



## **Intrauterine Growth Restriction and risk factors associated in Brazil**

### **Restrição de Crescimento Intrauterino e os fatores de risco associados no Brasil**

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#### **ABSTRACT**

**Introduction:** Intrauterine Growth Restriction is defined as the inability of the fetus to reach its growth potential and can be caused by maternal, placental, and fetal factors. **Objective:** The study aims to bring great social contribution, to help the health sectors in the development of actions aimed at improving the quality of life of pregnant women, promoting changes in behaviors harmful to the fetus and thus contributing to reduce infant morbidity and mortality. **Methodology:** A bibliographic survey was carried out in the Scielo, PubMed and VHL databases, between 2010-2020, with the descriptors and their combinations in Portuguese and English, using the Boolean operators: "fetal growth retardation" OR "intrauterine growth retardation" OR "intrauterine growth restriction" AND "risk factors" AND "intrauterine growth restriction" AND "Brazil". After applying inclusion and exclusion criteria, 10 articles were selected. **Results:** The analysis of the articles showed that Intrauterine Growth Restriction is strictly related to five themes: evolution in prenatal treatment; socioeconomic factor; low birth weight; fetal mortality and serum leptin concentration, eclampsia, and HIV. **Conclusion:** The available analyses on the main categories related to IUGR showed that the lack of prenatal care, precarious socioeconomic status, low leptin concentration during pregnancy, preeclampsia, and viral infections, such as HIV, are risk factors present for IUGR in Brazil.

**Keywords:** Growth restriction, Risk factors, Intrauterine.

#### **1 INTRODUCTION**

Intrauterine Growth Restriction (IUGR) is defined as the inability of the fetus to reach its growth potential. The diagnosis is made in the intrauterine period, through serial ultrasound



evaluations (LAUSMAN et al., 2013). After birth, the diagnosis is clinical through the clinical evaluation of nutritional status and anthropometric measurements (METCOFF et al., 1994) and has been considered as a synonym of small newborn for gestational age (one who has weight below the 10th percentile for gestational age and sex) (NAUFEL, 2003). The occurrence of IUGR varies according to the risk factors involved and the sociodemographic profile of the population studied (ZANETTE et al., 2010). This condition is also associated with the clinical measure of low birth weight (LBW) (SADOVSKY et al., 2016), which leads to an investigation into a possible relationship between the associated risk factors and the cause of an IUGR.

IUGR can be caused by maternal, placental, and fetal factors. The main maternal factors are chronic hypertension, diabetes mellitus, cardiovascular diseases, illicit drug use and autoimmune diseases. As placental causes are placental infarcts, vascular malformations, placental insufficiency and, among the fetal causes are infections, congenital malformations, and chromosomal disorders (BRODSKY, CHRISTOU, 2004). In addition to these factors, IUGR is related to the precarious socioeconomic situation of the pregnant woman, smoking, malnutrition, and lack of prenatal care and during childbirth. It is noteworthy that growth restriction leads to a higher risk of death and neonatal diseases (VETTORE et al., 2010 apud FONSECA et al., 2012).

Analyzing the epidemiology of IUGR Sharma (2016) points out that, in developing countries, the incidence of intrauterine growth restriction is six times higher when compared to developed countries, it also points out that this incidence differs between countries, populations and races and increases with the decrease in gestational age.

As long-term consequences, newborns with IUGR develop complications, both in the school environment and in health, and may have their physical, mental, and cognitive development impaired (RUGOLO, 2005 apud FONSECA et al., 2012).

It is noteworthy that fetal growth restriction, when associated with low birth weight and prematurity, is considered a serious public health problem, being responsible for an increase in perinatal morbidity and mortality (FONSECA et al., 2012).

In this context, this study is justified because it can bring great social contribution, and can help the health sectors in the development of actions aimed at improving the quality of life of pregnant women, promoting changes in behaviors harmful to the fetus and thus contributing to reduce infant morbidity and mortality, with the objective of raising the main risk factors associated with IUGR in Brazil.



## 2 METHODOLOGY

This is an Integrative Literature Review study. To survey the articles in the literature, a search was conducted in the following databases: *Scielo*, *PubMed* and *VHL*. The following descriptors and their combinations in Portuguese and English were used to search for the articles, using the Boolean operators: "*fetal growth retardation*" OR "*intrauterine growth retardation*" OR "*intrauterine growth restriction*" AND "*risk factors*" AND "*intrauterine growth restriction*" AND "*Brazil*".

