51.15) | 0.53 | 168(47.86) | 183(52.14) | 0.22 |
| Thyroid disorder | Yes | 3(27.27) | 8(72.73) | | 1(33.33) | 2(66.67) | |
| | No | 85(49.71) | 86(50.29) | 0.14 | 171(47.37) | 190(52.63) | 0.62 |
| Oral and dental disease | Yes | 28(44.44) | 35(55.56) | | 46(48.42) | 49(51.58) | |
| | No | 60(50.42) | 59(49.58) | 0.44 | 126(46.84) | 143(53.16) | 0.79 |
| History of bleeding | Yes | 13(46.43) | 15(53.57) | | 4(44.44) | 5(55.56) | |
| | No | 75(48.7) | 79(51.3) | 0.82 | 168(47.32) | 187(52.68) | 0.86 |

**Fig.1**:The frequency of gender in the case and control group.

**Table-3:** The results of univariate conditional logistic regression analysis, the impact of diseases of pregnancy on LBW in rural areas of west of Iran

| Variables | Cases N (%) | Controls N (%) | Unadjusted OR (95% CI) | P-value |
|---|---|---|---|---|
| **Gestational Diabetes** | | | | |
| No | 172(94.51) | 346(95.05) | 1 | |
| Yes | 10(5.49) | 18(4.95) | 1.09(0.47-2.52) | 0.82 |
| **Gestational hypertension** | | | | |
| No | 167(91.76) | 360(98.90) | 1 | |
| Yes | 15(8.24) | 4(1.01) | 13..8(3.14-60.65) | 0.000 |
| **Iron deficiency anemia** | | | | |
| No | | | 1 | |
| Yes | 111(60.09) | 349(95.88) | | |
| | 71(39.01) | 15(4.12) | 18.55(8.51-40.41) | 0.000 |
| **Urogenital infection** | | | | |
| No | 174(95.60) | 351(96.43) | 1 | |
| Yes | 8(4.40) | 13(3.75) | 1.22(0.47-3.16) | 0.67 |
| **Thyroid disorder** | | | | |
| No | 171(93.96) | 361(88.98) | 1 | |
| Yes | 11(6.04) | 3(0.2) | 7.33(2.04-26.28) | 0.02 |

| | | | | |
|---|---|---|---|---|
| **Oral and dental disease** | | | | |
| No | 119(38.65) | 269(73.9) | 1 | |
| Yes | 63(34.62) | 95(26.10) | 1.47(1.02-2.15) | 0.03 |
| **History of bleeding** | | | | |
| No | 154(84.62) | 355(97.53) | 1 | |
| Yes | 28(15.38) | 9(2.47) | 7.59(3.30-17.44) | 0.000 |

**Table-4**: The results of multivariate conditional logistic regression analysis, the impact of diseases of pregnancy on LBW in the case and control groups in rural areas of west of Iran.

| Variables | Cases N (%) | Controls N (%) | Unadjusted OR (95% CI) | P-value | adjusted OR (95%Cl) | P-value |
|---|---|---|---|---|---|---|
| **Gestational hypertension** | | | | | | |
| No | 167(91.76) | 360(98.90) | 1 | | 1 | |
| Yes | 15(8.24) | 4(1.1) | 13.8(3.14-60.65) | 0.000 | 6.11(2.91-14.36) | 0.00 |
| **Iron deficiency anemia** | | | | | | |
| No | 111(60.09) | 349(95.88) | 1 | | 1 | |
| Yes | 71(39.01) | 15(4.12) | 18.55(8.51-40.41) | 0.000 | 23.86(9.31-61.11) | 0.00 |
| **Thyroid disorder** | | | | | | |
| No | 171(93.96) | 361(99.8) | 1 | | 1 | |
| Yes | 11(6.04) | 3(0.2) | 7.33(2.04-26.28) | 0.02 | 2.26(0.42-12.07) | 0.33 |
| **Oral and dental disease** | | | | | | |
| No | 119(65.38) | 269(73.9) | 1 | | 1 | |
| Yes | 63(34.62) | 95(26.01) | 1.47(1.02-2.15) | 0.03 | 1.88(0.43-3.13) | 0.08 |
| **History of bleeding** | | | | | | |
| No | 154(84.62) | 355(97.53) | 1 | | 1 | |
| Yes | 28(15.38) | 9(2.47) | 7.59(3.30-17.44) | 0.000 | 9.21(3.39-25.01) | 0.00 |

