Factors Relating to Iron Deficiency Anemia in Pregnancy: An Integrative Review

Abstract

Introduction: Anemia is a condition in which the blood’s hemoglobin concentration is abnormally low as a result of the lack of one or more essential nutrients. Caused by iron deficiency, this condition can impair the mental and psychomotor development, reduce the individual’s work performance, reduce resistance to infection and cause increased maternal and child morbidity and mortality. In pregnant women, the causes for the development of this anemic context are varied and include a nutritional deficiency and hormonal problems related to the menstrual cycle and endometrial and pregnancy complications.

Objective: Identifying the factors associated with iron deficiency anemia in pregnancy.

Method: This is an integrative literature review. The databases were consulted LILACS and PubMed. It used the descriptors: anemia, iron deficiency anemia, pregnant and pregnancy. The results were obtained through the selection of 06 articles through a detailed reading and then data were organized in frames summaries.

Results: Anemia during pregnancy is not caused by an isolated factor and should be treated as a problem of different causes. The factors related to iron deficiency anemia in pregnancy, referred to by the authors were: socio-economic, with reports in three articles; obstetric, mentioned by five analyzed products; and health indicators in four articles. All the evidence has been proven statistically by multivariate analysis with logistic regression model or linear, except for one study, whose analysis was univariate.
Introduction

Anemia is considered a serious public health problem today; it is defined by the World Health Organization (WHO) as “a condition in which the blood’s hemoglobin concentration is abnormally low as a result of the lack of one or more essential nutrients, any that is the origin of this lack”[1].

Caused by iron deficiency, it is the most common nutritional deficiencies and accounts for over 90% of cases, resulting in a negative balance between the amount of biologically available iron and an organic need. This condition can impair the mental and psychomotor development, reduce the individual’s work performance, reduce resistance to infection and cause increased maternal and child morbidity and mortality[2].

In Brazil, anemia has been found in various states of the country and is committed sensitive groups such as children, adolescents and women of childbearing age, pregnant and lactating women. This disease affects much of the female population, since their physiology makes it more suited to the development of this framework. From this perspective, the United Nations, in 1990, outlined goals for the coming decade, among which the reduction in the prevalence of anemia in women and in pregnant women seemed to be relevant[3]. However, especially in pregnant women, the causes for the development of this framework anemic are varied and include a nutritional deficiency and hormonal problems related to the menstrual cycle and endometrial and pregnancy complications.

The pregnancy, in turn, results in countless modifications to the woman’s body, and some can trigger anemic frames. The passage of iron through the placenta into the fetal needs, for example, has a negative balance of this nutrient in the body of the woman, as is the maternal organism responsible for the complete nutrition of the embryo.

Thus, this research aims to answer the following questions: What factors are related to anemia during pregnancy? There are diseases that affect pregnant women and that interfere in the occurrence of anemia? The objective is to identify factors related to iron deficiency anemia in pregnancy.

Method

It is an integrative literature review, an approach that allows, from the analysis of the data, having a support helps in decision-making and improve clinical practice. The integrative review process includes six distinct stages, similar to conventional research stages of development[4]:

1st) Issue identification and selection of the research question - begins with the definition of a problem and formulate a research hypothesis that

Conclusion: We can see the need to prioritize the socio-economic condition of the poorest populations in the planning of public policies and the need for a more effective prenatal care as a primary goal to reduce the gestational anemia index, including active search of these women in the community. Health education is also relevant, parallel to the improvement of health conditions of the population.
has relevance to health. In this sense, to think of anemia in pregnant women, the central question of this study was: What factors are related to iron deficiency anemia during pregnancy?

2nd) Criteria for the selection of the sample - In April 2015, the survey of information by searching the databases of the Virtual Health Library (BVS) was performed: Latin American and Caribbean Health Sciences (LILACS) and the international database Medical Published - service of the US National Library of Medicine (PubMed). We used the descriptors: anemia, iron deficiency anemia, pregnancy, pregnant (2086 articles in PubMed); In LILACS database, using the descriptors anemia, iron deficiency anemia, pregnancy, pregnancy, and pregnant women were found 92 articles.

For best direction in the pre-selection of items and to increase the amount of these was decided to use two descriptors for search. So they used the descriptors anemia or iron deficiency anemia is: pregnancy, pregnancy and pregnant women (totaling six searches in each database). The filters were applied: survey conducted in humans in the past decade, published in Portuguese, English or Spanish, with abstracts and full text available clinical studies.

