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# Maternal age and adverse perinatal outcomes in a birth cohort (BRISA) from a Northeastern Brazilian city

*Idade materna e desfechos perinatais adversos em uma coorte de nascimentos (BRISA) de uma cidade do Nordeste brasileiro*

## Keywords

Maternal age  
Gestational age  
Premature birth/etiology  
Fetal growth retardation  
Pregnancy outcome

## Palavras-chave

Idade materna  
Idade gestacional  
Nascimento prematuro/etiologia  
Retardo do crescimento fetal  
Resultado da gravidez

## Abstract

**PURPOSE:** To verify the existence of associations between different maternal ages and the perinatal outcomes of preterm birth and intrauterine growth restriction in the city of São Luís, Maranhão, Northeastern Brazil. **METHODS:** A cross-sectional study using a sample of 5,063 hospital births was conducted in São Luís, from January to December 2010. The participants comprise the birth cohort for the study "Etiological factors of preterm birth and consequences of perinatal factors for infant health: birth cohorts from two Brazilian cities" (BRISA). Frequencies and 95% confidence intervals were used to describe the results. Multiple logistic regression models were applied to assess the adjusted odds ratio (OR) of maternal age associated with the following outcomes: preterm birth and intrauterine growth restriction. **RESULTS:** The percentage of early teenage pregnancy (12–15 years old) was 2.2%, and of late (16–19 years old) was 16.4%, while pregnancy at an advanced maternal age (>35 years) was 5.9%. Multivariate analyses showed a statistically significant increase in preterm births among females aged 12–15 years old (OR=1.6; p=0.04) compared with those aged 20–35 years. There was also a higher rate in preterm births among females aged 16–19 years old (OR=1.3; p=0.01). Among those with advanced maternal age (>35 years old), the increase in the prevalence of preterm birth had only borderline statistical significance (OR=1.4; p=0.05). There was no statistically significant association between maternal age and increased prevalence of intrauterine growth restriction.

## Resumo

**OBJETIVOS:** Verificar a existência de associações entre diferentes idades maternas e desfechos de nascimentos pré-termo e restrição de crescimento intrauterino no município de São Luís, no Maranhão. **MÉTODOS:** Estudo transversal no qual se utilizou uma amostra composta de 5.063 nascimentos hospitalares em São Luís, região Nordeste do Brasil, de janeiro a dezembro de 2010. As participantes compõem a coorte de nascimentos da pesquisa "Fatores etiológicos do nascimento pré-termo e consequências dos fatores perinatais na saúde da criança: coortes de nascimento em duas cidades brasileiras" (BRISA). Para a descrição dos resultados, utilizaram-se medidas de frequência e intervalo de confiança de 95%. Modelos de regressão logística múltipla foram aplicados para avaliar o *odds ratio* (OR) ajustado da idade materna associado com os seguintes desfechos: nascimento pré-termo e restrição de crescimento intrauterino. **RESULTADOS:** O percentual de gestantes adolescentes precoces (12 a 15 anos) foi de 2,2%, e daquelas tardias (16 a 19 anos) de 16,4%, enquanto o de grávidas com idade avançada (>35 anos) foi de 5,9%. As análises multivariadas demonstraram um aumento estatisticamente significativo na ocorrência de partos pré-termo entre as mulheres na faixa etária dos 12 aos 15 anos (OR=1,6; p=0,04) quando comparadas àquelas de 20 a 35 anos. Também houve aumento entre as mulheres dos 16 aos 19 anos (OR=1,3; p=0,01). Entre aquelas com idade materna avançada (acima de 35 anos), apesar do aumento na prevalência de parto pré-termo, houve significância estatística limítrofe (OR=1,4; p=0,05). Não houve associação estatisticamente significativa entre a faixa etária materna e o aumento da prevalência de restrição do crescimento intrauterino.

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## Introduction

Though female fertility begins around 10 years of age, the period ranging from 18 to 30 years old is when pregnancy has the best chance for success from a biological perspective<sup>1</sup>.

