Epidemiology of low birth weight in Iran: A systematic review and meta-analysis

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ABSTRACT

Introduction: Low birth weight (LBW) is an important general health indicator. The present study was conducted to evaluate the prevalence and risk factors of LBW in Iran.

Method: This meta-analysis was reported based on the PRISMA guidelines. All stages were independently performed by two authors. This review is registered with PROSPERO (CRD42020163446). We searched epidemiological studies at international databases of Scopus, Embase, Science Direct, PubMed/Medline, CINAHL, EBSCO, Cochrane Library, Web of Science, and Google Scholar search engine, as well as Iranian databases of SID, IranDoc, Iranian National Library, Barakat Knowledge Network System, RICST and Magiran using MeSH keywords without time limit until 2019. After selecting the studies, applying the inclusion and exclusion criteria, data extraction and qualitative assessment, the data were analyzed based on random effects model using Comprehensive Meta-Analysis Software version 2. P < 0.05 was considered significant.

Results: The prevalence of LBW in Iran was 7.95% (95% confidence interval [CI]: 7.36–8.58) in 62 studies with a sample size of 301,839 newborns. The prevalence of LBW in girls and boys was 8.41% (95% CI: 7.47–9.45) and 6.67% (95% CI: 5.86–7.59), respectively. The girls-to-boys odds ratio of LBW was 1.25 (95% CI: 1.13–1.39, P < 0.001) very LBW and extremely LBW prevalence was estimated to be 0.61% (95% CI: 0.40–0.93) and 0.29% (95% CI: 0.18–0.45), respectively. The risk factors for LBW were age of < 20 vs. ≥ 20 years (P < 0.001), education of middle school and lower vs. high school and higher (P < 0.001), weight under 50 kg (P = 0.001), employed vs. housekeeper (P < 0.001), inadequate prenatal care (P = 0.046), interval with previous pregnancy < 2 vs. ≥ 2 (P < 0.001), prematurity (P < 0.001), history of LBW (P < 0.001), multiple birth (P < 0.001), abortion (P < 0.001), vaginal bleeding (P < 0.001), hypertension (P = 0.001) and preeclampsia (P < 0.001).

Conclusion: The results of this meta-analysis showed that LBW is prevalent in Iran. This study can be a national database for LBW that would be of interest to Iranian health policy-makers and planners.

1. Introduction

Low birth weight (LBW) is an important general health indicator, which is defined by the World Health Organization (WHO) as weight at birth less than 2500 g [1]. It is estimated that around 15.5% of newborns are born with LBW each year, and more than 95.6% of them are born in developing countries, while about 72% of LBW newborns are born in Asia and 8% are born in the eastern Mediterranean region, including Iran [2, 3]. The prevalence of LBW in developed and developing countries was estimated to be 5–7% and 19%, respectively [2].

LBW is one of the main causes of neonatal mortality, accounting for about 40% of all mortality among children under five years of age, and the mortality rate in LBW infants is approximately twenty times higher than heavier infants [1, 4]. The etiology of LBW is complex and is influenced by several factors such as demographic factors, maternal nutrition, reproduction and socioeconomic factors such as inadequate care and difficult physical labor during pregnancy, family's deprivation of social protection, low levels of education and financial poverty [5, 6, 7]. Additionally, infections, multiple pregnancies and complications of pregnancy such as preeclampsia, maternal emotional distress,
Substance abuse, smoking, infertility, preterm labor, and intrauterine growth restriction (IUGR) are associated with LBW [8, 9, 10, 11].

LBW imposes an economic burden on the health care system, which is equal to one-third of the world’s medical expenses [12]. In addition to health-related issues such as the need for hospital care, infants with LBW are at risk for chronic diseases and mental disabilities compared to infants with normal weight [13, 14]. LBW can be one of the major factors affecting growth disorder, cognitive development defects, and increased rate of diseases such as infectious diseases during pregnancy and childhood [15]. It is worth noting that recent epidemiological studies have shown that in people with LBW, the risk of developing chronic diseases in adulthood such as hypertension, coronary disease, kidney disease, diabetes, stroke and obesity is higher [16, 17]. Education level, age, poor diet, gravidity and parity, lack of proper prenatal care, as well as economic and social status are most important factors predicting of LBW risk [17, 18, 19, 20].

Several studies have been conducted in Iran on LBW [18, 19, 20, 21, 22, 23, 24]. In systematic reviews and meta-analyses, a complete picture of the dimensions of a problem in society can be presented by examining all relevant documentation and providing a general assessment [25, 26, 27]. Obviously, with the increase in the number of studies involved in the process of analysis, the confidence interval is reduced and the overall estimate is more reliable [27, 28]. Therefore, the present meta-analysis was conducted to determine the prevalence and risk factors of LBW in Iran.

