

The Risk Factors Affecting Low Birth Weight in Iran: An Updated Systematic Review

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ABSTRACT

Background & Objective: Given the significant role of low birth weight (LBW) in infant death and disability and relevant childhood diseases, the present systematic review was conducted to determine the factors affecting newborns' birth weight in Iran.

Materials & Methods: This study systematically reviewed all the observational studies carried out in Iran between 1990 and 2021 (retrieval date: April 28, 2021) in four steps and through searches in Persian databases (including Magiran, SID, and IranDoc) and English databases (including Embase, Cochrane Library, Web of Sciences, Google Scholar, PubMed, and Scopus). All the relevant articles were searched by two researchers separately and collected using research keywords, Boolean operators, and a combination of relevant tags depending on the type of database. The quality of the articles was evaluated with 22-item Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and Ottawa checklists, respectively.

Results: Of the 251 articles collected, 31 met the study inclusion criteria. Variables such as the mother's age (35%), body mass index (BMI) (25%), preterm childbirth, and diagnosis with a maternal chronic disease (25%) were found to be the most common causes of LBW in the reviewed studies, by order of prevalence.

Conclusion: Based on the results of this review study and given that many of the known risk factors of LBW are preventable, the timely diagnosis, proper treatment, and follow-up of women at risk can prevent the birth of LBW infants.

Keywords: Birth weight, Iran, Low birth weight, Systematic review



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Introduction

Birth weight is a major factor determining infants' survival and a reliable sign of intrauterine growth that is positively related to the child's growth and development (1). Given that low birth weight (LBW) causes mortality and increases the risk of childhood disabilities and diseases, identifying and eliminating factors that contribute to LBW is crucial (2). Studies suggest that children with a proper birth weight are at a lower risk of infant mortality, even in adverse conditions (3). On average, one in every seven children in the world is born weighing less than 2,500 g (4). LBW is defined as any birth weight of less than 2,500 g, and very low birth weight (VLBW) and extremely low birth weight (ELBW) are any weight of less than 1,500 and 1,000 g, respectively. The survival rate of infants belonging to the latter two groups is reportedly less than that in LBW

infants and has been reported as 43% in developing countries (5) and over 90% in developed countries (6). In Iran, two-thirds of the infant mortalities in the first 24 hours of birth occur in LBW babies (7).

The exorbitant costs of hospitalization and therapeutic interventions for the survival of these children and the future consequences of LBW for the child's growth and development have turned this problem into a distinct health indicator in different countries (1). Epidemiologic studies show that the risk of middle-age diseases, such as middle-age hypertension and renal diseases (8), mental disorders (9), autism (10), and diabetes and obesity (11), is higher in patients with a history of LBW. Different studies have demonstrated that various factors can be associated with LBW, including heredity (12),

parents' lifestyle (especially the mother's) (13, 14), mother's body mass index (BMI) (15, 16), mother's age and gravidity (17), socioeconomic factors (13, 16), mother's physical diseases (16), and mother's psychological disorders and history of taking sedatives during pregnancy (17). Nevertheless, factors such as economic and cultural poverty (15, 16) and environmental conditions such as environmental pollutants (18) might play a more significant role in this problem compared to the noted factors. Although maternal and neonatal health services have developed extensively, women still face many health problems during pregnancy that threaten their lives (12). First-line preventive therapy can therefore play a major part in eliminating the risk factors related to LBW. Different methods have been used in studies in Iran to investigate the effect of factors such as the mother's age, nutritional status during pregnancy, mother's medical disorders, and obstetric complications on the risk of LBW (19) and its consequences (20).

Objectives

Given the importance of the timely diagnosis of the underlying factors related to intrauterine growth restriction (IUGR) in preventing the occurrence of LBW, besides the limited number of systematic reviews carried out on this subject in recent twenty years, the current study was conducted to perform a systematic review of the factors affecting infants' birth weight in Iran. Systematic reviews investigate and summarize the results of other studies (21). The present review can therefore provide valuable information gathered from numerous studies in Iran and facilitate proper planning for the management of these risk factors in pregnancy so as to prevent LBW and its negative complications.