The importance of maternal age on perinatal outcomes has been the subject of numerous studies. Pregnancies that happen at either end of a woman's reproductive life have been associated with adverse perinatal outcomes<sup>2-5</sup>.

Pregnancy during adolescence (from 10 to 19 years old)<sup>6</sup> is often associated with poor obstetric and perinatal outcomes. Studies have shown that pregnant adolescents have lower socioeconomic and educational levels, poor prenatal care, and give birth to children with higher rates of low birth weight (LBW) or intrauterine growth restriction (IUGR), and neonatal/childhood mortality<sup>7-9</sup>. Several investigations have demonstrated that teenage pregnancy is associated with LBW or IUGR and preterm birth as a result of biological immaturity, which is often worsened by socioeconomic deprivation<sup>10,11</sup>. Ribeiro et al.<sup>8</sup>, analyzing pregnancy in both early (13–17 years old) and late (18–19 years old) adolescences reinforced this idea when they found adverse social and biological outcomes more frequently in the first group. Younger adolescents were associated with fewer prenatal visits and stable civil unions, and higher rates of LBW and preterm birth. The authors indicated that the negative obstetric outcomes among younger mothers could be related to age and other independent adverse factors.

At the other end of the spectrum, we can mention the pregnancies at advanced maternal age (after 35 years of age). In the past three decades, Brazilian<sup>12,13</sup> and worldwide<sup>14,15</sup> studies have detected a considerable increase in the number of women who delay motherhood. This phenomenon is driven by the change in women's social roles, the option of investing in training and career developments, and the variety of contraceptive methods available<sup>16</sup>.

The effects of pregnancy at an advanced maternal age (35 years old or more) in perinatal outcomes have been described by several authors. Two studies conducted in Nigeria showed that primigravidae aged 35 years or older had higher preterm birth rates<sup>17</sup> and LBW ones<sup>18</sup> than younger women. An investigation carried out in Norway<sup>19</sup>, in 2011, found no significant differences in the rates of preterm birth and LBW between older and younger women. A retrospective study of 1,255 women conducted in Brazil, in 2012<sup>16</sup>, found no differences in the rates of LBW and preterm birth.

Data from studies published in the 1980s that analyzed the influence of maternal age on perinatal outcomes are controversial, which can be partly explained by different methodological approaches, sample sizes, and sample

representativeness in addition to significant regional differences. Another factor that may contribute to the controversial nature of these studies is the period during which the studies were developed. In 2000, Mariotoni et al.<sup>5</sup> studied 18,262 births from 1971 to 1995 in Campinas, São Paulo State, Brazil, divided into five-year periods, and found an association between LBW with pregnancy during adolescence or above 35 years of age. However, this was observed in some of the surveyed periods, but not in all of them. Population-based studies are needed to achieve greater reliability in the observed trends.

The present study used a population-based sampling method and therefore has the potential to fill gaps in our knowledge about the influence of different maternal ages on two adverse perinatal outcomes: IUGR and preterm birth. The objective of this study was to confirm the presence and dimension of these associations in São Luís, which is the capital of Maranhão State, Northeastern Brazil, assuming that these results should resemble the patterns occurring in other capitals in the same region.

In Brazil, particularly in the Northern and Northeastern regions, few studies have addressed the association between maternal age and preterm birth, and even fewer studies have examined the relationship between maternal age and intrauterine growth restriction.

## Methods

This study is part of a project entitled "Etiological factors of preterm birth and consequences of perinatal factors on children's health: birth cohorts from two Brazilian cities (BRISA)", which was developed by *Universidade Federal do Maranhão (UFMA)* in partnership with the *Universidade de São Paulo (USP)*, in Ribeirão Preto campus.

The cross-sectional cohort was composed of 5,063 single live-born infants, who were born in São Luís from January to December 2010. Data were collected in all hospitals in such city, which recorded more than 100 births/year in the previous year, representing 98.7% of the total of hospital births in the city.