2. Materials and methods

2.1. Study protocol

This meta-analysis was reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses [26]. The study stages included the search strategy, the selection of studies, the qualitative assessment of studies, data extraction and statistical analysis. All these steps were independently performed by two authors. In the case of dispute, a third author was consulted. This review is registered with PROSPERO (CRD42020163446). Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020163446.

2.2. Search strategy

We searched epidemiological studies at nine international databases of Scopus, Embase, Science Direct, PubMed/Medline, CINAHL, EBSCO, Cochrane Library, Web of Science, and Google Scholar search engine, as well as six Iranian databases of Scientific Information Database (SID) (http://www.sid.ir/), Iranian Research Institute for Information Science and Technology (IranDoc) (https://irandoc.ac.ir), Iranian National Library (http://www.nlai.ir/), Barakat Knowledge Network System (http://health.barakatkins.com), and Regional Information Center for Science and Technology (RICST) (http://en.ricest.ac.ir/), and Magiran (http://www.magiran.com/) using MeSH and non MeSH keywords including “prevalence”, “Incidence”, “epidemiology”, “frequency”, “newborn”, “infant”, “neonate”, “underweight”, “abnormal birth weight”, “birth outcome”, “low birth weight”, “preterm birth” and “Iran” without time limit until 2019. To perform a combined search, the ‘AND’ and ‘OR’ functions were used. An example of the PubMed search strategy were (prevalence OR epidemiology OR frequency) AND (newborn OR Infant OR neonate OR underweight OR abnormal birth weight OR birth outcome OR low birth weight OR preterm birth) AND (Iran). The manual search was also done using the list of references in the selected or review articles.

2.3. Selection of studies

First, all related articles, whose affiliation included Iranian authors, were collected and after completing the search and removal of duplicates, two independent researchers screened the titles. After the screening process, we reviewed the summary. If there were doubts about eligibility of the article based on the abstract, the full text was examined and if the full text was not available, we contacted the author.

Figure 1. PRISMA flowchart.
Table 1. Summary of studies entered into meta-analysis.