Exclusion criteria were literature review articles of the narrative type and preliminary study. Articles published in Portuguese, English and Spanish were included, with abstracts and full text available on the selected databases; which they referred to factors related to iron deficiency anemia in pregnancy, the method adopted allowed to obtain strong evidence (level 1, 2, 3 and 4), ie, systematic review with or without meta-analysis, randomized clinical study (RCS) with over 1000 patients, RCS with less than 1000 patients and cohort study. These evidences were adopted considering the question that guided this review, because it is clinical question[5].

However, given the minimal publishing with these designs, it was decided to include the observational/transversal studies. The strategies used to search for articles in the databases were adapted, because such bases present specific characteristics. Thus, the research was guided by the question and inclusion and exclusion criteria, to maintain consistency in the search for articles and avoid possible biases. Thus, in PubMed and LILACS, searching totaled 42 articles and 35 articles, respectively.

3rd) Identification of pre-selected and selected studies - was held at first reading the summaries; in reading were found repeated articles in LILACS and PubMed databases, applying the combination of descriptors in pairs, as mentioned. Pre-selected were six articles of LILACS and PUBMED.

It was later performed in full, a close reading of the pre-selected articles and verified their suitability for inclusion criteria of the study. In this reading of the LILACS items was excluded for not presenting statistical analysis on the results. Then, the consolidation of the findings of this research was based on six selected articles.

4th) Categorization of studies - analogous stage to collecting the conventional survey data. For data collection of articles has been used an instrument validated by Ursi[6], containing the following items: identification of the original article, methodological characteristics of the study, assessment of the methodological rigor of measured interventions and findings. Through data collection instrument it was possible an individual assessment of the studies included, both methodologically, and in relation to the synthesis of the results. Keeping in mind the issue problem, the findings were listed by reading and the inclusion criteria previously mentioned.

5th) Analysis and interpretation of results - for the analysis and subsequent synthesis of the articles that met the inclusion criteria was used a summary table specially built for this purpose, which included the following aspects considered relevant: the name of research, the authors name and fac-
tors related to iron deficiency anemia in pregnancy. Finally, analyzed descriptively in the light of scientific evidence.

6th) Presentation of synthesis of knowledge - the evidence was gathered and synthesized and conclusions of studies questioned because of their limitations.

Results

Frame 1 shows the articles, title, purpose, study type and level of evidence. Regarding the articles published by year of publication, are: 2013 with 2 (two) articles; 2009 and 2008 with one (1) item a year; 2006 two (2) items.

Regarding the language found, there were 02 articles in English, three in Portuguese and one in Spanish. A publication was the result of the research carried out in Vietnam, Southeast Asia[7]; one in Cienfuegos, Cuba city[8]; and four were studies conducted in Brazil, in the South, an article[9]; Northeast Region, one article[10]; one in the Central West Region[11] and one in the South and Midwest[12].


In the analysis of the journals subject of publications, stood out Periodicals area of obstetrics and gynecology[8-10], magazines nursing area[12], area of Science and Medicine[7] and the area of Nutrition[11].

The method used in four articles was the Cross study, considered weak evidence (level 5)[8,10-12]; an intervention (level 4), to be carried out <1000 patients[9]; and population prospective study (level 2)[7].

Although most studies have applied analytical statistics with reliable statistical tests, casts doubt on generalizations about the studied object, because besides the methodological designs were of weak evidence, the sample size was small, which does not reveal representation.

Evidence about factors related to iron deficiency anemia in pregnancy

In response to the main question of this integrative review: “What factors are related to anemia during pregnancy”, the frame 02 presents a summary of the analyzed articles.

After analysis of the publications, the factors related to iron deficiency anemia in pregnancy, referred to by the authors were: socio-economic, with reports in three articles[9,10,12]; obstetric, cited by all analyzed productions, except Vitolo et al.[9]; health indicators in four articles[8,10-12]. It is worth mentioning that all the evidence, as expressed in Frame 2, were statistically proven, through multivariate analysis with logistic regression model or linear, except for one study[11], whose analysis was univariate.

Discussions

In Frame 02 citations were grouped corresponding to the above subject. Among the approaches to the factors related to iron deficiency anemia during pregnancy, it has been seen that the obstetrical are the ones that stood out in the studies, highlighting the multipregnancies, advanced gestational age, previous miscarriage, late onset of pre-natal and pre few queries natal. As regards health indicators factors were cited overweight/obese pre-pregnancy and during pregnancy, pre-pregnancy weight below 50kg, son of loss history for abortion or mortality in the first year of life. Socioeconomic included: education less than eight years, marital status - with a partner, younger age of the mother and or his companion, reside in rural areas, do not have toilet in residence, per capita income less than US$ 1.00/day largest number of family members.