Materials and Methods

Search Strategy

The present systematic review was conducted on all the observational studies carried out in Iran between 1990 and 2021 (retrieval date: April 28, 2021) in four steps by searching Persian databases (including Magiran, SID, and IranDoc) and English databases (including Embase, Cochrane Library, Web of Sciences, Google Scholar, PubMed, and Scopus). In the first step, all the relevant articles were searched and collected using keywords and appropriate Boolean operators, including "and" and "or" and a combination of related tags depending on the type of database. The strategy used for search in PubMed is as follows:

("Low Birth Weight" OR "Low-Birth-Weight Infant" OR [Infant AND "Low-Birth-Weight"]) OR "Low Birth Weight Infant" OR "Low-Birth-Weight Infant" OR ["Birth Weight" AND Low] AND [Iran (tiab) OR Iran (PL) OR Iran (ad)]

In the second step, the researchers prepared a list of titles and abstracts of the relevant articles, which was separately and carefully examined by two researchers to determine and select the relevant titles.

Inclusion and Exclusion Criteria

The observational studies written in Persian or English on the causes and variables associated with LBW (<2,500 g) in Iranian society were included in the study. Exclusion criteria included case report studies, review studies, animal studies, studies conducted in non-Iranian society, lack of access to the original article, unrelated reports, interventional study, and IUGR.

Data Extraction

Using the inclusion criteria as a foundation, two reviewers independently screened the article titles and abstracts. Then, the bodies of these articles were evaluated if they met the present research criteria. Necessary information was extracted individually by two skilled reviewers, and a third reviewer was involved in case of disagreement. Necessary data, such as authors, year, place of research, population and sample size, statistical methods, type of study, and results, were extracted from the studies.

Quality Evaluation

To evaluate standard reporting of initial studies, the 22-item Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (22) was used. This checklist evaluates the title and objectives of the articles, their study population and samples, sampling method, method of controlling the sources of bias, validity and reliability of data collection tools, method of data analysis, and the results and discussion sections; it classifies the articles as poor, medium, and strong. Articles irrelevant to the study objectives, poor or repeated articles, and abstracts lacking adequate evidence (such as conference reports/lectures and translations of foreign studies) were excluded from this review. In the fourth step, the Ottawa checklist was used to investigate the quality of the reviewed studies. This checklist was designed to examine observational studies, and its maximum score is nine (23). To ensure that this systematic review was written in accordance with the proper order, we utilized the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Outcome Measures

The major outcome in the present work was the existence of LBW. The study was based on the report of LBW in the studies, as well as the expression of related risk factors. Most of the studies used questionnaires and information recorded in the patients' files.

Results

The present study investigated all the research articles conducted in Iran. In this review, at first, 2,983 papers were identified; 1,517 articles were entered and assessed according to the inclusion criteria. Of the 251 articles collected, 31 met the eligibility criteria, including 11 descriptive-analytical studies, 12 descriptive studies, one longitudinal study, and seven case-control studies (Figure 1).