| Ref. | First author, Published Year | Year Design Place | Sample size (N*) | LBW (%) | Quality |
|------|-----------------------------|-------------------|-----------------|---------|---------|
| [18] | Mirahmadizadeh A, 2017      | 2014 Cross-sectional Fars | 3594 1811 1778 | 8.7     | High    |
| [19] | Momeni M, 2017              | 2014-5 Cross-sectional Kerman | 6027 29961 28226 | 9.42    | High    |
| [20] | Golestan M, 2011            | 2008 Cross-sectional Yazd | 5897 | 8.79    | Moderate |
| [21] | Rafiei M, 2007              | 2005 Cross-sectional Arak | 4022 2051 1971 | 9.1     | High    |
| [22] | Delaram M, 2008             | 2005 Cross-sectional Shahr-e-Kord | 5102 2637 2465 | 8.5     | Moderate |
| [23] | Shadzi Sh, 2000             | 1996-7 Cross-sectional Isfahan | 848 391 445 | 6       | Moderate |
| [24] | Zarbakhsh Bhari M, 2012     | 2008-9 Cross-sectional Gilan | 32471 6.95 | High    |
| [25] | Hajian K, 2011              | 1998 Cross-sectional Babol | 1087 550 528 | 6.2     | Moderate |
| [26] | Eslami Z, 2002              | 2005-10 Cross-sectional Ardabil | 6832 | 6.32    | Moderate |
| [27] | Pasdary, 2010               | 2010 Cross-sectional Kerman | 32450 5.7 | Moderate |
| [28] | Hashemian Nejad, 2014       | 2011-12 Cross-sectional Sabzevar | 7599 | 6.32    | High    |
| [29] | Karamzad N, 2013            | 2014 Cross-sectional Tabriz | 7353 | 6.4     | High    |
| [30] | Roudbari M, 2013            | 2011 Cross-sectional Yasuj | 1000 | 7.19    | High    |
| [31] | Khoori E, 1999              | 1996 Cross-sectional Gorgan | 2183 1107 1076 | 6.3     | Moderate |
| [32] | Wafaie SM, 2005             | 2004 Cross-sectional Neishabour | 1240 587 522 | 11.79   | High    |
| [33] | Zahed Pasha Y, 2004         | 2000 Cross-sectional Babol | 2228 1134 1082 | 7.7     | High    |
| [34] | Yousefi J, 2015             | 2007-8 Cross-sectional Mashhad | 866 | 16.5    | Moderate |
| [35] | Khorsheid M, 2013           | 2011-12 Cross-sectional Mazandaran | 3792 1899 1893 | 2.9     | Moderate |
| [36] | Rafati S, 2005              | 2002-3 Cross-sectional Tehran | 1927 985 921 | 11.79   | Moderate |
| [37] | Talebian MH, 2013          | 2009 Cross-sectional Isfahan | 9579 | 9.5     | High    |
| [38] | Jafari F, 2010              | 2004 Cross-sectional Zanjan | 4510 2368 2142 | 6.80    | Moderate |
| [39] | Vahdaninia M, 2005          | 2005 Cross-sectional Tehran | 3734 | 4.7     | High    |
| [40] | Taheri FA, 2006             | 2004 Cross-sectional Birjand | 2558 | 7.9     | Moderate |
| [41] | Toootoonchi P, 2007         | 2005-6 Cross-sectional Tehran | 905 395 514 | 8.6     | High    |
| [42] | Younesi F, 2008             | 2004-7 Cross-sectional Fars | 2228 1134 1082 | 7.7     | High    |
| [43] | Saeedi R, 2011              | 2012 Cross-sectional Mashhad | 461 221 240 | 6.72    | High    |
| [44] | Ranjbaran M, 2015           | 2013-4 Cross-sectional Arak | 461 221 240 | 6.72    | High    |
| [45] | Nachvak SM, 2012            | 2002-7 Cross-sectional Tehran | 866 | 16.5    | Moderate |
| [46] | Ahmadi P, 2017              | 2005-9 Cross-sectional Tehran | 600 237 312 | 9.5     | High    |
| [47] | Safari M, 2013              | 2013 Cross-sectional Garmser | 681 340 340 | 4.7     | High    |
| [48] | Mahmoodi Z, 2013            | 2012 Cross-sectional Tehran | 7353 | 6.4     | High    |
| [49] | Mousa-farkhani E, 2002      | 2001 Cross-sectional Quchan | 803 426 377 | 12      | Moderate |
| [50] | Shahika M, 2008             | 2000-1 Cross-sectional Rasht | 5897 | 4.92    | High    |
| [51] | Veghari G, 2009             | 2007 Cross-sectional Gorgan | 2881 | 9.8     | Moderate |
| [52] | Nili F, 2002                | 1999-2000 Cross-sectional Tehran | 2357 | 16      | Moderate |
| [53] | Fadaii B, 2009              | 2009-10 Cross-sectional Isfahan | 941 | 9.35    | Moderate |
| [54] | Fallah MH, 2008             | 2007 Cross-sectional Yazd | 941 | 9.35    | Moderate |
| [55] | Ebrahimian M, 2008          | 1995-6 Cross-sectional Tehran | 1500 812 688 | 19.1    | Moderate |
| [56] | Eghbalian F, 2007           | 2004-5 Cross-sectional Hamedan | 350 | 8.57    | High    |
| [57] | Tayebi T, 2013              | 2010 Cohort Sari | 1500 812 688 | 19.1    | Moderate |
| [58] | Bahrami N, 2014             | 2010 Cross-sectional Qazvin | 3076 1572 1407 | 6.7     | High    |
| [59] | Shahiri P, 2012             | 2008 Cross-sectional Alborz | 808 379 429 | 4.9     | High    |
| [60] | Tabatabi S, 2010            | 2007 Cross-sectional Tehran | 2050 | 7.7     | High    |
| [61] | Eftekhari H, 2007           | 2005 Cross-sectional Bandar Abbas | 5893 | 4.395   | Moderate |
| [62] | Koohdani F, 2010            | 2001-3 Cross-sectional Tehran | 225 | 7.10    | Moderate |
| [63] | Garmaroudi Gh, 2001         | 1996-7 Cross-sectional Tehran | 5893 | 4.395   | Moderate |
| [64] | Sharififard G, 2012         | 2010 Cross-sectional Isfahan | 225 | 7.10    | Moderate |
| [65] | Faramarzi M, 2005           | 2001-3 Cross-sectional Babol | 3275 | 11.20   | High    |