The inclusion criteria defined for the selection of articles were: articles published in Portuguese, English; clinical trial articles, meta-analysis, systematic review that portray the theme related to the review and articles published and indexed in these databases in the last 10 years.

The exclusion criteria defined for the selection of articles were: non-original articles, articles of integrative reviews, books, dissertations and theses and articles that addressed the theme, but from a different point of view.

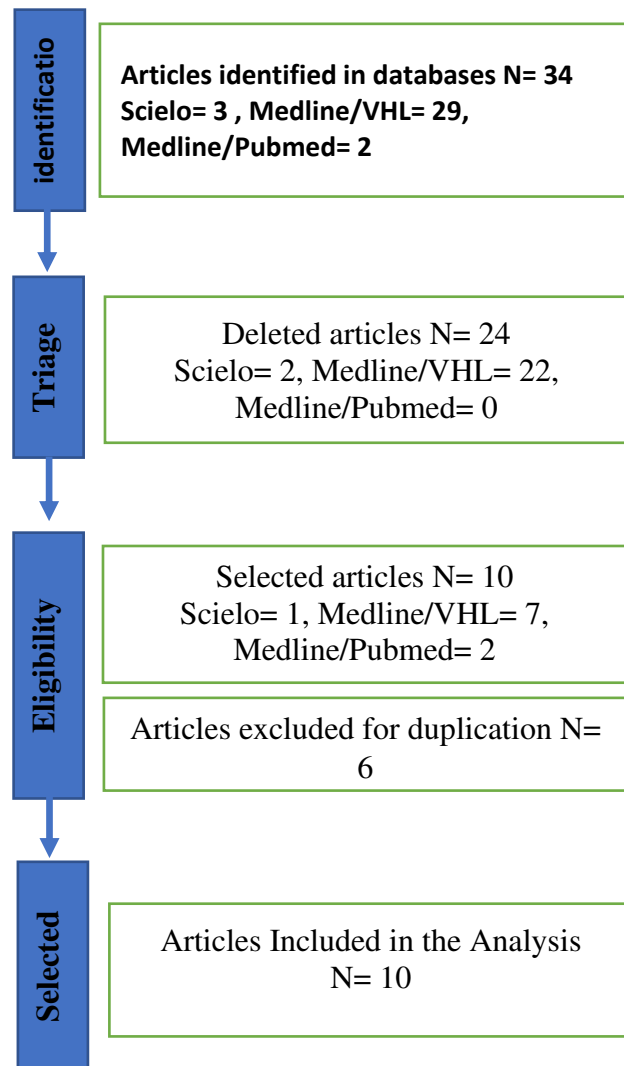
The analysis and synthesis of the selected studies were carried out descriptively, making it possible to observe, count, describe and classify the data, in order to gather the knowledge produced on the theme explored in the review.

The final sample of this review consisted of 10 scientific articles, selected by the inclusion and exclusion criteria previously established.

### 3 RESULTS AND DISCUSSION

Characteristics of the reviewed articles:

Figure 1 – Flowchart of identification and selection of publications according to the PRISMA *Statement*



Of the 34 articles on **Intrauterine Growth Restriction and Associated Risk Factors**, published in the period 2010 – 2020, initially identified, 10 were included in this review. The other 24 articles were excluded because they did not meet the previously established inclusion criteria. In addition, the selected articles were published mostly in (Portuguese/English) in journals such as *Cadernos de Saúde Pública*, *Revista da AMRIGS*, *BMC Pediatrics*, *Revista do Instituto de Medicina Tropical de São Paulo*, *BMC Research Notes*, *Karger*, *Journal of Biosocial Science*, *Cambridge University Press* and *BMC Pregnancy and Childbirth*.

The quantitative study design was the majority, being 90% of the articles, followed by the qualitative design (10% of the articles).

The use of secondary databases was the most used data source and method (40% of the articles), followed by interviews with structured forms (30%), document analysis (10%) and direct observation following patients (10%). It is important to emphasize that approximately 40% of the articles used the composition of more than one method/source (Chart 1).

Table 1. Characteristics of the articles included in the review.