The sample was proportionally allocated to the number of births. For the study, a total of 6,000 ones were calculated, representing one third of those of the city in one year. For each hospital participating in the study, a random number from 1 to 3 was drawn to identify the starting point, with a sampling interval of 3. Losses due to refusal or early discharge from the hospital represented 4.6%.

Three survey instruments were used: a birth record, and mother and newborn survey questionnaires.

In the present research, a newborn was considered preterm when the gestational age was less than 37 weeks as calculated from the first day of the last menstrual period.

When the only available information was the month, its 15<sup>th</sup> day was used to calculate the gestational age. An algorithm was applied to identify the gestational age for cases without last menstrual period information, which was determined using a regression model based on birth weight, parity, per capita household income, and newborn's sex. In addition, birth weights above the 99<sup>th</sup> percentile (British reference curve)<sup>20</sup> and considered incompatible with gestational age were coded as unknown.

The birth weight ratio described by Kramer et al.<sup>21</sup> was used to establish IUGR. It defines newborns with IUGR presenting a birth weight ratio lower than 0.85. Such ratio is obtained dividing the newborn weight by the weight corresponding to the 50<sup>th</sup> percentile of the weight curve for the gestational age.

The independent variables analyzed were maternal age, marital status, parity, whether the mother received prenatal care, age-appropriate education, type of delivery, type of hospital (public or private), hypertension during pregnancy, risks for abortion and preterm labor, anemia, and smoking during pregnancy. Maternal age-appropriate education was classified into age-appropriate or not age-appropriate education according to a modified method described by Hellerstedt et al.<sup>22</sup>, as follows: 19 years or older — 12 years of education was considered age-appropriate; younger than 19 years — the number schooling period was subtracted from age, and results higher than 7 indicated not age-appropriate education.

For the statistical analysis, multiple logistic regression modeling was used to control the influence of each variable alone on the rates of preterm birth or IUGR. The risk between the independent variables and the perinatal outcomes was calculated using odds ratios (OR) with 95% confidence interval (95%CI). All analyses were performed using STATA 11.0 software (Stata Corp., College Station, TX, USA) and the stepwise method to select variables, firstly considering a probability of  $p < 0.20$  for inclusion in the model; subsequently, variables with  $p > 0.10$  were removed from it. In the final version,  $p < 0.05$  was regarded as statistically significant.

This study followed the criteria of Resolution 196/96 of Health National Council, and its complementary resolutions. The interviewees were invited to participate in the study, and they signed informed consent forms, if they agreed to participate. It was approved by the Research Ethics Committee of the University Hospital of UFMA (223/2009).

## Results

This study consisted of a sample including 5,063 births after excluding twins, stillbirths and 4 cases

of missing birth weight information. Herein, 2.2% of the mothers were women aged 12 to 15 years (early adolescence); 16.4% were 16 to 19 years old (late adolescence); 75.4%, 20 to 35 years; and 5.9%, older than 35 years old. Sociodemographic characteristics, clinical aspects of pregnancy, including frequency of prenatal visits, number of pregnancies and parity, and the most common complications during pregnancy are shown in Table 1.

**Table 1.** Sociodemographic, clinical, and perinatal characteristics of pregnant women (n=5,063)

Characteristics	n	%
<b>Maternal age</b>		
12–15 years	113	2.23
16–19 years	832	16.43
20–35 years	3,818	75.41
>35 years	300	5.93
<b>Education</b>		
Age-appropriate	3,129	62.93
<b>Marital status</b>		
Married/stable union	4,100	80.98
<b>Gainful employment</b>		
Yes	1,698	33.54
<b>Smoking during pregnancy</b>		
Yes	204	4.03
<b>Prenatal visits</b>		
Yes	4,965	98.06
<b>Parity</b>		
Primiparous	2,410	47.60
<b>Hypertension</b>		
Yes	827	16.33
<b>Diabetes</b>		
Yes	106	2.09
<b>Anemia</b>		
Yes	2,377	46.95
<b>Types of delivery</b>		
Vaginal delivery	2,690	53.13
<b>Gender of newborn</b>		
Female	2,479	48.96
<b>Kind of hospital</b>		
Public	4,277	84.48
<b>Intrauterine growth restriction</b>		
Yes	818	16.20
<b>Preterm birth</b>		
Yes	612	12.09

In this research, 16.2% of the infants were born with IUGR, while 12.1% were preterm births. Other perinatal characteristics, such as type of delivery, newborn's sex, and place of birth are presented in Table 1.