(continued on next page)
Table 1 (continued)

| Ref. | First author, Published Year | Year | Design | Place | Sample size (N*) | LBW (%) | Quality |
|------|-----------------------------|------|--------|-------|-----------------|---------|---------|
| [88] | Nojomi M, 2006              | 2003 | Cross-sectional | Tehran | 430               | 12.79   | High    |
| [89] | Sobhi A, 2013               | 2008–2011 | Cross-sectional | Fariman | 7763              | 6.1     | Moderate |
| [90] | Khojateh F, 2016           | 2014 | Cross-sectional | Zahedan | 2227              | 4.84    | Moderate |
| [91] | Delvarianzadeh M, 2007     | 2005 | Cohort | Shahrood | 424              | 13      | Moderate |
| [92] | Sharifzadeh F, 2012        | 2008 | Cohort | Tehran   | 576               | 13.02   | High    |
| [93] | Moghadam-Banaei L, 2010    | 2008 | Cross-sectional | Tehran | 344              | 3.5     | High    |
| [94] | Goujani R, 2014            | 2011 | Cross-sectional | RafaSanjan | 5532            | 7.066   | High    |
| [95] | Hoseini M, 2009             | 2004–5 | Cohort | Tehran-Shemiran | 610          | 11.79   | Moderate |
| [96] | Alizadegh Sh, 2014          | 2010–11 | Cross-sectional | Guilan | 590              | 4.10    | High    |
| [97, 98] | Omani-Samani R, 2018    | 2015 | Cross-sectional | Tehran | 4899             | 5.16    | High    |
| [99] | Rafiei M, 2008              | 2004 | Cross-sectional | Arak | 10241           | 5241    | 5000    | 8.99 High   |
| [100] | Judipour Z, 2015           | 2013 | Cross-sectional | Sistan and Baluchestan | 1712         | 9.3     | Moderate |
| [101] | Amani R, 2000              | 1995–6 | Cross-sectional | Ahvaz | 876              | 7.3     | Moderate |
| [102] | Oskouie F, 2006            | 2005 | Cross-sectional | Tehran | 1000             | 14.7    | Moderate |
| [103] | Adlshoar M, 2005           | 2003 | Cohort | Rasht   | 2500             | 5.2     | Moderate |
| [104] | Golestani M, 2008          | 2004 | Cohort | Yazd    | 6016             | 8.4     | Moderate |
| [105] | Momenabadi V, 2017         | 2015 | Cross-sectional | Shiraz | 250              | 1811    | 1778    | 18 High    |

Number.

2.4. Inclusion and exclusion criteria

The inclusion criteria according to PICO (based on Evidence Based Medicine) [28] were: 1) Population: Epidemiologic studies (cross-sectional, cohort, and case-control) that examined the prevalence and risk factors of LBW; 2) Intervention: Weight less than 2500 g to confirm LBW and subcategories include very low birth weight (VLBW), which is less than 1500 g, and extremely low birth weight (ELBW), which is less than 1000 g; 3) Comparison: Evaluation of the demographic, medical diseases, obstetrics and gynecology variable in infants with LBW and without LBW for risk factors; 4) Outcome: Estimating the prevalence and risk factors of LBW.

The exclusion criteria were: 1) Non-Iranian studies; 2) Studies with non-random sample size to estimate the prevalence of LBW; 3) Non-related studies; 4) Duplicate studies; 5) Case reports, Case series, Letter to Editor, Editorial, Commentary and review; and 6) Low quality studies.

2.5. Definition

LBW defined by the WHO as weight at birth less than 2500 g. Subcategories include VLBW, which is less than 1500 g, and ELBW, which is less than 1000 g [1].

2.6. Qualitative assessment

To assess the quality of selected studies, the Modified Newcastle-Ottawa scale for non-randomized studies and its adapted form for cross-sectional studies was used [29]. This checklist includes 7 questions, each receiving up to 10 stars. Therefore, the quality of studies was divided into three categories: unsatisfactory (less than 5 stars), satisfactory (5–7 stars) and good (8–10 stars). Finally, the scores given to the articles were compared by the two researchers and discussions were held on differences. The minimum score for entering the meta-analysis process was 5.

2.7. Data collection

The two authors independently extracted the data, including the first author, year of publication, year of study, sample size (total, girl, and boy), study design, LBW prevalence, VLBW prevalence, ELBW prevalence, geographic area of study, number of LBW and normal LBW in available variables. Any disagreement was resolved in consultation with a third person as a judge.

2.8. Evidence assessment

The overall methodological quality of each analysis was classified according to the Grading of Recommendations, Assessment, Development, and, Evaluation (GRADE), taking into account study limitations (risk of bias), inconsistency, imprecision, indirectness, and publication bias. Then, the quality of the evidence was divided into three categories: high, moderate, low or very low [30].