Title	Author, year and approach	Subject and sample (n) of the study	Objectives of the study	Data Sources and Methods Used	Periodic
Risk factors for fetal mortality in a maternity hospital of the Unified Health System, Rio de Janeiro, Brazil: a study case-control	Fonseca, Sandra Costa, Coutinho, Evandro Silva Freire, 2010. Case-control study.	Population attended at the Leila Diniz Maternity, linked to the Municipal Health Department of Rio de Janeiro.	To discuss the process of determining fetal mortality of the population attended at the Leila Diniz Maternity Hospital in the period from 2002 to 2004.	A nested case-control study was conducted, with density sampling, in which the birth cohort was followed from October 2002 to October 2004	Public Health Notebooks.
Caracterização de gestantes com diagnóstico de Restrição de Crescimento Intrauterino internadas em um hospital do Sul do Brasil/ Characterization of pregnant women with a diagnosis of intrauterine growth restriction admitted to a hospital in South Brazil	Zanette, Nicole Vieira; Costa, Aline Zanette Dalla; Corrêa, Thiago Ricardo Kerber. 2016. Cross-sectional study.	1,995 pregnant women hospitalized during the study period.	To determine the prevalence of Intrauterine Growth Restriction in pregnant women admitted to the Hospital Nossa Senhora da Conceição, in Tubarão, Santa Catarina.	A cross-sectional study was carried out, in which the medical records of all pregnant women who were admitted to the Rooming-in Unit of the Hospital Nossa Senhora da Conceição (HNSC) were analyzed.	AMRIGS Magazine.
LBW and IUGR temporal trend in 4 population-based birth cohorts: the role of economic inequality.	Sadovsky, Anna D I; Matijasevich, Alicia; Santos, Iná S; Barros, Fernando C; Miranda, Angelica E; Silveira, Mariangela F. 2016. Prospective cohort.	Mothers and their newborns born in hospitals in the city of Pelotas throughout 1982, 1993 and 2004.	To analyze the inequality of absolute and relative income in the occurrence of low birth weight and small size for gestational age in neonates in four birth cohorts from southern Brazil in 1982, 1993, 2004 and 2011.	Four birth cohort studies were conducted in the city of Pelotas during 1982, 1993 and 2004.	BMC Pediatrics
Changes in perinatal health in two birth cohorts (1997/1998 and 2010) in São Luís, Maranhão State, Brazil.	Silva, Antonio Augusto Moura da; Batista, Rosângela Fernandes Lucena; Sylvester Roberts; Thomaz, Erika Barbara Abreu Fonseca; Ribeiro, Cecilia Claudia Costa; Lamy-Son,	Data on live births $\geq$ 20 weeks of GA or weighing $\geq$ 500 g born to mothers living in the municipality. In 1997/1998.	To analyze changes in perinatal health in two birth cohorts conducted in 1997/1998 and 2010 in São Luís, Maranhão, Brazil	The temporal analysis of maternal and child health indicators in São Luís comparing the 1997/1998 cohort with the BRISA 2010 cohort	Public Health Notebooks.