Only statistically significant results obtained in the multivariate analysis are shown in the tables. There was a significant difference in preterm birth rates between women in the age ranges of 12 to 15 (18.6%; OR=1.6; p=0.04) and 16 to 19 years (14.9%; OR=1.3; p=0.01) with those aged 20 to 35 years, who were considered the baseline category. Among the subjects who are older than 35 years old, despite an increased prevalence of preterm birth compared with the baseline category, only borderline statistical significance was observed (14.3%; OR=1.4; p=0.05).

Among the independent variables analyzed in this study, marital status “without a partner”, smoking during pregnancy, lack of prenatal care, primiparity and not age-appropriate education were associated with higher preterm birth rates. In addition, clinical complications of pregnancy, such as hypertension and risk of preterm labor, were associated with higher preterm birth rates.

Multivariate analysis results for preterm birth are shown in Table 2.

There was no statistically significant association between maternal age and increased IUGR rates. Primiparity, smoking during pregnancy, lack of prenatal care, hypertension in pregnancy, and risk of preterm labor were associated with increased prevalence of IUGR (Table 3).

**Table 2.** Adjusted analysis of the association between preterm birth and maternal age, marital status, parity, smoking during pregnancy, prenatal visits, education, hypertension, and risks of preterm labor (n=5,063)

	Term		Preterm		Total	OR	95%CI	p-value
	n	%	n	%				
<b>Maternal age</b>								
12–15 years	92	81.4	21	18.6	113	1.6	1.0–2.7	0.04
16–19 years	708	85.1	124	14.9	832	1.3	1.1–1.6	0.01
20–35 years	3,394	88.9	424	11.1	3,818	1	–	–
>35 years	257	85.7	43	14.3	300	1.4	0.99–1.96	0.05
<b>Marital status</b>								
With a partner	3,636	88.7	464	11.3	4,100	1	–	–
Without a partner	815	84.6	148	15.4	963	1.2	1.0–1.3	0.01
<b>Parity</b>								
Non-primiparous	2,359	88.9	294	11.1	2,653	1	–	–
Primiparous	2,092	86.8	318	13.2	2,410	1.2	1.0–1.5	0.04
<b>Smoking during pregnancy</b>								
Non-smoking	4,286	88.2	573	11.8	4,859	1	–	–
Smoking	165	80.9	39	19.1	204	1.7	1.1–2.5	0.01
<b>Prenatal visits</b>								
Yes	4,377	88.2	588	11.8	4,965	1	–	–
No	74	75.5	24	24.5	98	2.1	1.2–3.5	0.01
<b>Education</b>								
Age-appropriate	2,775	88.7	354	11.3	3,129	1	–	–
Not age-appropriate	1,595	86.5	248	13.5	1,843	1.3	1.0–1.5	0.02
<b>Hypertension</b>								
No	3,768	88.9	468	11.0	4,236	1	–	–
Yes	683	82.6	144	17.4	827	1.4	1.1–1.7	0.01
<b>Risks of preterm labor</b>								
No	4,047	91.8	359	8.1	4,406	1	–	–
Yes	404	61.5	253	38.5	657	7.3	5.9–9.0	<0.01

OR: odds ratio, 95%CI: 95% confidence interval.