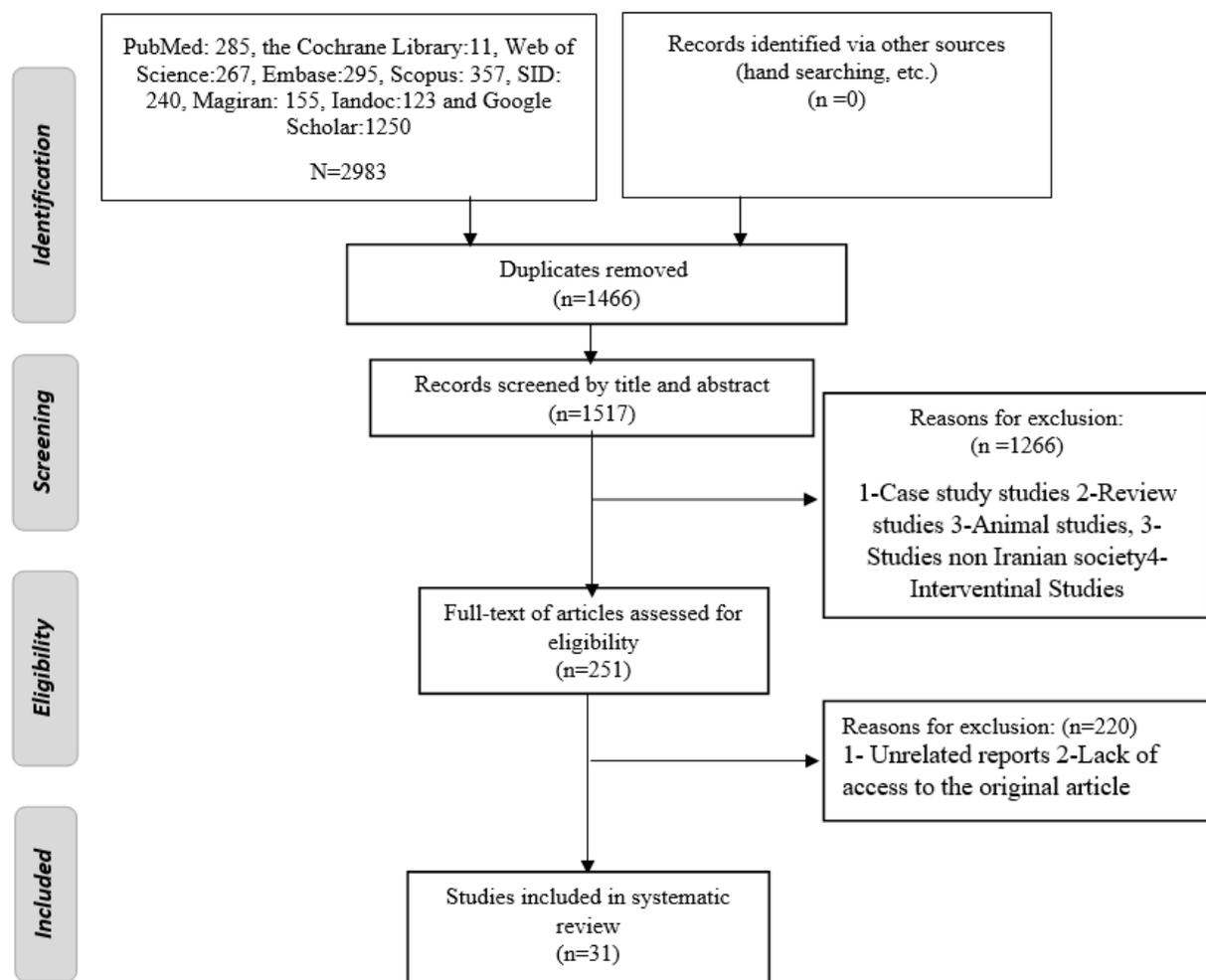


Figure 1. Flowchart for selection of studies

The sample included 156,273 pregnant women and 41,372 infants. [Table 1](#) presents the general characteristics of the reviewed articles, including author's name, study year/location, sample size, and study type. The standard reporting of all the studies was investigated using the STROBE checklist, and the scores obtained ranged from 15 to 21 ([Table 1](#)).

The studies investigated different factors that affected birth weight, and the most important ones included the mother's age (11 studies, 35%), mother's BMI (eight studies, 25%), and preterm delivery and mother's chronic diseases (eight studies, 25%), as well as gestational age, maternal education level, underlying

diseases, and infections during pregnancy (four studies, 13%). Three studies (0.09%) demonstrated a relationship between weight and two variables of gender and birth interval. Some other factors also affect birth weight; these factors that have been rarely discussed in the literature included the seasonal pattern of delivery, multiple pregnancies, marital dissatisfaction, mother's attitude to weight changes during pregnancy, planned or unplanned pregnancy, congenital anomalies, smoking, history of abortion/bleeding, no iron intake, birth order, low fruit intake, level of income, mother's occupation, awareness, place of residence, air pollution, and agent and mode of delivery.