## 4- DISCUSSION

LBW in each community is as one of the factors affecting infants' mortality as well as represents socio-economic status and also is an indicator of the health status of that community (30). In Iran, LBW is the main cause of Infant Mortality Rate (IMR) (14, 26, 27). LBW depends on many factors including diseases of pregnancy, mental and psychological tensions, risky behaviors during pregnancy, socio-economic level of the family, the number of previous pregnancies, the interval between pregnancies, exposure to cigarette smoke and other factors (20, 28). The results of this study which was conducted for 6 months in rural areas of west of Iran show that LBW is influenced by factors including diseases of pregnancy such as iron deficiency anemia, oral and dental problems, and a history of bleeding during pregnancy.

### 4-1. Gestational hypertension and the Risk of LBW

Gestational hypertension is a common disorder which will have fatal risks for mother and fetus along with bleeding and infection during pregnancy. About 5-7% of pregnant women during pregnancy are with gestational hypertension which includes a major part of maternal complications during pregnancy (29). Preterm delivery, stillbirth, impairment of fetal growth can be mentioned as complications of gestational hypertension (26, 27). The prevalence of hypertension in the study is 8.24% in the case group and 1.10% in the control group which was consistent with the results of the study of Keshavarz and Babaei study (30).

The results of this study showed that the risk of LBW in mothers with gestational hypertension is about six times more than the mothers who do not have gestational hypertension [OR=6.11, (95% CI=2.91-14.36)]. This study was consistent with the results of the studies of Eshraghiyan et al., Namakin et al.,Tootoonchi et al., as well as Bahrami et al., in Iran (31-34), and also the results of the studies of Aregay et al. in Northern Ethiopia (35), Demelash et al. (36), as well as the study of Xia et al. (37), which these results are consistent with the results of our study. In a study which was conducted by Reime et al. in Germany (38), there was no relationship between gestational hypertension and LBW. This may be due to differences in type of study, genetic and racial characteristics of mothers, or method of sampling among these studies which these results are unlike the results of our study. Gestational hypertension reduces blood flow of many organs such as the liver and kidneys. Reduction of uterine blood flow can cause problems such as reduction of fetal growth, reduction of amniotic fluid, and placental abruption, and it can lead to preterm delivery and preterm fetus may be born (27, 33, 39).

**4-2. Iron deficiency anemia and the Risk of LBW**

During pregnancy, the daily needs of pregnant women for food increases due to fetal growth through nutritional relationship between fetus and mother; so that, amount of required iron is 1,000 mg per day which of this amount, about 300 mg is actively transferred to the fetus (40). Required iron for the fetus is actively transferred from mother to infant through receptors which amount of these receptors increases in case of mother's iron deficiency that the fetus can use of mother's body as much as possible (41).

According to the World Health Organization, the prevalence of iron deficiency anemia is 25% in developing countries and is 22% in developed countries (40). The prevalence of anemia during pregnancy is 42% in India, and 11.5% in Germany (31, 40-42). The prevalence of anemia during pregnancy was reported 2.6 to 27 percent in the study of Mostajeran et al. in 2013 in Isfahan (43). Also, iron deficiency anemia especially in first and second trimester of pregnancy is associated with the increase in preterm delivery and LBW infant delivery (41, 42). In several studies, the relationship between iron deficiency anemia of mother and preterm delivery and LBW has been specified and it is shown that anemia at week 24 of pregnancy increases the probable risk of preterm delivery and LBW (44, 45).

Some studies have shown a positive relationship between mother's anemia during pregnancy and the Apgar score of infant (14, 32). It is specified that the probability of mortality of the infants who their mothers have not received supplementary iron during pregnancy is about 22% higher than other infants. Also, anemia of mother may be associated with intrauterine growth reduction and LBW (36, 40, 46). This study showed that there is statistically significant relationship between iron deficiency anemia and LBW in the case and control groups [(OR=24.42

(95% CI=5.87-101.6)]. This means that the risk of LBW delivery in the mothers who have iron deficiency anemia during pregnancy is about 24 times higher than the mothers who do not have the problem of iron deficiency anemia during pregnancy. The results of this study was consistent with the study of Tootoonchi et al. (47) in Iran, and the study of Aregay et al. in Ethiopia in 2010 (35), as well as the study of Badshah et al. in Pakistan in 2008 (48), and the study of Elhassan et al. in 2010 in Sudan under the title of iron deficiency anemia and LBW (49).