2.9. Statistical analysis

To determine the prevalence of LBW, the total number and the number of events were used. To estimate the risk factors of LBW, we used the total number and the number of events in both case and control groups and we calculated the odds ratio (OR) and 95% confidence interval (CI). Heterogeneity of studies was evaluated using Cochran’s Q test and I² index. In this regard, the interpretation is as follows: 0–25% may not be important, 25–49% may indicate a moderate heterogeneity, 50–75% indicates substantial heterogeneity, and over 75% indicates significant heterogeneity [31]. Moreover, in order to find the cause of heterogeneity, subgroup analysis and meta-regression were performed [32]. Based on the Dersimmonian-Laird test, the random effects model was used in this study to combine the data [33]. To ensure the strength and validity of the findings, sensitivity analysis was performed by omitting a study at a time [34]. Specifically, the subgroup analysis was performed based on year of study, type of study, sample size, study quality, geographical region and province. Any probable bias in the publication was evaluated using the Egger and Begg’s tests [35]. Data were analyzed using Comprehensive Meta-Analysis Software (CMA) version 2. In this study, p < 0.05 was considered statistically significant.

3. Results

3.1. Overview of search

In the initial search, 640 studies were obtained and 320 duplicate studies were deleted. After reviewing the full text of 138 related articles, 63 articles were excluded due to lack of necessary criteria and finally, 75 eligible studies entered the qualitative assessment stage (Figure 1). Table 1 shows the characteristics of each study.
3.2. LBW, VLBW, and ELBW prevalence

Total heterogeneity for prevalence of LBW, VLBW, and ELBW was very high in the studies (Heterogeneity test: $P < 0.001$, $I^2 = 97.03\%$ for LBW, $P < 0.001$, $I^2 = 94.17\%$ for VLBW, and $P < 0.001$, $I^2 = 85.29\%$ for ELBW). The prevalence of LBW in Iran in 62 studies with sample size of 301,839 infants was estimated to be 7.95\% (95\% CI: 7.36–8.58). The lowest and highest LBW were related to studies in Mazandaran (2011-2) (2.9\%) and Hamadan (2004–5) (19.1\%), respectively (Figure 2). VLBW and ELBW prevalence was estimated to be 0.61\% (95\% CI: 0.40–0.93) and 0.29\% (95\% CI: 0.18–0.45), respectively (Figure 3).

3.3. Subgroup analysis

The subgroup analysis of LBW is shown in Table 2. The variables of geographical area ($P = 0.066$), study design ($P = 0.196$), quality ($P = 0.957$), sample size ($P = 0.241$) and year of studies ($P = 0.088$) were not significant, but the subgroup analysis of provinces ($P < 0.001$) was significant (Table 2).

3.4. LBW based on gender

Total heterogeneity was very high for prevalence of LBW in girls and boys (Heterogeneity test: $P < 0.001$, $I^2 = 93.18\%$ for girls gender and...
heterogeneity test: $P < 0.001$, $I^2 = 93.40\%$ for boys gender). The prevalence of LBW in girls in 25 studies with a sample size of 60,557 infants was 8.41% (95% CI: 7.47–9.45). The prevalence of LBW in boys in 25 studies with a sample size of 64,989 infants was 6.67% (95% CI: 5.86–7.59) (Figure 4-A,B). The female-to-male OR of LBW was 1.25 (95% CI: 1.13–1.39, $P < 0.001$) (Figure 4-C).

3.5. LBW based on place of residence

Total heterogeneity was very high for prevalence of LBW in urban and rural studies (Heterogeneity test: $P < 0.001$, $I^2 = 95.13\%$ for urban studies and heterogeneity test: $P < 0.001$, $I^2 = 95.18\%$ for rural studies). The prevalence of LBW in urban areas (14 studies with a sample size of 41,454 infants) and rural areas (13 studies with a sample size of 58,593 infants) were 6.94% (95% CI: 5.82–8.26) and 6.93% (95% CI: 5.72–8.38). The urban-to-rural OR of LBW was 1.01 (95% CI: 0.86–1.19; $P = 0.842$) (Figure 5).

3.6. Risk factors for LBW

The demographic risk factors for LBW, including age of $>35$ versus $\leq 35$ (1.41 [95% CI: 1.04–1.90], $P = 0.024$), age of $<18$ vs. $\geq 18$ years (1.39 [95% CI: 1.20–1.61], $P < 0.001$), education of middle school and lower vs. high school and higher (1.56 [95% CI: 1.28–1.90], $P < 0.001$), weight under 50 kg (2.49 [95% CI: 1.45–4.26], $P = 0.001$), employed vs. housewife (2.40 [95% CI: 1.52–3.80], $P < 0.001$) were significant, but smoking (3.52 [95% CI: 0.85–14.48], $P = 0.081$) was not significant (Table 3).