**Table 3.** Adjusted analysis of the association between intrauterine growth restriction and maternal age, type of delivery, parity, smoking during pregnancy, prenatal visits, hypertension, and risks of preterm labor (n=5,049)

	Appropriate weight		IUGR		Total	OR	95%CI	p-value
	n	%	n	%				
<b>Maternal age</b>								
12–15 years	87	77.7	25	22.3	112	1.1	0.7–1.7	0.75
16–19 years	671	80.9	158	19.1	829	1	0.8–1.2	0.83
20–35 years	3,223	84.6	587	15.4	3,810	1	–	–
>35 years	250	83.9	48	16.1	298	1.3	0.9–1.8	0.13
<b>Type of delivery</b>								
Vaginal	2,192	81.8	489	18.2	2,681	1	–	–
Caesarean	2,039	86.1	329	13.9	2,368	0.7	0.6–0.8	<0.01
<b>Parity</b>								
Non-primiparous	2,286	86.5	358	13.5	2,644	1	–	–
Primiparous	1,945	80.9	460	19.1	2,405	1.7	1.4–2.0	<0.01
<b>Smoking during pregnancy</b>								
Non-smoking	4,080	84.2	765	15.8	4,845	1	–	–
Smoking	151	74.0	53	26.0	204	1.8	1.3–2.5	0.01
<b>Prenatal visits</b>								
Yes	4,167	84.1	787	15.9	4,954	1	–	–
No	64	67.4	31	32.6	95	2.5	1.6–4.0	<0.01
<b>Hypertension</b>								
No	3,572	84.6	651	15.4	4,223	1	–	–
Yes	659	79.8	167	20.2	826	1.4	1.2–1.7	<0.01
<b>Risks of preterm labor</b>								
No	3,727	84.8	668	15.2	4,395	1	–	–
Yes	504	77.1	150	22.9	654	1.6	1.3–2.0	<0.01

IUGR: intrauterine growth restriction.

## Discussion

The present study demonstrated that, in this Brazilian population, maternal age of less than 20 years old, and not only early adolescence (younger than 16 years old) but also late one (aged 16 to 19 years) are associated with higher preterm birth rates, while advanced maternal age (>35 years) showed only a borderline association with this outcome. However, maternal age was not associated with IUGR in any of the age groups defined in this study.

In the present study, the percentage of adolescents who gave birth was 18.6%, with 2.2% corresponding to early adolescents and 16.4% to late ones. This value was higher than those observed in developed countries, such as Finland<sup>23</sup> (7.8%) or the United Kingdom<sup>24</sup> (7.7%), as well as in emerging countries like India<sup>25</sup> (10%). However, this rate was lower than those verified in other Brazilian studies, such as those conducted

in 2002 in Rio Grande do Norte<sup>26</sup> (25.3%) and in 1997/98 in São Luís<sup>27</sup> (29.7%). Our data thus show a decrease in teenage pregnancy rates compared with previous studies carried out in Brazil. Nevertheless, they also reveal that these rates are still high in this population, highlighting the percentage of pregnant women aged 12 to 15 years (2.23%) compared, for instance, with the Finnish<sup>23</sup> study, where only 0.09% of the pregnant women belonged to this age group.

The percentage of mothers at an advanced age (>35 years) was 5.9%. This ratio is lower than the proportion found in developed countries, such as the United Kingdom<sup>24</sup> (16.6%) or Norway<sup>19</sup>, where one third (33.4%) of pregnant women are older than 35 years, and higher than that found in São Luís in 1997/98<sup>27</sup> (4.2%). Data indicating that an increased number of women delay motherhood have been confirmed by several Brazilian<sup>12,13</sup> and worldwide<sup>14,15</sup> studies.

The preterm birth rate was 12.1% in this investigation. A Norwegian study of 6,619 pregnant women conducted between 2004 and 2007<sup>19</sup> had a preterm birth rate of 9.6%. A cohort with more than 200,000 women from 2004 to 2008 in the United Kingdom<sup>24</sup> encountered a 7.54% preterm birth rate. Among the Brazilian studies, 2,160 pregnant women in *Hospital do Servidor Público de São Paulo*, in the period from 2000 to 2003<sup>12</sup> presented a preterm birth rate of 11.7%, while a group of 2,429 subjects in the city of São Luís in 1997/98<sup>27</sup> found one of 12.6%.