There was not statistically significant relationship between iron deficiency anemia in the first three months of pregnancy and the risk of low birth weight in the study of Ghavi et al. (42), Saberi et al. (40), and Bhaskar et al. (50), that the results of these studies were not consistent with the results of our study.

## 4-3. Thyroid disorders and the Risk of LBW

Thyroid problems during pregnancy is also one of other diseases that affect the health of the mother and consequently infant (51). Abortion, preterm delivery, and delay in fetal growth can be mentioned as undesirable consequences of hypothyroidism (52-54).

Regarding hypothyroidism in pregnant mothers and its effect on birth weight, the results of this study has introduced it an important factor as weight disorder during pregnancy, but these results were not statistically significant [OR=2.26 95%CI=(0.42-12.07)]. These results are consistent with the results of the study of Razi et al. in Rafsanjan (55), Stagnaro-Green in New Jersey (56), and Idris et al. in Nottingham (57).

Thyroid and growth hormones are of the most important hormones that affect the development and growth process during fetal and childhood (52, 58). In the first

months of pregnancy, ten fetal thyroids are not still active and the fetus is highly dependent on the mother in terms of thyroid hormones; therefore, disorder in maternal thyroid hormones will have a significant impact on growth and development in infants (59).

## 4-4. Periodontal Disease and the Risk of LBW

Oral health is one of the important indicators in public health. It is more important during pregnancy (60). According to many studies, it is proven that periodontal diseases during pregnancy are associated with undesirable perinatal consequences including preeclampsia, preterm delivery, LBW, and hospitalization of infant in the Neonatal Intensive Care Unit (NICU) (30, 60). The results of this study showed that there is no statistically significant relationship between oral and dental problems and LBW [OR=1.88 95% CI= (0.34-3.13)]. This means that the mothers who have had periodontal problems during pregnancy will have the probability of LBW delivery 1.88 times higher than the other mothers who have not had periodontal problem during pregnancy, but this relationship was not statistically significant (P=0.08).

In the study of Clothier et al., after investigating 31 published studies in relation to periodontal during pregnancy and LBW in infants, the results of 22 studies have shown a positive relationship between periodontal and preterm (61). As well as in the study of Naseh et al., a statistically significant relationship was observed between periodontal disease and the risk of LBW in infants (62) which these results are not consistent with the results of our study sample size, racial and cultural differences can be an effective factor in this regard. In the study of Michalowicz et al., no statistically significant relationship was observed between periodontal and the risk of LBW

despite the large sample size of 823 people (413 people) case and (410 people) control (63). Also in the meta-analysis study of Rosa et al. in 2012 under the title of periodontal disease, no relationship was observed between LBW and periodontal disease (64) which this study was consistent with the results of our study.

## 4-5. Bleeding during pregnancy and the Risk of LBW

Bleeding during pregnancy is a risk factor for mother and fetus. Bleeding in first trimester of pregnancy is a threat to abortion (65). Bleeding in late pregnancy has another concept. Two important factors of it are placental abruption and placenta previa which both are dangerous and will face the fetus with the lack of oxygen (66, 67). If bleeding occurs frequently during pregnancy, the probability of preterm delivery and prom will increase in them. Placental abruption and placenta previa may cause a lot of bleeding that it causes fetal death very soon (1, 41).

In current study, statistically significant relationship was observed between history of bleeding during pregnancy and LBW in the case and control groups [OR=7.74 (95% CI= 1.83-33.15)]. This means that the probability of LBW infants in the mothers who have history of bleeding during pregnancy is 7.74 times higher than the mothers who do not have history of bleeding during pregnancy. The results of this study were consistent with the study of Rezaeian et al. in 2013 (68), the study of Zarbakhsh Bhari et al. in 2011 (20), the study of Tootoonchi et al. in Iran (47), and the study of Sharma et al. in 2014 in Nepal that statistically significant relationship was observed between bleeding during pregnancy and the risk of LBW which was consistent with our study (69).