The obstetrics and gynecology risk factors for LBW, including inadequate prenatal care (1.54 [95% CI: 1.00–2.30], $P = 0.046$), interval with previous pregnancy $<2$ vs. $>2$ years (2.14 [95% CI: 1.46–3.14], $P < 0.001$), prematurity (13.86 [95% CI: 4.99–38.49], $P < 0.001$), history of LBW (3.57 [95% CI: 1.91–6.67], $P < 0.001$), multiple birth (13.20 [95% CI: 4.82–36.12], $P < 0.001$), abortion (1.28 [95% CI: 0.60–2.73], $P = 0.651$), vaginal bleeding (2.56 [95% CI: 1.83–3.57], $P < 0.001$) but unwanted pregnancy (1.64 [95% CI: 0.90–3.00], $P = 0.106$), nulliparity (1.14 [95% CI: 0.99–1.32], $P = 0.059$) and cesarean section (1.11 [95% CI: 0.76–1.62, $P = 0.584$]) were not significant (Table 3).

Risk factors of medical diseases for LBW, including hypertension ($P = 0.001$) and preeclampsia ($P < 0.001$) were significant but diabetes mellitus ($P = 0.77$), urinary tract infection ($P = 0.133$), pregnancy-induced hypertension (0.094) were not significant (Figure 6).

3.7. Meta-regression

The meta-regression model showed that the changes in the prevalence of LBW were not significant based on the year of study (meta-regression coefficient: -0.003, 95% CI: -0.019 to 0.012, $P = 0.663$). In addition, this model was not significant for the prevalence of LBW in girls (meta-regression coefficient: -0.009, 95% CI: -0.035 to 0.17, $P = 0.497$) and boys (meta-regression coefficient: -0.003, 95% CI: -0.031 to 0.024, $P = 0.801$) and also VLBW (meta-regression coefficient: 0.067, $P = 0.001$, $I^2 = 94.17\%$)
3.8. Sensitivity analysis and publication bias

The sensitivity analysis showed a strong point estimate by eliminating a study at a time for prevalence of LBW, VLBW, and ELBW (SF 3, 4). Publication bias was not significant for the prevalence of LBW based on P-values of Egger and Begg’s tests were 0.746 and 0.836, respectively. The publication bias was not significant for the female-to-male odds ratio of LBW based on Egger (P = 0.829) and Begg’s test (P = 0.387). Publication bias is shown in SF 5 file in the form of a funnel plot.

4. Discussion

The Millennium Development Goals (MDGs) are aimed at reducing the mortality of children under the age of 5 to two-thirds. The most important factor that can affect the survival of infants is LBW. This is an important health index in any country [106]. One of the goals of sustainable development is to reduce the mortality rate of infants to below 12 per 1,000 live births in all countries by 2030. The neonatal mortality rates in Iran have been reported to be 13.3 infants according to the World

95% CI: -0.004 to 0.139, P = 0.065 and ELBW (meta-regression coefficient: 0.055, 95% CI: -0.041 to 0.151, P = 0.262) (SF [Supplementary figure] 1, 2).

Table 2. Subgroup analysis of LBW based on region, quality of studies, study design, Provinces, year, and sample size.