Table 1. The general characteristics of the eligible articles

Author (Year)	Location	Population	Statistical Methods	Type of Study	Results	STROBE Score
Nasim Bahrami (2012) (24)	Qazvin	3076 women given birth	Software: SPSS-17; Tests: Independent t-test, ANOVA, linear regression; Level of significance: P<0.05	Descriptive cross-sectional	Significant relationships were observed between the seasonal pattern and the birth of low-weight infants, and the highest frequency of LBW was observed in the summer	21
Alireza Khalilian (2011) (25)	Sari	466 mothers and newborns	Software: LISREL 8 Tests: Path analysis and correlational test; Level of significance: P<0.05	Cross-sectional analytical	Preterm delivery and gestational age affected LBW	18
Arezoo Ghavi et al (2011) (26)	Rasht	83 mothers with LBW newborns	Software: SPSS-16; Tests: Kolmogorov-Smirnov, Spearman, Mann-Whitney and Kruskal; Level of significance: P<0.05	Descriptive analytical	LBW was related significantly to the type of treatment received as well as nausea and vomiting during pregnancy	16
Masoumeh Delaram (2010) (27)	Shahrekord	5102 newborns	Software: SPSS; Tests: Chi-squared and regression; Level of significance: P<0.05	Descriptive cross-sectional	Multiple pregnancies, prematurity and a female gender were predictors of LBW	17
Fariba Kahnamoeei et al. (2009) (28)	Rasht	206 pregnant women	Software: SPSS; Tests: ANOVA and correlational test; Level of significance: -	Descriptive-analytical	Positive correlations were observed between the mothers' BMI at the beginning of pregnancy and the infants' weight (P<0.00001)	17
Jamshid Yousefi et al. (2008) (29)	Mashhad	866 LBW newborns	Software: SPSS; Tests: Chi-squared, Fisher and t-test; Level of significance:-	Descriptive cross-sectional	A history of preterm delivery affected birth weight	17
Mohammadhossein Fallah et al. (2008) (30)	Yazd	941 newborns	Software: SPSS; Tests: logistic regression; Level of significance:-	Descriptive analytical	Pregnancy at below age 19, severe marital dissatisfaction, hypertension and the mother being employed increased the risk of LBW significantly (P<0.05)	18

Author (Year)	Location	Population	Statistical Methods	Type of Study	Results	STROBE Score
Flora Younesi et al. (2008) (31)	Fars	353 LBW newborns and 279 control newborns	Software: SPSS; Tests: Chi-squared and Cramér's phi; Level of significance:-	Case control	Marital satisfaction, the mother's attitude toward weight changes during pregnancy and paying attention to them and the pregnancy being wanted or unwanted differed between the case and control groups	18
Razieh Zahedi et al. (2008) (32)	Jahrom	92 LBW newborns	Software: SPSS-11; Tests:- ; Level of significance:-	Descriptive	Immaturity and preterm delivery were the most common causes of LBW	20
Baghiani Moghaddam et al] (2015) (33)	Urmia	250 newborns	Software: SPSS-15; Tests: Chi-squared and t-test; Level of significance: P<0.05	Descriptive cross-sectional	The mother's age and weight was related significantly to the infant's birth weight	21
Parichehr Tootoonchi (2007) (34)	Tehran	905 newborns	Software: SPSS; Tests: Chi-squared and Fisher; Level of significance: P<0.05	Descriptive cross-sectional	LBW was related significantly to gestational age, birth spacing, congenital anomalies, multiple pregnancies, mother's age, smoking history in recent pregnancy, medication history, previous history of LBW infants, education, mother's weight gain during pregnancy, chronic diseases, history of infertility, abortion and bleeding, pregnancy-related illnesses, infection in recent pregnancy and iron intake during pregnancy	19
Mohammadreza Eshraghian et al (2007) (35)	Tehran	191 LBW newborns and 191 control newborns	Software: SPSS; Tests: Chi-squared, independent t-test and multiple logistic regression; Level of significance: P<0.05	Case control	Birth weight was related significantly to gestational age, height and weight, mother's age, mother's bleeding or disease history, mother's education and birth order	18
Maryam Adlshoar et al. (2005) (36)	Rasht	2500 newborns	-	Descriptive correlational	LBW was related significantly to age, low intake of fruits and the father's unemployment and income (P<0.05)	18