	Fernando; Lamy, Zeni Oak; Alves, Maria Teresa Seabra Soares de Britto and; Loureiro, Flávia Helen Furtado; Cardoso, Viviane Cunha; Bettiol, Heloisa; Barbieri, Mark Antony. 2015. Prospective cohort.				
Preterm birth and fetal growth restriction in HIV-infected Brazilian pregnant women.	Dos Reis, Helena Lucia Barroso; Araujo, Karina da Silva; Ribeiro, Lilian Paula; Da Rocha, Daniel Ribeiro; Rosato, Drielli Petri; Passos, Mauro Romero Leal; Merçon De Vargas, Paulo Roberto. 2015. Observational and analytical study.	250 deliveries of HIV-infected mothers who gave birth in a tertiary public university hospital in the city of Vitória, ES	To determine the prevalence of low birth weight and IUGR in low-income women, users of antiretrovirals, publicly attended, HIV-infected women and to verify its relationship with the stage of HIV infection.	This is an observational and analytical case series study conducted at the Cassiano Antonio Moraes University Hospital (HUCAM), a public tertiary hospital with 314 beds in the city of Vitória, Espírito Santo State, southeastern Brazil.	Journal of the Institute of Tropical Medicine of São Paulo
Risk factors for low birth weight in Botucatu city, SP state, Brazil: a study conducted in the public health system from 2004 to 2008.	Fonseca, Cátia Regina Branco; Strufaldi, Maria Wany Louzada; de Carvalho, Lydia Rachel; Puccini, Rosana Fiorini. 2012. Case-control study with secondary data.	The case group consisted of all low birth weight newborns (less than 2,500g) totaling 860 babies, and the control group consisted of a random sample of 860 newborn children weighing $\geq$ 2,500g.	To identify factors related to low birth weight in lactating women from Botucatu that contribute to a better understanding of this problem during the approach in the public health system in Brazil, and triggering discussion about the importance of public policies to support and health actions for women and babies.	A case-control study was conducted in Botucatu - SP with newborns divided into two groups: low birth weight newborns (LWNB) and a control group ( $\geq$ 2500 g). Secondary data were collected using the Live Birth Certificate (LBC) and records of medical records of pregnant women in Basic Health Units (UBS) and in a Public University Hospital (HU) from 2004 to 2008.	BMC Research Notes
Low leptin concentration in the first gestational trimester is associated with being born small for gestational age: prospective study in Rio de Janeiro, Brazil.	Franco-Sena, Anne Beatrice; Goldani, Marcelo Zubaran; Tavares do Carmo, Maria das Graças; Velasquez-Melendez, Gustavo; Kac, Gilbert. 2010. Prospective cohort.	195 pregnant women followed in a health service center in the city of Rio de Janeiro	To investigate the effect of serum leptin concentration in the 1st trimester of pregnancy on the incidence of SGA newborns and to identify other determining factors for its occurrence.	The prospective cohort study resulted from a main study composed of pregnant women followed in a basic health service center in the city of Rio de Janeiro. These women were selected for 22 months between 2005 and 2007.	Karger
Secular trend of very low birth weight rate in Porto Alegre, Southern Brazil.	Da Silva, Clécio Homrich; Agranonik, Marilyn; Da Silva, Antonio Augusto Moura; Bettiol,	257,740 newborns from 1994 to 2005 in the city of Porto Alegre were included in the study.	To evaluate the secular trend of IUGR in the city of Porto Alegre, a large city	The study was the cohort study and data were obtained from the birth certificates of all live births in the city of	Journal of Biosocial Science

	Heloisa; Barbieri, Mark Antony; Goldani, Marcelo Zubaran. 2010. Cohort.		in a developed area in southern Brazil, and the potential determinants of this trend during the 1990s and early 2000s.	Porto Alegre between 1994 and 2005.	
PREPARE: protocol for a stepped wedge trial to evaluate whether a risk stratification model can reduce preterm deliveries among women with suspected or confirmed preterm pre-eclampsia	Marcos Augusto Bastos Dias, Leandro De Oliveira, Arundhanthi Jeyabalan, Beth Payne, Christopher W. Redman, Laura Magee, Lucilla Poston, Lucy Chappell, Paul Seed, Peter von Dadelszen, James Michael Roberts and research group PREPARE 2019 Randomized trial	Women with suspected or confirmed preeclampsia between 20 + 0 and 36 + 6 weeks gestation in any one will be eligible of the seven tertiary centers. Women with any comorbidities (e.g., chronic hypertension, kidney disease, diabetes) will also be included.	To test the hypothesis that risk stratification of women with suspected or confirmed preeclampsia based on objective criteria reduces the proportion of preterm deliveries with medical indication and improvement of neonatal outcome	This is a randomized, clustered, staggered trial that will include women with suspected or confirmed PE between 20+0 and 36+6 weeks of gestation. All pregnant women who present these findings in seven tertiary centers in geographically dispersed areas throughout Brazil will be considered eligible and evaluated for risk stratification at admission. Sites will transition to risk stratification performed according to the sFlt-1/PIGF (Roche Diagnostics) measurement and the complete PIERS score with both results will be revealed to caregivers. Health care providers of women stratified as low risk for adverse outcomes (sFlt-1/PIGF $\leq$ 38 E fullPIERS <10% risk) will be recommended to postpone delivery. sFlt-1/PIGF will be repeated once and the fullPIERS score twice a week.	BMC Pregnancy and Childbirth
Aspirin plus calcium supplementation to prevent superimposed preeclampsia: a randomized trial	E.V. Souza M.R. Torloni A.N. Atallah G.M.S. dos Santos L. Kulay Jr N. Sass 2014 Randomized Clinical Trial	To calculate the sample size, the records of all women with chronic hypertension who received prenatal care at the clinic in the last 5 years were reviewed and those with abnormal uterine artery Doppler in the second trimester were selected. The incidence of overlapping preeclampsia in this group was greater than	The aim of this study was to investigate the efficacy of aspirin combined with calcium supplementation to prevent preeclampsia in women with chronic hypertension.	This randomized, double-blind, placebo-controlled study was conducted at the prenatal outpatient clinic for hypertensive diseases of a large tertiary university hospital located in the southern region of the city of São Paulo, SP, Brazil. This clinic offers free prenatal care for low-income women. Throughout the study	Cambridge University Press