Regarding IUGR, we found a 16.2% rate. This value is similar to that seen in a study conducted with Mexican pregnant women between 2009 and 2010<sup>28</sup> (13.5%). In Brazil, studies carried out in São Paulo<sup>12</sup> and Rio Grande do Norte<sup>26</sup> achieved IUGR rates of 10.0 and 7.1%, respectively. The high proportion of this outcome in the current study seems to be also associated with the poor socioeconomic conditions of the studied population, as previously demonstrated by Matijasevich et al.<sup>29</sup>

Despite several reports in the literature demonstrating the increased risk of preterm birth and IUGR in women at either end of their reproductive lives, this subject remains controversial<sup>2-5,7-9</sup>. Currently, however, it is thought that living conditions and health of the pregnant woman, particularly the quality of prenatal care and delivery, are more important than age<sup>9-11</sup>.

We obtained rates of preterm births of the early (18.6%) and late adolescents (14.9%) significantly higher than that of the Control Group (20 to 35 years; 11.1%). This trend is consistent with data from several studies performed in Brazil<sup>26</sup> and in other countries<sup>23,30,31</sup>. Nonetheless, the actual preterm births rates reported for these age groups (adolescents and controls) vary considerably among these studies, possibly as a result of the different characteristics of the studied populations.

It is noteworthy that the strength of the association between early adolescence and preterm birth (OR=1.6) was greater than that observed between late adolescence and this outcome (OR=1.3). In addition to all of the social problems associated with teenage pregnancy, these data suggest that biological immaturity has a greater influence on this age group than on older adolescents. Ribeiro et al.<sup>8</sup> mentioned that adolescents aged 13 to 17 years had a 2-fold higher rate of LBW and one nearly to this of preterm birth regarding adolescents aged 18 to 19 years in a cohort studied in 1994 in Ribeirão Preto, Brazil, thus corroborating the results of the current study.

IUGR rates for both early (22.3%) and late adolescences (19.1%) were higher than that of the

Control Group (15.4%), although this difference was not significant. Studies that have attempted to associate teenage pregnancy with increased IUGR rates are contradictory; in fact, some of them attributed it to demographic and socioeconomic factors that were not actually controlled<sup>9-11</sup>. An Australian study concluded that the risk of maternal morbidity is significantly increased by social disadvantage<sup>32</sup>.

Preterm birth was more prevalent among pregnant women of advanced age (14.3%) compared with those aged 20 to 35 years; however, the statistical significance was borderline (OR=1.4; 95%CI 0.99–1.96; p=0.05). Regarding IUGR, a small but not significant difference was found between the group of women older than 35 years (16.1%) and the Control Group (15.4%; OR=1.3; 95%CI 0.9–1.8; p=0.13). These findings do not concur with several previous studies that reported higher rates of adverse obstetric outcomes in pregnant women of advanced age<sup>33-35</sup>. However, similar to our findings, other studies have found no association between advanced maternal age and adverse obstetric outcomes<sup>19,36,37</sup>, suggesting that without risk factors such as hypertension and/or diabetes, the course and outcome of the pregnancy of women of advanced age could be similar to those of younger women. Consequently, advanced maternal age alone cannot be associated with the studied perinatal outcomes (preterm birth and IUGR). Risk factors like hypertension and diabetes, which were more prevalent in pregnant women of advanced age, may instead be the factors responsible for the adverse outcomes. These findings indicate that minimizing the risks associated with these adverse outcomes will require improved prenatal care for women at either end of their reproductive life.

This study has some limitations. The cross-sectional design of the study did not allow more robust conclusions about the risk of the studied outcomes, indicating only the associations. Furthermore, although the number of studied patients was appropriate, extremes of the age categories were not represented by optimal numbers of individuals; some of the borderline associations could therefore potentially reach significance in larger samples.

The present research makes an important contribution to the discussion about the influence of maternal age on two studied perinatal outcomes because this was a population-based study, and the sample size, despite the problems mentioned, was larger than those of most studies on this subject. The work also adds essential information on a subject that is poorly understood, particularly in the Northeastern region of Brazil.

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