Also, in the study of Saberi et al., no statistically significant relationship was observed between iron deficiency anemia

in the first trimester of pregnancy and the risk of LBW (40). Although pregnancy is a normal issue which can lead to a healthy infant with the process of vaginal delivery, this natural issue can lead to death of mother and infant with the smallest negligence and ignorance which three-quarters of deaths during pregnancy namely about 5.7 million deaths in developed countries annually that more than 90% of them is due to LBW can be prevented with proper nutrition and providing care during pregnancy with high quality, and practical training. Due to amount of study and cultural differences between Kurdistan and other provinces of the country (Iran), it is suggested to implement above study in nested case-control study method in other provinces and to present more generalizable results.

## 4-1. Limitations of the study

Since this study has conducted in rural areas of Kurdistan province, Iran, and this province is different with 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 in more examples and size than the other provinces are necessary to fix this problem.

## 5- CONCLUSION

Our study showed that there was a relationship between blood pressure during pregnancy, iron deficiency anemia, and history of bleeding during pregnancy with low birth weight in neonates in rural areas in Kurdistan province, Iran. Improving the quality of pregnant mothers' care and the need for awareness and identification and continuous monitoring of pregnant mothers is essential in preventing the birth of LBW infants, especially in rural areas.

## 6- CONFLICT OF INTEREST

This research has had no conflicts of interest for authors.

## 7- ACKNOWLEDGMENT

## 8- REFERENCES

1. Chaman R, Naieni KH, Golestan B, Nabavizadeh H, Yunesian M. Neonatal mortality risk factors in a rural part of Iran: a nested case-control study. Iranian Journal of Public Health 2009; 38(1):48-52.

2. Preventation (CDC). CfDCa. National Center for Health Satisticics Vitalsat. 2010. Available at: URL: http: //www.cdc. gov/ nchs/ Vital/ Stats.htm.

3. Alexander G, Wingate M, Mor J, Boulet S. Birth outcomes of Asian-Indian-Americans. International Journal of Gynecology & Obstetrics 2007; 97(3):215-20.

4. de Bernab JV, Soriano T, Albaladejo R, Juarranz M, Calle MaE, Martínez D, et al. Risk factors for low birth weight: a review. European Journal of Obstetrics and Gynecology and Reproductive Biology 2004; 116(1):3-15.

5. Ettinger AS. Children's Health, The Nation's Wealth: Assessing and Improving Child Health. National Institute of Environmental Health Science; 2004. Available at: http://aidforthehuman.org.uk/our-missions/supporting-the-children/gclid.

6. Sharifzadeh Gh, Ayatallahi A, Rajaeefard A, Namakin K. Epidemiologic study of infant mortality and its risk factors in Birjand health houses in rural areas are covered. Journal of Babol University of Medical Sciences 2013; 10(3):9-15.

7. Solimani, F. Developmental Outcome of Low Birth-Weight Premature Infants. Iranian journal of pediatrics 2007; 17(1):125-32.

8. Babapor J, Satarzadeh N, Khodaei R. Physical violence against pregnant women: risk factors and its relation to some pregnancy outcomes in women referring to Tabriz educational hospitals in 1386. Journal of Urmia Nursing and Midwifery Faculty 2007; 5(4):29-44.

9. Rahmani K, Zokaei M, Bidarpoor F, Babahajiani S, Nessaei P, Moradi G. Children Mortality Rate Trend in Kurdistan Province During 2007 to 2011. Iranian Journal of Epidemiology 2014; 10(1):65-72.

10. Muglia LJ, Katz M. The enigma of spontaneous preterm birth. New England Journal of Medicine 2010; 362(6):529-35.

11. Lim JW, Chung SH, Kang DR, Kim CR. Risk factors for cause-specific mortality of very-low-birth-weight infants in the Korean neonatal network. Journal of Korean Medical Science 2015; 30(Suppl.1):S35-44.

12. Khanal V, Sauer K, Karkee R, Zhao Y. Factors associated with small size at birth in Nepal: further analysis of Nepal Demographic and Health Survey 2011. BMC pregnancy and childbirth 2014; 14(1):32.

13. Daliri S, Karimi A, Sayeh Miri K, Bazyar J, Sayeh Miri F. Infant and maternal factors during pregnancy previous relationship with Iran underweight at birth: a systematic review and meta-analysis. The Iranian Journal of Obstetrics, Gynecology and Infertility 2016; 19(31):23-32.