		<p>50%. Based on an expected rate of overlapping preeclampsia of 55% in the participants, and an estimated reduction of approximately 50% in this incidence in the group receiving aspirin plus calcium, with an alpha of 5% and a power of 80%, a total of 22 women would have to be randomly assigned to each group.</p>		<p>period, the same team of physicians and nurses cared for all the women enrolled in the study. All participants gave birth at the university hospital and were followed for 6 weeks after delivery. All women receiving antenatal care and planning to give birth at the university hospital, and carrying a living, structurally normal, single fetus between 20 and 27 weeks gestation were eligible if they had chronic hypertension and an abnormal uterine Doppler exam. Chronic hypertension was defined as a known history of pre-existing hypertension prior to pregnancy, or blood pressure readings <math>\geq 140</math> systolic and/or <math>\geq 90</math> mmHg diastolic on two occasions 6 hours apart before the 20th week of gestation. The two-sample test for equal proportions, the chi-square test or Fisher's exact test, the independent samples t-test and the Mann-Whitney test were used to compare the results in the placebo and study groups. <math>P &lt; 0.05</math> was considered significant. All analyses were conducted according to the intention to treat.</p>	
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As a result of the research, initially 34 articles on the subject were found in the databases previously discussed. Based on the criteria established to restrict the research, 10 articles were selected for study and data collection. After the characterization of the articles, a reading of the legal documents was carried out to discuss the approaches found in the studies, which gave rise to five major categories relevant to Intrauterine Growth Restriction: evolution in prenatal treatment; fetal mortality; low birth weight; serum leptin concentration, eclampsia, HIV, and IUGR; socioeconomic factor and IUGR.



### 3.1 IMPACTS OF PRENATAL CARE ON IUGR

The Prenatal and Birth Humanization Program (PHPN) was created in 2000 to offer strategic actions to improve the quality of care for pregnant women and their children, and brought at its core the discussion about prenatal practices and their conceptual bases according to the standards used worldwide. The main strategy of the PHPN is to ensure improvement in access, coverage and quality of prenatal care, delivery and puerperium, to the care of pregnant women and newborns, from the perspective of citizenship rights, following specific guidelines and well-defined actions that should be closely monitored during prenatal care (FONSECA et al., 2012).

Care for pregnant women should include procedures and tests necessary to reduce maternal and fetal morbidity and mortality. This care would be preventive for early diagnosis of changes such as intrauterine growth restriction and maternal infections that can be transmitted vertically. A good prenatal follow-up ensures a protective effect for the pregnant woman and the fetus through better nutritional control, access to resources to reduce smoking, early diagnosis and adequate treatment of infections and diseases that could prevent low birth weight in newborns (FONSECA et al., 2012).

In prenatal care, ultrasonography is the exam of choice to raise the hypothesis of the occurrence of IUGR. With it, it is possible to estimate fetal weight and biometrics, thus evaluating its growth during pregnancy, as well as reducing morbidity and mortality associated with intrauterine growth deviations, through the follow-up and adoption of specific protocols for fetal vitality surveillance (ZANETTE et al., 2016).

And the importance of prenatal care is increasingly widespread in Brazilian society, as shown by Silva et al. (2015) in which the city of São Luís - MA presented an increase in prenatal coverage by 6.8%, from 1997 to 2010. Similar results were seen in Ribeirão Preto - SP from 1994 to 1998 and in Pelotas - RS from 1982 to 2004. Another positive point, shown by the study in São Luís, was the early start of prenatal care, with an absolute increase of 11% in the first prenatal visit in the first trimester, covering up to 67.5% of pregnant women in 2010. It is also observed the assertion on the part of the authors the sharp increase in prenatal coverage, in the adequate number of prenatal consultations and in the prenatal period from the first trimester. There are positive and stimulating results, and this favorable trend in the care of pregnant women, contributed to the decline in the rate of IUGR (SILVA et al., 2015), in addition to it is shown by Fonseca and Coutinho (2010) as a protective factor for fetal death, when an adequate prenatal care is done.