Author (Year)	Location	Population	Statistical Methods	Type of Study	Results	STROBE Score
Ziba Mosayebi et al. (2004) (37)	Tehran	10187 LBW newborns	-	Descriptive	The mother's age was a significant contributor to LBW	19
Alireza Zohour (2002) (38)	Kerman	487 mothers given birth	Software: SPSS; Tests: Chi-squared, ANOVA and stepwise regression; Level of significance: P<0.01	Descriptive	Weight at the start of pregnancy and the mother's education were significant predictors of the infant's birth weight	17
Maryam RF RF et al. (2002) (39)	Marand	91 pregnant women	Software: SPSS-6; Tests: t-test, ANOVA and correlation test; Level of significance:-	Descriptive analytical	As an independent variable, pre-pregnancy weight was related significantly to birth weight (P<0.00002)	18
Gholamreza Garmaroudi et al. (2001) (40)	Tehran	263 LBW newborns and 277 control newborns	-	Case control	The mother's age was related significantly to birth weight (P<0.01) and primiparous women were at a higher risk of LBW than multiparous women	16
Shahin Shazeri et al. (2000) (41)	Isfahan	848 newborns	Software: SPSS Tests: Chi-squared, Mantel-Haenszel and ANOVA; Level of significance: P<0.05	Cross-sectional	Birth order and birth spacing had significant relationships with birth weight	18
Hamid Tavakkoli Ghouchani et al. (1998) (42)	Bojnord	118 newborns	-	Descriptive analytical	Birth spacing was related significantly to birth weight (P<0.002)	17
Salehi et al. (2016) (43)	Tehran	156 mothers with LBW newborns and 433 controls	Software: SPSS-16 and LISREL 8.8; Tests: Pathway analysis, logistic regression; Level of significance:-	Case control	The mother's occupation had the greatest impact on the infant's weight gain	15
Monjezi et al. (2017) (44)	Ahvaz	1500 newborns	Software: SPSS-20; Tests: ANOVA, t-test and logistic regression; Level of significance: P<0.05	Descriptive analytical	Cardiovascular diseases, anemia before pregnancy, hypertension and urinary tract infection during pregnancy and gestational diabetes were related to birth weight	19