14. Eghbalian F. Low birth weight causes survey in neonates. Iranian Journal of Pediatrics. 2007; 17(Suppl 1):27-33.

15. Russell RB, Green NS, Steiner CA, Meikle S, Howse JL, Poschman K, et al . Cost of hospitalization for preterm and low birth weight infants in the United States. Pediatrics 2007; 120(1): 1-9.

16. Talebian MH, Afrooz GA, Hooman HA, Aghaei A. The relationship between biological cognitive and psychosocial characteristics of parents and the weight of infant at the time of birth in Isfahan. Journal of education and health promotion 2013; 2: 34-41.

17. Gisselmann MD. Education, infant mortality, and low birth weight in Sweden 1973—1990: Emergence of the low birth weight paradox. Scandinavian Journal of Social Medicine 2005; 33(1):65-71.

18. Goodarzi E, Ghaderi E, Khazaei S, Alikhani A, Ghavi S, Mansori K, Ayubi E, Gholamaliee B, Beiranvand R, Dehghani SL, Ghotbi N. The Prevalence of Transient and Permanent Congenital Hypothyroidism in Infants of Kurdistan Province, Iran (2006-2014). International Journal of Pediatrics 2017; 5(2):4309-18.

19. Khazaei S, Mansori K, Khazaei Z, Sani M, Ayubi E. Infant and Young Child Feeding Status in Iran Compared the Different United Nation Regions. International Journal of Pediatrics 2016; 4(10):3639-41.

20. Zarbakhsh Bhari M, Hoseinian S, Afrooz G, Hooman H. Prevalence of Low Birth Weight and Comparison of Many Biological Characteristics of Low Birth Weight–Newborns, Mothers with those of normal weight-newborns' counterparts. Journal of Guilan University of Medical Sciences 2012; 21(81):3744.

21. Ansari H, Parisai Z, Rahimi E, Rakhshani F. Relationship between violence exposure pregnancy and neonatal low birth weight: A case-control study. J Jahrom Univ Sci. 2008; 6(2):17-26.

22. Baker JL, Olsen LW, Sørensen TI. Weight at birth and all-cause mortality in adulthood. Epidemiology 2008; 19(2):197-203.

23. Guyer B, Ma S, Grason H, Frick KD, Perry DF, Sharkey A, et al. Early childhood health promotion and its life course health consequences. Academic Pediatrics 2009; 9(3):142-9. e71.

24. Kliegman RM, Behrman RE, Jenson HB, Stanton BM. Nelson Textbook of Pediatrics E-Book. Elsevier Health Sciences; 2007 Aug 15.

25. Holakouie Naieni K, Ostovar A, Danesh A, Sadjedinejad S, Ghalichee L, Moradi G, et al. Comparison of Nested Case-control and Cohort Analysis Methodologies using a District TB Registry Data. Iranian Journal of Epidemiology 2010; 6(2):1-6.

26. Khalilian AR, Hamta A, Farhadi R, Ranjbaran H. Investigating the Factors Affecting the Low Birth Weight of the Infants Using Path Analysis 2011.3(2):14

27. Chaman R, Yunesian M, Golestan B, Holakoi Naeini K. The effect on morbidity and mortality in high-risk pregnancies using the method-country. Iranian Journal of Epidemiology 2007; 3(3):1-6.

28. Khazaei S, Mansori K, Khazaei Z, Ayubi E. A Look at the Phenomenon of Child Marriage in Iran and the World. International Journal of Pediatrics 2016; 4(9):3499-501.

29. Villar J, Carroli G, Wojdyla D, Abalos E, Giordano D, Ba'aqeel H, Farnot U. and et al. Preeclampsia, gestational hypertension and intrauterine growth restriction, related or independent conditions?. American journal of obstetrics and gynecology 2006; 194(4):921-31.

30. Keshavarz M, Babaei G. Comparison of pregnancy complications and healthy and gestational diabetes: a cohort study. Journal of Endocrinology and Metabolism 2004; 5(4):325-31.

31. Bahrami N, Soleimani MA, Chan YH, Masoudi R, Rabiei L. Study of Some Determinants of Birth weight in Qazvin. Journal of Clinical Nursing and Midwifery 2015; 3(4):56-64.

32. Karimlou M, Sajadi H, Dejman M. Low birth weight and its association factors in Iran: according world health organization model. Journal of Rehabilitation 2012; 13(2):75-87.

33. Namakin K, Sharifzadeh G, Malekizadeh A. To identify the risk factors in prematurity birth in Birjand, Iran: a case–control study. Iranian Journal of Epidemiology 2011; 7(3):1-5.