However, for Fonseca et al. (2012), although prenatal care is widespread in Brazilian society (in their study it is shown that in Brazil there are high rates of coverage of prenatal care



with 80.7% of women having 5 or more prenatal consultations between 2006 and 2007), one should be concerned with the quality of care. It was observed in the result of their study that children who were born with growth restriction, presented a higher percentage of adequate number of consultations, but with inadequate quality of care (31.3%), when compared to the control group (19.3%). Showing the importance of a health promotion to improve the quality of prenatal care and that it is an important strategy to prevent IUGR.

### 3.2 SOCIOECONOMIC FACTOR AND IUGR

Public health policies in low- and middle-income countries are constantly challenged by socioeconomic and demographic inequalities. We can note that factors such as schooling, wealth, employment and access to health, for example, contribute to these inequalities and, thus, have an impact on the socioeconomic level of individuals in society and, throughout life, reflect on health.

It is noted that in terms of economy and schooling, in disadvantaged regions that present great inequalities in health, there is an increase in the rates of critical neonatal outcomes such as intrauterine growth restriction. Unfortunately, these outcomes contribute to increased infant morbidity and mortality. According to Sharma et al. (2016), the following are included as maternal causes of IUGR: low socioeconomic status and developing countries.

After observing the discussion of Sadovsky et al. (2016) and Sharma et al. (2016), it is noticeable the importance of analyzing the prevalence pattern of neonates with intrauterine growth restriction due to socioeconomic impact, in order to seek new health policy measures in order to reduce infant morbidity and mortality resulting from this factor.

According to the analysis of four cohorts, Sadovsky et al. (2016) observed that all showed that poorer mothers were more likely to have newborns with growth restriction, concluding that the mother's unfavorable socioeconomic level, based on income, schooling and other sociodemographic factors, may favor growth restriction in the newborn.

The income of the mother and the family affects the health of the mother and her children in several ways, such as access to adequate prenatal care, nutritional quality or the identification of morbidities in the gestational period, for example, which may result in intrauterine growth restriction. Thus, it is understood that low income is an important socioeconomic factor related to the social exclusion of the individual in the community and a reflection of health inequalities.

### 3.3 RISK FACTORS ASSOCIATED WITH UNDERWEIGHT AND IUGR

According to the study DA SILVA, C. H. et al. (2009), a sample of data from the Live Birth Information System (SINASC) in Porto Alegre was surveyed, presenting a distribution of data collected regarding significant variables in relation to the birth of babies diagnosed with Very Low Birth Weight (VLBW). Poisson progression (IRR) was used to record the progression of VLBW and to evaluate the biological, sociodemographic and economic influence for this purpose.

Table 2. Incidence Rate Ratio (IRR) for VLBW according to independent variables from 1994 to 2005 in Porto Alegre, Brazil.

VARIABLES	n	1994	1996	1998	2000	2002	2004	2005	IRR
<b>Births</b>	257.740	23.844	23.326	22.525	22.856	19.425	18.957	18.325	%MBPN
<b>Maternal schooling (years)</b>									
<8	112.034	1,38	1,20	1,15	1,41	1,44	1,31	1,48	1,019
>8	143.638	1,20	1,00	0,99	1,36	1,23	1,23	1,12	1,011
<b>Maternal Age</b>									
<20	61.860	1,64	1,20	1,20	1,49	1,73	1,30	1,56	1,001
21-30	121.120	1,04	1,00	0,90	1,20	1,12	1,24	0,95	1,020
>36	29.276	1,71	1,60	1,32	2,03	1,82	2,17	1,76	1,015
<b>Medium of birth</b>									
Vaginal	161.107	1,09	0,82	0,86	1,08	0,88	0,80	0,89	0,995
Cesarean section	96.609	1,76	1,65	1,49	1,89	1,94	1,98	1,64	1,010
<b>Hospital</b>									
Private	41.510	0,87	0,72	0,99	0,73	0,90	1,20	0,65	0,996
Mixed	49.014	0,67	0,71	0,72	1,17	1,09	1,05	1,05	1,064
Public	166.809	1,58	1,31	1,20	1,61	1,49	1,42	1,46	1,004
<b>Gestational Age (month)</b>									
<28	1.079	73,0	90,7	79,3	99,0	98,6	97,4	98,8	1,030
28-36	19.812	12,0	10,6	10,9	10,9	10,9	9,9	9,1	0,979

Source: Elaborated by the authors based on the study of DA SILVA, C. H. et al, 2009.