| Variable                  | Studies (N°) | Sample (N) | Heterogeneity | 95% CI | Pooled prevalence (%) |
|----------------------------|--------------|------------|---------------|--------|------------------------|
| **Region**                 |              |            |               |        |                        |
| Center                     | 29           | 94154      | 7577          | 95.69  | 0.001                  |
| East                       | 9            | 27442      | 2106          | 96.87  | 0.001                  |
| North                      | 15           | 73969      | 4916          | 95.75  | 0.001                  |
| South                      | 7            | 72333      | 6602          | 92.70  | 0.001                  |
| West                       | 2            | 33950      | 2136          | 99.73  | 0.001                  |
| Test for subgroup differences: Q = 8.800, df(Q) = 4, P = 0.066 |
| Quality                    |              |            |               |        |                        |
| High                       | 30           | 173298     | 14254         | 95.45  | 0.001                  |
| Moderate                   | 32           | 128541     | 9084          | 97.68  | 0.001                  |
| Test for subgroup differences: Q = 0.003, df(Q) = 1, P = 0.957 |
| Study design               |              |            |               |        |                        |
| Cross-sectional            | 57           | 291713     | 22500         | 98.17  | 0.001                  |
| Cohort                     | 5            | 10126      | 837           | 94.14  | 0.001                  |
| Test for subgroup differences: Q = 1.67, df(Q) = 1, P = 0.196 |
| Provinces                  |              |            |               |        |                        |
| Khuzestan                  | 2            | 1684       | 104           | 75.86  | 0.042                  |
| Qazvin                     | 2            | 3326       | 229           | 51.47  | 0.151                  |
| Kerman                     | 2            | 65805      | 6069          | 96.99  | 0.001                  |
| Mazandaran                 | 5            | 12398      | 800           | 98.02  | 0.001                  |
| Tehran                     | 12           | 29811      | 2259          | 97.67  | 0.001                  |
| Sistan and Baluchestan     | 3            | 5179       | 413           | 96.41  | 0.001                  |
| Hamadan                    | 1            | 1500       | 287           | 0      | -                      |
| Kermanshah                 | 1            | 32450      | 1850          | 0      | -                      |
| Qom                        | 1            | 1927       | 227           | 0      | -                      |
| Markazi                    | 3            | 14724      | 1318          | 31.55  | -                      |
| Chaharmahal va Bakhtiari    | 1            | 5102       | 434           | 0      | -                      |
| Kohgiloyeh and Boyerahmad  | 1            | 1000       | 72            | 0      | -                      |
| Semnan                     | 2            | 1105       | 87            | 95.63  | 0.001                  |
| South Khorasan             | 1            | 2558       | 202           | 0      | -                      |
| Ardabil                    | 2            | 14815      | 902           | 0.845  | 0.001                  |
| Fars                       | 2            | 3844       | 358           | 95.60  | 0.001                  |
| Gilan                      | 4            | 41548      | 2799          | 93.71  | 0.001                  |
| Golestani                  | 3            | 5414       | 450           | 89.85  | 0.001                  |
| Isfahan                    | 4            | 16157      | 1257          | 96.88  | 0.001                  |
| Razavi Khorasan            | 5            | 19705      | 1491          | 97.98  | 0.001                  |
| Zanjan                     | 1            | 4510       | 307           | 0      | -                      |
| Test for subgroup differences: Q = 560.43, df(Q) = 21, P < 0.001 |
| **Year**                   |              |            |               |        |                        |
| 1996-2005                  | 31           | 91883      | 7356          | 96.97  | 0.001                  |
| 2006-2015                  | 31           | 209956     | 15982         | 97.10  | 0.001                  |
| Test for subgroup differences: Q = 2.91, df(Q) = 1, P = 0.088 |
| **Sample**                 |              |            |               |        |                        |
| ≤1000                      | 22           | 13838      | 1305          | 90.43  | 0.001                  |
| 1001-10000                 | 35           | 142379     | 10066         | 97.35  | 0.001                  |
| >10000                     | 5            | 145622     | 11426         | 99.14  | 0.001                  |

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a Number.

b Confidence interval.
Figure 4. Prevalence of LBW in girls (A), boys (B) and an odds ratio of girls-to-boys (C).
Bank collection of development indicators [107], which could be due to improvements in Iran's national health system.

The prevalence of LBW in Iranian studies has been reported between 2.9% and 19.1% in different regions. In the present meta-analysis, the national prevalence of LBW in Iran among 301,839 infants was estimated to be 7.95%. The prevalence of LBW in 2015 was estimated to be worldwide (14.6%), Sub-Saharan Africa (14.0%), Southern Asia (26.4%), Northern Africa (12.2%), Southeastern Asia and Oceania (12.2%), Central Asia (5.4%), Eastern Asia (5.3%), Western Asia (9.9%), Latin America and Caribbean (8.7%) [108]. Considering high heterogeneity of LBW prevalence in Iranian studies, subgroup analysis was done to find its cause, and province (P < 0.001) was the only significant factor. Therefore, the prevalence of LBW varies according to differences in health care quality, sample size, and socioeconomic and cultural conditions in different regions of Iran, so it should be considered by policy makers and health care providers.
The meta-regression model for LBW prevalence did not change significantly based on the year of study (between 1993 and 2017). In a systematic global review article, its prevalence was 17.5% in 2000 and 20.6% in 2015 [108].

The sickest and youngest infants are often missed from information systems, including those who die soon after birth, or are hospitalized elsewhere. The information system and communication system should be improved to obtain information about these vulnerable infants. Incorrect classification of premature infant mortality as “stillbirths” still exists. Since these infants are more likely to suffer from LBW, failure to consider mortality may lead to underestimation of the prevalence of LBW. Therefore, it is important that any newborn, whether alive or dead, is registered in the information system [109]. Social and family demand for birth weight data is an issue that is not discussed. There is little information about family and community perceptions and the demand for birth weight measurement, including cultural barriers to birth weight measurement, especially in some areas of the community and for stillbirths.

Preterm delivery plays a major role in developing LBW. A systematic review and meta-analysis reported the prevalence of preterm labor to be 9.2% in Iran and considered it a relatively common problem in Iran [110].

In evaluating the effect of gender on LBW, we found that the prevalence of LBW in females was significantly higher than that of males. In a study conducted in Japan, there was a significant relationship between female gender and low birth weight [111], and it was also found that the mean birth weight of male infants was higher than that of female infants [112].