34. Eshraghian M, Abou AJ, Ghafari Z, Rajaei S. The Effects of Riskfactor of Pregnancy Period on Infant's Weight. The Journal of Qazvin Univ. of Med. Sci. 2008; 11(4):60-5.

35. Aregay A, Wendafrash M, Berhe S. Maternal Risk Factors Associated With Low Birth Weight in Tigray Region, Northern

Ethiopia, 2010 International Journal of Nursing Didactics 2015;5(6):11-20.

36. Demelash H, Motbainor A, Nigatu D, Gashaw K, Melese A. Risk factors for low birth weight in Bale zone hospitals, South-East Ethiopia: a case–control study. BMC pregnancy and childbirth 2015; 15(1):264.

37. Xia W, Du X, Zheng T, Zhang B, Li Y, Bassig BA, et al. A case–control study of prenatal thallium exposure and low birth weight in China. Environmental health perspectives 2016; 124(1):164.

38. Reime B, Ratner PA, Tomaselli-Reime SN, Kelly A, Schuecking BA, Wenzlaff P. The role of mediating factors in the association between social deprivation and low birth weight in Germany. Social science & medicine 2006; 62(7):1731-44.

39. Karimlou M, Sajadi H, Dejman M. Low birth weight and its association factors in Iran: according world health organization model. Journal of Rehabilitation. 2012 Jul 15; 13(2):75-87

40. Saberi M, Rahmani S. Associated anemia during pregnancy and birth weight. The Iranian Journal of Obstetrics, Gynecology and Infertility 2015; 18(142):6-10.

41. Emamghoreishi F, Iranmahbob E, Rezaei M. Iron status in mothers and their newborns. Hormozgan Medical Journal 2004; 7(3):145-9.

42. Ghavi A, Kazemnejad E. Survey associated maternal Factors with low-weight infants in Women referred to health centers in Rasht. Holistic Nursing and Midwifery Journal 2011; 21(2):35-9.

43. Mostajeran M, Hassanzadeh A, Majlessi F, Shariat M, Aghdak P. Prevalence of iron deficiency anemia in unwanted and high risk pregnancy in Isfahan province, Iran. Journal of Health System Research 2013, 9(1): 66-75.

44. Lelic M, Bogdanovic G, Ramic S, Brkicevic E. Influence of maternal anemia during pregnancy on placenta and newborns. Medical Archives 2014; 68(3):184.

45. Mosha D, Chilongola J, Ndeserua R, Mwingira F, Genton B. Effectiveness of intermittent preventive treatment with sulfadoxine–pyrimethamine during pregnancy on placental malaria, maternal anaemia and birthweight in areas with high and low malaria transmission intensity in Tanzania. Tropical Medicine and International Health 2014; 19(9):1048-56.

46. Wilken M, Bartmann P. Posttraumatic feeding disorder in low birth weight young children: a nested case–control study of a home-based intervention program. Journal of pediatric nursing 2014; 29(5):466-73.

47. Tootoonchi P. Low birth weight among newborn infants at Tehran hospitals. Iran J Pediatr. 2008; 17(2):186-92.

48. Badshah S, Mason L, McKelvie K, Payne R, Lisboa PJ. Risk factors for low birthweight in the public-hospitals at Peshawar, NWFP-Pakistan. BMC Public Health 2008; 8(1):197.

49. Elhassan EM, Abbaker AO, Haggaz AD, Abubaker MS, Adam I. Anaemia and low birth weight in Medani, Hospital Sudan. BMC research notes 2010; 3(1):181.

50. Bhaskar RK, Deo KK, Neupane U, Chaudhary Bhaskar S, Yadav BK, Pokharel HP, et al. A case control study on risk factors associated with low birth weight babies in Eastern Nepal. International journal of pediatrics 2015:6(3).1-7.

51. van den Boogaard E, Vissenberg R, Land JA, van Wely M, van der Post JA, Goddijn M, et al. Significance of (sub) clinical thyroid dysfunction and thyroid autoimmunity before conception and in early pregnancy: a systematic review. Human reproduction update 2011; 17(5):605-19.

52. Khazaei Z, Goodarzi E, Ghaderi E, Khazaei S, Alikhani A, Ghavi S, et al. The prevalence of Transient and Permanent Congenital Hypothyroidism in Infants of Kurdistan Province during 2006 to 2014. International Journal of Pediatrics 2017; 5(2):4309-18.