The results of this table indicate that the increase in VLBW rates was significant among mothers with lower schooling, births attributed in mixed hospitals and mothers aged 21 to 30 years.

In the study by DA SILVA et al (2009), it was noted that the main risk factors related to VLBW were in mothers with low education, public hospitals, multiparity and nulliparity.

This finding suggests that such variables are related to the birth of these low birth weight babies, in which they interfere with their intrauterine development, leading to relative fetal risks, increasing the likelihood for IUGR.



### 3.4 SERUM LEPTIN CONCENTRATION, ECLAMPSIA, HIV AND IUGR

It is observed that preeclampsia is still a disorder not fully understood. However, it is notorious that processes such as imbalance in thromboxane-prostacyclin production and activity and low calcium intake play a major role in the development of this multifactorial disorder.

A pilot study was conducted by Souza et al. (2014) to observe the effect of the hypothesis on the benefits of aspirin and calcium supplementation in the prevention of preeclampsia in women with chronic hypertension. This thesis would possibly be associated with the reduction of inflammatory factors and oxidative stress.

According to the analysis, combined aspirin and calcium supplementation from 20-27 weeks gestation produced a non-significant decrease in the incidence of overlapping preeclampsia and fetal growth restriction in hypertensive women with abnormal uterine artery Doppler findings.

In this sense, a positive and stimulating result for further investigations is observed. However, because it is a small sample, more results and tests are still needed to be able to conclude about the benefit of this supplementation.

For Dos Reis et al. (2015), another point that draws attention in the results was the high trend of larger fetal dimensions such as birth weight, birth length, head and abdominal circumferences in babies born with AIDS compared to mothers without AIDS.

What's more, in the study by Franco-Sena et al. (2010), it was found that lower leptin concentrations are associated with a significant risk in young children for gestational age. Thus, maternal serum leptin in early pregnancy can be used as a marker for the early detection of indication of young children for gestational age.

### 3.5 NEONATAL MORTALITY AND MORBIDITY SECONDARY TO IUGR

The risk factors mentioned above along with IUGR can cause neonatal mortality and morbidities, as stated by Sharma (2016).

According to Sadovsky (2016), to reduce neonatal mortality, which has as one of the causes low birth weight, investments and the improvement of maternal and child policies should be prioritized. In addition, welcoming and ensuring access to full prenatal care for low-income pregnant women can diagnose pregnancy-specific morbidities, thus avoiding IUGR.

According to Fonseca and Coutinho (2010), intrauterine growth restriction is among the main causes of the 134 fetal deaths that occurred at the Leila Diniz Maternity. The study used 360 control cases to be associated with this cause, demonstrating a positive association (OR = 2.14; CI95%: 1.31-3.48). Although the mechanisms that cause growth restriction are not all elucidated,



placental insufficiency is present in several obstetric morbidities. The present studies validate IUGR as one of the reasons for fetal death, but leave a gap about what the etiologies of this mechanism would be.

Therefore, this requires further investigation in order to explain and highlight the factors that cause intrauterine growth restriction in Brazilian pregnant women. Once explained about the risk factors, it is possible to centralize health investments in screening methods for early diagnosis during pregnancy and prenatal campaigns.

#### **4 CONCLUSIONS**

The available analyses on the main categories related to IUGR showed that the lack of prenatal care, precarious socioeconomic status, low leptin concentration during pregnancy, preeclampsia and viral infections, such as HIV, are risk factors present for IUGR in Brazil.

The importance of prenatal follow-up for the prevention and early diagnosis of IUGR is highlighted, and ultrasound is used to observe changes in fetal growth, so it is necessary to perform the appropriate number of quality prenatal consultations to prevent this and other pathologies.

Small advances in the prevention of IUGR were observed, such as calcium and aspirin supplementation, which demonstrated positive results, but little significant due to the sample size.

Thus, knowing that one of the main risk factors for intrauterine growth restriction is related to the socioeconomic situation of the pregnant woman, contributing to the increase in infant morbidity and mortality, a policy focused on facilitating the access of these pregnant women to prenatal care should be encouraged, making the hours of care more flexible and increasing the team of obstetric professionals, facilitating the performance of essential examinations for a possible identification of morbidity and a support for an improvement in the nutrition of these women and their fetuses.