All factors had representative significance for research, demonstrating the relevance of this study to
Frame 1. Characterization of the analyzed publications, according to author(s), title, goals, type of study and level of evidence.

<table>
<thead>
<tr>
<th>Articles</th>
<th>Title/Language/Journal (Database)</th>
<th>Objective</th>
<th>Type of the study / Sample</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fujimori et col. [12]</td>
<td>Anemia in pregnant women of municipalities in the southern and Central-Western Brazil. Portuguese Rev Esc Enferm USP (LILACS)</td>
<td>Analyze the distribution of anemia in pregnant women served in basic network public health services of two municipalities a in the South, and another in the Central-Western Brazil.</td>
<td>Cross-sectional study Medical records of 954 and 781 pregnant women in Cuiaba-MT and Maringa-PR, respectively.</td>
<td>5</td>
</tr>
<tr>
<td>Vitolo et col. [9]</td>
<td>Low educational level as a limiting factor for combating anemia among pregnant women Portuguese Rev. Bras. Ginecol. Obstet. (LILACS)</td>
<td>Assess the impact and the accession of an intervention based on prescription iron supplement and food guidelines in the hemoglobin levels in pregnant women of a Basic Health Unit. Evaluate the prevalence and risk factors for anemia.</td>
<td>Intervention study 92 pregnant women in the control group 76 in the intervention group (Clinical with &lt; 1000 patients)</td>
<td>Level 4</td>
</tr>
<tr>
<td>Álvarez et col. [8]</td>
<td>Iron deficiency and anemia in pregnant women in urban area of the municipality of Cienfuegos. Spanish Rev Cubana Obstet Ginecol (LILACS)</td>
<td>Determine the relationship between the presence of anemia and socioeconomic demographic variables, obstetric history and nutritional habits.</td>
<td>Cross-sectional study 150 pregnant women, 50 in each quarter, randomly selected.</td>
<td>5</td>
</tr>
</tbody>
</table>

**Frame 2.** Characterization of publications as the factors related to iron deficiency anemia in pregnancy.

<table>
<thead>
<tr>
<th>Article</th>
<th>Statistics/Results</th>
<th>Factors related to iron deficiency anemia in pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tran et col.[7]</td>
<td>Multivariate Analysis: Chi-square test for the model fitting with values of p greater than 0.05, indicating a good fit, Root Mean Square error of approximation (RMSEA) with values less than 0.05, indicating a good fit and Tucker-Lewis index (TLI) and comparative fit index (CFI), with values greater than 0.95, indicating a good fit.</td>
<td>Women with 2 or more pregnancies, they were at the end of gestation and had iron deficiency anemia in early pregnancy [OR: 16.72 (CI 95% 3.46 - 29)].</td>
</tr>
<tr>
<td>Camargo et col. [11]</td>
<td>Univariate analysis: Kolmogorov-Smirnov test, Student’s t-test and Mann-Whitney test, Chi-square test or Fisher exact. The significance level was set at 5%.</td>
<td>- Prior Abortion - low iron serum (p = 0.03) and low transferrin saturation (p = 0.02). - Overweight or obesity before pregnancy - low iron levels (p = 0.04).</td>
</tr>
<tr>
<td>Fujimori et col. [12]</td>
<td>Multivariate Analysis: Odds ratio (OR), Chi-square tests, student’s t test and variance analysis.</td>
<td>In Maringa-PR the Hb differ statistically in function of: - Marital status-with companion (p = 0.013). - Previous pregnancies (&gt; 2) (p = 0.006); - III quarter Gestations (p &lt; 0.001). In Cuiabá-MT this difference can be observed: - The age (&lt; 20) (p = 0.011). In Cuiabá-MT this difference can be observed: - Number of previous pregnancies (&gt; 2) (p = 0.020); - III quarter Gestations (p &lt; 0.001). In Cuiabá-MT this difference can be observed: - Nutritional status (overweight/obesity) (p = 0.039).</td>
</tr>
<tr>
<td>Article</td>
<td>Statistics/Results</td>
<td>Factors related to iron deficiency anemia in pregnancy</td>
</tr>
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<td>-------------------------</td>
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</tbody>
</table>
| Ferreira et col. [10]   | Identified the Gaussian distribution (Kolmogorov - Smirnov test) and homogeneity of the variances of the errors (test Levene); we decided to perform the multiple linear regression analysis (MCRLM). | - Live in rural areas (p = 0.03).  
- Prenatal onset (after the first trimester of gestation) (p = 0.002).  
- Child loss history by effecting or mortality in the first year of life (p < 0.001).  
- Do not have toilets in residence (p < 0.001).  
- Before pregnancy Weight < 50 kg (p = 0.03).  
- Per capita Income of less than $ 1.00/ day (p = 0.02);  
- Largest number of members in the family (p = 0.02).  
- Lower maternal age (p = 0.04) and/or your partner (p = 0.03) |  

- Before pregnancy Weight < 50 kg (p = 0.03).  
- Univariate analysis:  
  - Increased number of pregnancies (p < 0.001) and abortions (p < 0.001);  
  - Short pregnancy time (p = 0.002);  
  - Greater gestational age (3rd quarter) (p = 0.008).  