Author (Year)	Location	Population	Statistical Methods	Type of Study	Results	STROBE Score
Moradi et al. (2017) (45)	Kordestan	182 mothers with LBW newborns and 364 controls	Software: SPSS-20; Tests: ANOVA, t-test, logistic regression; Level of significance: P<0.05	Case control	The mother's diseases were related to birth weight	17
Momeni et al. (2017) (46)	Kerman	6027 newborns	Software: SPSS-21; Tests: Chi-squared, t-test and logistic regression; Level of significance: P<0.05	Descriptive cross-sectional	Preterm delivery, a female gender, mother's age, C-section, pregnancy risk factors, mother's illiteracy, living in rural areas and delivery performed by a specialist were related to LBW	18
Karamzad et al. (2016) (47)	Tabriz	6027 newborns	Software: STATA; Tests: Chi-squared, Fisher and OR; Level of significance: P<0.01	Case control	Mother's age, age at marriage and mother's weight gain before pregnancy were related significantly to LBW	16
Khorshidi et al. (2012) (48)	Mazandaran	3792 LBW newborns	Software: SPSS-15; Tests: Chi-squared, Fisher; Level of significance: P<0.05	Longitudinal	Gender, place of residence and mother's age did not affect birth weight	16
Hashemian et al. (2012) (49)	Sabzevar	481 LBW infants	Software: SPSS-11.5; Tests: ANOVA and t-test; Level of significance: P<0.05	Descriptive analytical	Income, mother's awareness and urinary tract infections affected birth weight	18
Ahmadi et al. (2017) (50)	Tehran	600 pregnant women	Software: Statistical R version 3.2.2; Tests: PPV, NPV and regression; Level of significance:-	Cross-sectional	Gestational age, BMI in the third trimester of pregnancy and mother's age and BMI in the first trimester of pregnancy were predictors of birth weight	17

Author (Year)	Location	Population	Statistical Methods	Type of Study	Results	STROBE Score
Manouchehri et al. (2021) (51)	Kashmar	327 LBW neonate	Software: SPSS-11 Tests: ANOVA and t-test; Level of significance: P<0.05	Cross sectional	The maternal factors including history of hypertension, preeclampsia, infertility, the use of assisted reproductive techniques, and self-medication had relationship with LBW	18
Sarizadeh et al. (2020) (52)	Ahvaz	150,766 pregnant women	Software: R, Amulti-pollutant Test: generalized additive model (GAM) was used to estimate the risk ratio (RR), Level of significance: P<0.05	A time-series	Air pollution had significantly associated with LBW	20
Asgarian et al. (2020) (53)	Qom	602 newborns	Software: SPSS-18 Tests: Chi-square, Fisher exact, and independent t-tests; Level of significance: P<0.05	Retrospective	According to results preterm labor, premature rupture of membrane (PROM), showed significant association with LBW.	18
Sharifi et al. (2020) (54)	Mashahd	160 women	Software: SPSS-18 Tests: Pearson regression and linear logistics tests. Level of significance: P<0.05	Cross-sectional	low maternal hemoglobin levels associated with LBW.	17

Discussion

The present systematic review study investigated 31 articles on LBW and factors that affect birth weight. According to the results, the most frequent factors contributing to LBW in the studies included maternal age, maternal BMI, preterm delivery, and maternal chronic diseases, respectively. Adolescent mothers are naturally at risk for pregnancy complications due to biological factors and inadequate access to nutrients. A study conducted in the US showed that childbirth complications were more prevalent in adolescent mothers compared to older mothers (55, 56). However, recently, there has been greater concern about LBW in mothers over the age of 35. The mechanism proposed to explain the correlation between the mother's increased age and LBW is the higher frequency of underlying diseases and reduced cardiovascular reserves in women over the age of 35. Other mechanisms proposed include relative infertility and complications associated with it. The higher prevalence of LBW in the two age ranges (adolescence and age over

35) may also be caused by socioeconomic issues (56); nevertheless, the present study did not propose socioeconomic status as a significant risk factor contributing to LBW.

The present study revealed that BMI was another factor affecting birth weight. Women's nutritional status also played a key role in the health and growth of the fetus. The two independent factors of prenatal BMI and weight gain during pregnancy acted as important factors in maternal and fetal outcomes. Studies have confirmed the significant effect of these two factors on pregnancy outcomes, mainly in developing countries (57, 58). Certain studies have found a positive relationship between LBW and the mother's BMI at the beginning of pregnancy. Mothers with a BMI less than 18 were at a high risk of giving birth to LBW infants (59). Studies have also found a relationship between the mother's overweightness at the beginning of pregnancy and birth weight. Militic

and Murakami found that a high BMI was related to a significant increase in birth weight and proposed a positive relationship between BMI and birth weight (60, 61). A study conducted on 91 pregnant women by the faculty members of Tabriz University of Medical Sciences in Tabriz, Iran, showed a significant positive correlation between birth weight and the mother's prepregnancy weight and BMI (47). The findings of a descriptive study have shown that the mother's prepregnancy weight and BMI were the best predictors of birth weight (28). Based on the results, the mother's proper weight gain during pregnancy can be considered a significant factor preventing the birth of low-weight infants, and proper health interventions can therefore help prevent LBW (58).