53. Vaidya B, Hubalewska-Dydejczyk A, Laurberg P, Negro R, Vermiglio F, Poppe K. Treatment and screening of hypothyroidism in pregnancy: results of a European survey. European Journal of Endocrinology 2012; 166(1):49-54.

54.     Wang W, Teng W, Shan Z, Wang S, Li J, Zhu L, et al. The prevalence of thyroid disorders during early pregnancy in China: the benefits of universal screening in the first trimester of pregnancy. Eur J Endocrinol 2011; 164(2):263-8.

55.     Razi S, VaziriNejad R, Rezaeian M, Sheikh Fathollahi M, Manshouri A, Goujani R, et al. Survey of Birth Weight in Newborns among Mothers with and Without a Common Underlying Disease in Rafsanjan Niknafs Maternity in 2011-2012. Journal of Rafsanjan University of Medical Sciences 2014; 13(4):323-38.

56.     Stagnaro-Green A. Maternal thyroid disease and preterm delivery. The Journal of Clinical Endocrinology and Metabolism 2009; 94(1):21-5.

57.     Idris I, Srinivasan R, Simm A, Page RC. Maternal hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome. Clinical endocrinology 2005; 63(5):560-5.

58.     Kharb S, Sardana D, Nanda S. Correlation of thyroid functions with severity and outcome of pregnancy. Annals of medical and health sciences research 2013; 3(1):43-6.

59.     Lazarus JH. Thyroid function in pregnancy. British medical bulletin 2010; 97(1):137-48.

60.     Bahri N, Iliati HR, Bahri N, Sajjadi M, Boloochi T. Effects of oral and dental health education program on knowledge, attitude and short-time practice of pregnant women (Mashhad-Iran). J Mash Dent Sch. 2012; 36(1):1-12.

61.     Clothier B, Stringer M, Jeffcoat MK. Periodontal disease and pregnancy outcomes: exposure, risk and intervention. Best Practice & Research Clinical Obstetrics & Gynaecology 2007; 21(3):451-66.

62.     Naseh M, Azin V, Zangeneh N, Lalooha F, Rezaee M, Mohammadi N, et al. The Effects of Periodontal Treatment on Incidence of Preterm Low Birth Weight among Pregnant Women with Mild to Moderate Periodontitis Journal of Isfahan Medical School 2014;32(272):16-24.

63.     Michalowicz BS, Hodges JS, DiAngelis AJ, Lupo VR, Novak MJ, Ferguson JE, et al. Treatment of periodontal disease and the risk of preterm birth. New England Journal of Medicine 2006; 355(18):1885-94.

64.     Rosa MId, Pires PDS, Medeiros LR, Edelweiss MI, Martínez-Mesa J. Periodontal disease treatment and risk of preterm birth: a systematic review and meta-analysis. Cadernos de saude publica. 2012; 28(10):1823-33.

65.     Shankaran S, Fanaroff AA, Wright LL, Stevenson DK, Donovan EF, Ehrenkranz RA, et al. Risk factors for early death among extremely low-birth-weight infants. American journal of obstetrics and gynecology 2002; 186(4):796-802.

66.     Lim JW, Chung S-H, Kang DR, Kim C-R. Risk factors for cause-specific mortality of very-low-birth-weight infants in the Korean neonatal network. Journal of Korean medical science 2015; 30(Suppl.1):S35-S44.

67.     Muchemi OM, Echoka E, Makokha A. Factors associated with low birth weight among neonates born at Olkalou District Hospital, Central Region, Kenya. Pan African Medical Journal 2015; 20(1):1-11.

68.     Rezaeian M, Goujani R, Sheikh Fathollahi M, Vaziri Nejad R, Manshori A, Razi S. A Comparative Study on Prevalence of Preterm Birth and Low Birth Weight in Iranians and Afghans Races in Rafsanjan Nik-Nafs Hospital in 2011-2012. Journal of Rafsanjan University of Medical Sciences 2014; 13(1):67-82.

69.     Sharma SR, Giri S, Timalsina U, Bhandari SS, Basyal B, Wagle K, et al. Low birth weight at term and its determinants in a tertiary hospital of Nepal: a case-control study. PloS one. 2015; 10(4):e0123962.