- Logistic regression (p < 0.005):  
  - Pregnancy gemelar.  
  - Increased gestational age (3rd quarter). |

| Vitolo et col. [9]      | Logistic regression (OR: IC 95%) p < 0.05.  
Schooling less than 8 years (OR: 3.4 (IC 95% 1.6-7.1) p = 0.001). | -  
- -  
- -  

| Álvarez et col. [8]     | Logistic regression to relate the connection between the selected variables and the existence of iron deficiency and anemia. Accepted a p = 0.05 (95% reliability) | -  
Univariate analysis:  
- Increased number of pregnancies (p < 0.001) and abortions (p < 0.001);  
- Short pregnancy time (p = 0.002);  
- Greater gestational age (3rd quarter) (p = 0.008).  
Univariate analysis and logistic regression (p < 0.005):  
- Lower consumption of meat and egg in week.  
- Logistic regression (p < 0.005):  
  - Pregnancy gemelar.  
  - Increased gestational age (3rd quarter). |
control gestational anemia, problem that can lead to losses to the fetal maternal health.

We noted, from the results, that obstetric factors were the most important throughout the entire research, since on all items were present at least one of its variables. In three articles\cite{7-8,12} it observed that the number of pregnancies has been one of the factors related to anemia, ie women with more than two pregnancies are more likely to have low serum iron.

During pregnancy, maternal body undergoes many changes and there is a need to adapt. At that stage, it is common woman presents iron deficiency\cite{13}. This fact is understood by the increased blood volume from the first trimester of pregnancy, due to hormonal action, which influences the renin-angiotensin-aldosterone. Thus, there is a 50% increase in blood volume (1200 ml to 1500 ml) compared to non-pregnancy period. Even with the arrangements that the body seeks to adapt this stage, the increase in packed cell volume is disproportionate to the increase in plasma volume, resulting thus in a decrease of hematocrit, hemoglobin and blood viscosity, resulting in one body physiological state of anemia in pregnancy.

Nevertheless, the decrease in circulating hemoglobin concentration as a result of the pregnancy period, not always causes great damage to maternal and fetal health\cite{13}. However, multiple pregnancies can cause a progressive exhaustion causing a higher tendency to develop anemia, apart from the fact that every birth, a woman has blood loss, estimated between 500 and 1.000 ml, resulting from lacerations of tissues and/or uterine contractions which can result in a future organic overhead, leaving the body more fragile and prone to new episode of anemia.

Women with gestational age were also more likely to anemia, since, with the progression of pregnancy, there is an increased need for blood to the fetus and the mother, with a more pronounced blood dilution. Also in the first trimesters of pregnancy the mean corpuscular volume (MCV) increases slightly and may mask the iron deficiency\cite{13}. Therefore, hemoglobin values, hematocrit and ferritin levels are decreased, mainly from the second trimester of pregnancy. This corroborates research\cite{14} that found that ferritin levels decline with increasing gestational age.

The previous abortion related to gestational iron deficiency anemia was a factor pointed out and addressed in two studies\cite{10-11}, which showed low serum iron (\(p = 0.03\)) and low transferrin saturation (\(p = 0.02\)) in women with abortion prior. We can base the results by the fact that, when a woman has an abortion, there is a significant blood loss resulting in uterine atony that stems from uterine hypocontractility and leads to a hemorrhage that progresses to anemia due to heavy loss of blood volume. On abortion, women have greater difficulty in physiologically return to pre-pregnancy state of the body as it passes through various stages to achieve the balance of the body, before an event that is not physiological\cite{13}.

Prenatal is a variable that has meaning for this search, since it is a factor that can help prevent anemia during pregnancy, since in the professional prenatal visit has as one of the primary functions prevent, diagnose and treat maternal anemia. Two factors that can highlight the results were the high rate in the number of pregnant women with early prenatal care late and the fewest prenatal appointments, especially in women who had anemia\cite{7,10}.