Consequently, due to these factors, we achieved a higher quality and effective prenatal care for all national incomes and avoided a percentage of neonatal mortality and morbidity. In addition, the literature presents few studies on this topic in the Brazilian reality, showing that more in-depth research is necessary to measure the severity of IUGR, and thus promote health actions to reduce its prevalence in Brazil.



## REFERENCES

- BRODSKY, D.; CHRISTOU, H. Current concepts in intrauterine growth restriction. *Journal of Intensive Care Medicine*. Boston, v.19, n. 06, p.307-18, Nov. 2004.
- DA FONSECA, C. R. B. et al. Risk factors for low birth weight in Botucatu city, SP state, Brazil: a study conducted in the public health system from 2004 to 2008. *BMC Res Notes*, v. 5, p. 60, 2012.
- DA SILVA, C. H. et al. Secular trend of very low birth weight rate in Porto Alegre, Southern Brazil. *Journal of Biosocial Science*, v. 42, n. 2, p. 243–253, 2010.
- DIAS, M. A. B. et al. PREPARE: protocol for a stepped wedge trial to evaluate whether a risk stratification model can reduce preterm deliveries among women with suspected or confirmed preterm pre-eclampsia. *BMC Pregnancy and Childbirth*, v. 19, n. 1, p. 343, 2019.
- DOS REIS, H. L. B. et al. Preterm birth and fetal growth restriction in HIV-infected Brazilian pregnant women. *Rev Inst Med Trop Sao Paulo*, v. 57, n. 2, p. 111–120, 2015.
- FONSECA, S. C.; COUTINHO, E. S. F. Fatores de risco para mortalidade fetal em uma maternidade do Sistema Único de Saúde, Rio de Janeiro, Brasil: estudo caso-controlado TT - Risk factors for fetal mortality in a public maternity hospital in Rio de Janeiro, Brazil: a case-control study. *Cadernos de Saúde Pública*, v. 26, n. 2, p. 240–252, 2010.
- FRANCO-SENA, A. B. et al. Low leptin concentration in the first gestational trimester is associated with being born small for gestational age: prospective study in Rio de Janeiro, Brazil. *Neonatology*, v. 97, n. 4, p. 291–298, 2010
- LAUSMAN, A et al. Intrauterine growth restriction: screening, diagnosis, and management. *Journal of Obstetrics Gynecology Canada*. Toronto, v.35, n8, p.741-748, Aug 2013.
- METCOFF, J et al Avaliação clínica do estado nutricional ao nascimento. *Clínicas pediátricas da América do Norte*. v.5, p.911-26, 1994.
- MOREIRA NETO AR et al. Etiologia da restrição de crescimento intrauterino (RCIU). *Com. Ciências Saúde - 22 Sup 1:S21-S30*, 2011
- NAUFEL, H. G. Avaliação física e classificação. In COSTA, H. P. F. E., MARBA, S. T. O Recém-nascido de muito baixo peso. São Paulo: Ed Atheneu, 2003. P. 61-72.
- SADOVSKY, A. D. I. et al. LBW and IUGR temporal trend in 4 population-based birth cohorts: the role of economic inequality. *BMC Pediatrics*, v. 16, p. 115, 2016.
- SHARMA, D. et al. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. *Clinical Medicine Insights: Pediatrics* v. 10, p. 67, 2016.
- SILVA, A. A. M. DA et al. Changes in perinatal health in two birth cohorts (1997/1998 and 2010) in São Luís, Maranhão State, Brazil. *Caderno Saúde Publica*, v. 31, n. 7, p. 1437–1450, 2015.



SOUZA, E. V. et al. Aspirin plus calcium supplementation to prevent superimposed preeclampsia: A randomized trial. *Brazilian Journal of Medical and Biological Research*, v. 47, n. 5, p. 419–425, 2014.

ZANETTE, N. V.; COSTA, A. Z. D.; CORRÊA, T. R. K. Caracterização de gestantes com diagnóstico de Restrição de Crescimento Intrauterino internadas em um hospital do Sul do Brasil TT - Characterization of pregnant women with a diagnosis of intrauterine growth restriction admitted to a hospital in South Brazil. *Rev. AMRIGS*, v. 60, n. 3, p. 214–219, 2016