To assess the risk factors for preterm birth, a systematic review article in Ethiopia showed that maternal age (over 35) are more likely to suffer from LBW. This finding is similar to other studies [113, 114, 115]. The employment of pregnant women in hard, troublesome, and active jobs is among the factors affecting LBW, early delivery and fetal death [116]. Working conditions are also important predictors of the outcome of pregnancy and childbirth. Various studies have shown that type of occupation as well as working conditions may lead to LBW [117, 118, 119, 120]. Similarly, other studies have shown that economic status, education, and weight during pregnancy may play an important role [121].

In the present study, there was no significant relationship between smoking and LBW. But smoking should be considered as a dangerous side effect for pregnant women. Some studies show that any type of smoking during pregnancy may lead to LBW, cognitive impairment, respiratory problems, birth defects, early delivery, and even infant death [122, 123, 124, 125].

The risk factors for gynecologic and obstetric care in the present study included interval of less than 2 years with the previous pregnancy, inadequate prenatal care, prematurity, LBW history, multiple sclerosis, abortion and vaginal bleeding. In a review article in developing countries, maternal age of 35–49 years, illiteracy, inadequate antenatal care, delayed conception, and being in the poorest socioeconomic stratum were among the risk factors for increasing LBW [126].

Another review article emphasized the role of inter-pregnancy interval and found that it has significant effect on the short intervals between pregnancies for outcomes: extremely preterm birth (< 6 month aOR: 1.58 [1.40, 1.78], 6–11 month aOR: 1.23 [1.03, 1.46], moderate preterm birth (<6 m aOR: 1.41 [1.20, 1.65], 6–11 month aOR: 1.09 [1.01, 1.18]), low birthweight (<6 month aOR: 1.44 [1.30, 1.61], 6–11 month aOR: 1.12 [1.08, 1.17]), stillbirth (aOR: 1.35 [1.07, 1.71] and early neonatal death (aOR: 1.29 [1.02, 1.64]) [127]. A review article in Ethiopia showed that maternal age <20 years (aOR = 1.7; 95% CI: 1.5–2.0), BMI <18.5 kg/m2 (aOR = 5.6; 95% CI: 1.7–9.4), pregnancy interval <24 months (aOR = 2.6; 95% CI: 1.4–4.2), and premature (aOR = 6.4; 95% CI: 2.5–10.3) are among LBW risk factors [128].

In the present study, the relationship between cesarean section and LBW was not significant. Some studies show that LBW is higher in women with CS delivery. However, this conclusion is controversial, while in other studies, the risk of LBW was not reported to be higher in CS delivery [129].

The medical risk factors in the present study were LBW, hypertension and preeclampsia. The association between LBW and preeclampsia has
been confirmed in other countries [130, 131, 132]. Other meta-analytical studies have shown the effect of anemia on LBW and Small for gestational age [133, 134]. It is recommended that attention be paid to thyroid disorders and LBW in future meta-analytical studies [135].

The strengths of this study: 1. We used a comprehensive search strategy to maximize the identification of all relevant literature. 2. Following the PRISMA protocol, we were able to provide the largest data on LBW in Iran to date. 3. We contacted the first author or the corresponding author to eliminate the ambiguity of the articles. 4. We used random effects model to integrate the data to provide a conservative estimate of the prevalence of LBW, and subgroup analysis and meta-regression model were performed to detect the cause of heterogeneity and to evaluate the publication bias. Limitations of the present study: 1. Search in national databases was limited due to limitations in combined search in these databases. 2. Studies on specific infants such as preterm infants, etc. or non-random sample sizes were excluded and the resulting

Figure 6. Relationship of low birth weight and diabetes mellitus (AND), hypertension (B), urinary tract infection (C), induced pregnancy hypertension (D) and preeclampsia (E).
estimate may be attributable to the general public. 3. In addition, there was a high heterogeneity between studies in the meta-analysis, and based on available data, we could attribute this difference to the provinces under study (P < 0.001), but there appears to be other causes, including differences in lifestyle, dietary habits, ethnicity (given that Iran has different ethnicities with different customs [136]) may also be effective, which could not be investigated using the available data.

5. Conclusion

The results of this meta-analysis showed that LBW is prevalent in Iran. Effective risk factors in LBW in Iranian population include low and high maternal age, low level of education, low maternal weight, occupation, inadequate prenatal care, short interval with previous pregnancy, prematurity, LBW history, multiple sclerosis, abortion, income, inequality and poverty, maternal smoking, maternal alcohol and drug use, and the relationship of maternal subclinical hypothyroidism during pregnancy and preterm birth: a systematic review and meta-analysis, Iran. J. Obst. Gynecol. Infertil. 19 (40) (2017) 69–78.

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