In the context of health promotion, prenatal shows evidence that it is effective and can ensure better health for mother and child if done with quality, since the governmental public actions can prevent and control anemia in pregnancy cycle when prescribing supplementation with supplementary iron from the 20th week of pregnancy and also when guidance is provided as to adequate food and the treatment of chronic blood loss. Prenatal plays an important role in focused health education\cite{15},
since the guidelines given in prenatal consultation are of crucial importance, especially when started as early as possible. Prenatal consultation strategy must work to nutrition counseling throughout monitoring of pregnancy and, preferably, has been initiated in the period before pregnancy, adding to iron supplementation.

Health indicators in one of the variables most observed in the study was obesity/pre-pregnancy and pregnancy overweight as an important factor when it takes into account the occurrence of gestational anemia. In a survey\(^\text{[11]}\), among others, it was revealed that foods like spaghetti and other pastas were often consumed by pregnant women, often because they know that the common wheat food is fortified with iron. However, it should be noted that the consumption of fortified foods should be done with caution, since all exaggeration can bring harm, one of the main obesity/overweight, which can often have the effect of influence on anemia index, and other problems such as hypertension and diabetes.

On the other hand, some studies have shown that low gestational weight can also be an important indicator related to anemia. Four articles analyzed\(^\text{[7-8,10,12]}\), which showed this relationship, were guided directly to the precarious socioeconomic status, which can subsidize the speech that with low socioeconomic status, the pregnant woman has no way to have a power quality, rich in iron and protein necessary for gestational demand. This condition is associated with other factors limiting pregnant women’s access to better food and living conditions. Thus, the iron stores in these women are minimal. In that sense, public policies, among them the incentive to satisfactory completion of prenatal care may be important early detection strategy, prevention and treatment of iron deficiency anemia in pregnancy.

Among the socio-economic factors related to iron deficiency anemia in pregnant women, low education stands out\(^\text{[9]}\). In that case, explained the difficulty of pregnant women with less education to adhere to prenatal care and iron supplementation and understand the importance of proper nutrition for their health and nutrition.

The gestational anemia rates were also present in cases of marital status - with fellow residents in rural areas, do not have toilet, per capita income less than US$ 1.00/day and greater numbers of family members; all of which are influential factors and directly linked to poor social conditions\(^\text{[10]}\). The combination of these data is worrying, while presenting concrete result, since the population living conditions is a factor that defines a specific demographic profile. In this case, showing the poverty rate and its influence on pregnancy and bringing as one of its consequences the propensity to gestational anemia due to iron deficiency.

The younger the patient was slightly associated with gestational anemia. However, there was a study\(^\text{[10]}\) that this condition considered a risk factor for anemia, justifying the growing demand of pregnant teenager who needs a proper iron demand. Juxtaposing to gestational necessity culminates to iron deficiency anemia. Furthermore, financial instability affected by younger women and often mate, may also influence the relationship pregnancy and anemia, since socioeconomic factors influencing the proper acquisition of iron rich food.

**Synthesis of knowledge**

The survey results show the factors that are related to anemia during pregnancy, highlighting the socioeconomic, obstetric and health indicators. These results make us think that there is only one single factor that can explain the occurrence of gestational anemia and needs to be analyzed the history of pregnant women as a whole, as well as a rescue your health history. All the evidence has been proven statistically by univariate and multivariate or with logistic regression model and or linear. Howe-
ver, the methodological designs used in research are considered weak evidence; the sample size was small, revealing representation.

We know that the dependence of the human body by iron led him to create mechanisms that would allow its efficient absorption, storage and conservation, but some factors can bring imbalance in reserves and iron absorption in the body, like this pregnancy. During pregnancy, iron demand increases and with it, the body cannot balance the extra need for iron.

All the studies analyzed showed that anemia in pregnancy is not caused by a single factor and should be treated as a problem of varying causes. Thus, alternatives to treat it vary by individual. It is important; however, that further studies are carried out by addressing specific laboratorial examinations in various stages of pregnancy, so it is established, through analytical and descriptive statistics, what factors related to anemia during pregnancy. Therefore, effective action plans can be drawn, as well as mechanisms that enable the identification of anemia in pregnant women, so that action is taken early, reducing complications of this pathological condition so common during pregnancy.

Conclusion

It is understood, from a study of the articles in this research, that iron deficiency anemia during pregnancy is a complex phenomenon and the factors related to it are not isolated. We realize the need to prioritize the socioeconomic status of the poorest populations in the planning of public policies and the need for a more effective prenatal care, while primary goal to reduce the gestational anemia index, including the active pursuit of these women, in the community. Health education is also relevant, parallel to the improvement of health conditions of the population.

It should be noted that iron deficiency anemia, although it is a common problem in pregnant women, can bring great harm to health of the mother and child as it is related to preterm labor, low birth weight, among others, may lead to death.

References


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