Preterm delivery and IUGR can increase the risk of LBW. A study conducted in Yazd Province (Iran) found that the prevalence of low weight was ten times higher in premature infants than in normal infants (30). A study conducted in a central teaching hospital in Tehran found that 54.9% of the LBW infants were preterm, and 45% of the IUGR were term (37). A study conducted on 10,585 newborns in 18 Syrian hospitals found over half of the babies to be preterm (4). Given that the greatest part of fetal weight gain occurs in the last two months of pregnancy, a low gestational age can explain this finding.

Studies suggest that LBW is affected by the mother's diseases, such as cardiovascular and renal diseases, respiratory problems, hypertension, smoking and drinking during pregnancy, short birth spacing, and psychological tensions and depression (45). It is currently believed that hypertension in mothers is associated with a pathologic rise in their thromboxane/prostacyclin indexes and the defective trophoblastic production of prostacyclin and probably nitric oxide together with a constant rise in some nutrients (such as endothelin), which can then increase vascular resistance, decrease systemic perfusion, and thereby decrease intrauterine growth and fetal weight (62). Studies also suggest that fetal weight is significantly affected by renal diseases in the mother, including pyelonephritis, glomerulosclerosis, chronic glomerular disease, and lupus glomerulonephritis, which are significantly correlated with IUGR. In all these cases, IUGR is associated with the loss of the proteins related to these processes (63).

Fink *et al.* found that renal diseases in pregnancy were related to an increased risk of preterm labor and LBW (64). LBW is positively correlated with increased infant mortality and is a determining factor involved in infant mortality. In fact, the most common cause of infant mortality is LBW, followed by low Apgar scores and gestational age at pregnancy termination (51). A study conducted by Mosayebi *et al.* in Tehran, Iran, showed that the mortality of hospitalized LBW infants was 27.6%, and the most common causes of infant mortality were hyaline membrane disease, asphyxia, and sepsis, respectively (37).

The main causes of LBW were multi-factorial (multiparous mothers, maternal harmful substances exposure (pesticide, noise, radiation, and alcohol consumption) and undernutrition (no intake of fresh vegetables), bacterial infections, poor socioeconomic status, history of chronic diseases, hepatitis B carriers before conception, and placental abnormalities) in the world. Lack of or inadequate antenatal care (ANC) and pregnancy complications increased the risk of LBW in infants (65-67). In line with our study, most of the maternal factors are effective, and since race and culture are also effective, this difference is observed in different studies.

A limitation of the present study was the limited number of case-control and cohort studies among the evaluated articles. The non-homogeneity in the type of studies and the failure to investigate each confounding variable, which were beyond the researcher's control, comprised another limitation of this research.

Conclusion

Based on the results and since many of the known factors contribute to preventable risk factors, the timely diagnosis, proper treatment, and follow-up of women at risk can prevent the birth of low-weight infants. Providing pre-pregnancy care to adolescent women, women over age 35, and women with abnormal BMIs and underlying diseases can help alleviate pregnancy complications.

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Ethical Permission

The work proposal was permitted by the Ethics Committee affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran, with the code of ethics IR.SBMU.PHARMACY.REC.1397.107.

Authors' Contributions

NS and SH considered the study, interpreted the results, and co-wrote the manuscript. ZK and SH collected the data, assisted with information interpretation, and co-wrote the manuscript. All the authors read and accepted the last manuscript.

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Conflict of Interest

The author declared no conflict of interest.

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