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Late pregnancy: impact on prematurity and newborn's weight

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SUMMARY

OBJECTIVE: This study aimed to evaluate the frequency of late pregnancies in Brazil, the age-specific fertility rate (ASFR) in the regions, the rate of prematurity, and the rate of low birth weight (LBW) and their association with advanced maternal age compared with 20–34-year-old women.

METHODS: This was a cross-sectional study conducted by searching the Information System on Live Births (*Sistema de Informações Sobre Nascidos Vivos* [SINASC]). Data from 1995 to 2018 were collected, and pregnant women were divided into three categories based on their age range: 35–39, 40–44, and ≥45 years. The study calculated the frequency of deliveries of mothers of advanced age in Brazil, the ASFR, and the rates of prematurity and LBW in each group.

RESULTS: The frequency of newborns (NB) of mothers aged ≥35 years increased by 64%. The 35–39-year-old ASFR increased in all regions, except in the northeast. At maternal age ≥35 years, NB increased by 58% between 28 and 36 weeks during the study period. LBW increased between 500 and 1,499 g in 68.7% and between 1,500 and 2499 g in 57% of cases. In 2018, regarding the age range of 20–34 years, the chance of premature delivery was 29% at 35–39 years (OR=1.29), 54% higher at 40–44 years (OR=1.54), and 114% higher at ≥45 years (OR=2.14); while the chance of LBW increased by 28% at 35–39 years (OR=1.28), 56% at 40–44 years (OR=1.56), and 139% at 45 years or older (OR=2.39).

CONCLUSIONS: The frequency of deliveries and ASFR ≥35 years increased between 1995 and 2018. The chances of prematurity and LBW were higher with increased maternal age.

KEYWORDS: Prematurity. Maternal age. Fertility rate. Pregnancy complications. Low birth weight.

INTRODUCTION

In recent decades, there has been an increased presence of women in the labor market along with the advent of debates on female empowerment, gender roles, and reproductive rights. While taking on other roles and considering the political, economic, and cultural contexts, many women choose to postpone motherhood[1]. With this, many mothers aged 35 years or older will be considered as "late pregnancy"[2]. Data from the Information System on Live Births (*Sistema de Informações Sobre Nascidos Vivos* [SINASC])[2] in Brazil show that the number of live births in mothers aged ≥35 years was 275,277 in 2000 and 457,109 in 2018, with an increase of 66%, which justifies the study of this population[2,3].

Pregnancy with advanced maternal age is a risk factor for obstetric and neonatal complications such as preeclampsia,

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hypertension, and gestational diabetes, resulting in higher rates of cesarean delivery and low birth weight (LBW)[4]. Therefore, it is important to study women who choose to postpone pregnancy to decrease the rates of peripartum complications due to higher maternal-fetal risk[2,4,5].

This study aims to evaluate the frequency of late pregnancies in Brazil, the age-specific fertility rate (ASFR) per region, the rates of prematurity and LBW, and their association with advanced maternal age as compared with 20–34-year-old women.

METHODS

This cross-sectional study obtained information from the SINASC database of the Department of Informatics of the Unified Health System (*Departamento de Informática do Sistema Único de Saúde* [DATASUS]) of the Ministry of Health in Brazil from 1995 to 2018[3]. The estimated total female population was obtained from the SINASC database until 2000 and from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística* [IBGE]) after 2001[6].

The 24-year period was grouped into four groups for data analysis: 1995–2000, 2001–2006, 2007–2012, and 2013–2018.

The maternal ages that were considered advanced for pregnancy were divided into the following: 35–39 years, 40–44 years, and 45 years or more. The control group included pregnant women between 20 and 34 years of age.

Gestational age was subdivided into 22–27 weeks (limit of fetal viability), 28–36 weeks (premature newborns, NB), 37–41 weeks (full-term pregnancies), and 42 weeks or more (postdatism situations).

Birth weight was subdivided into four subgroups: <500 g, 500–1,499 g; 1,500–2,499 g, 2,500–3,999 g, and ≥4,000 g.

The exclusion criteria were gestational age of <22 weeks (for miscarriage) and ignored maternal age. Since cases with the studied variable marked as "ignored" were not computed, the distribution of some variables did not reach 100%.

The frequency of late pregnancies was calculated by dividing the number of live births (LB) with maternal age ≥35 years by the total number of LB in the same period and region multiplied by 100. The fertility rate was obtained as the ratio between the number of LB and the total number of women living in the same period and region multiplied by 1,000. Fertility rate growth was calculated as the rate difference between 2013–2018 and 1995–2000 on the initial period value. The relationship between maternal age and birth weight used the number of LB with a given birth weight at maternal age ≥35 years divided by the total number of LB in the same period of a given birth weight multiplied by 100.

The graphs and data analysis were performed using Excel and R-Project software.

RESULTS

After applying the exclusion criteria, the total number of LB in Brazil was 18,408,043 with 1,498,193 mothers aged ≥35 years in 1995–2000, which is equivalent to 8.1% of births in the period. Between 2001 and 2006, there were 18,219,699 LB and 1,655,517 mothers of advanced age (9.1%). Between 2007 and 2012, the total number of LB decreased to 17,388,554, but mothers aged ≥35 years increased to 10.4% (1,808,578). Between 2013 and 2018, the total number of LB (17,627,221) was stable, with a significant increase in the number of LB of mothers aged ≥35 years to 2,354,305 (13.4% of the total) (Figure 1).

The frequency of LB between 1995 and 2018 increased in mothers in the following age groups: ≥35 years (64% increase), 35–39 years (69.8% increase), and 40–44 years (51.7% increase).

The comparison between 1995–2000 and 2013–2018 showed a 13.7% increase in ASFR for mothers aged 35–39 years in Brazil.

In the north of the country, ASFR increased by 4.9% for mothers aged between 35 and 39 years. For mothers aged between 40–44 and 45–49 years, it reduced by 19.6% and 53.2%, respectively.

In the northeast region, ASFR decreased in the three age groups by 3.5, 28.7%, and 33.6%, respectively.

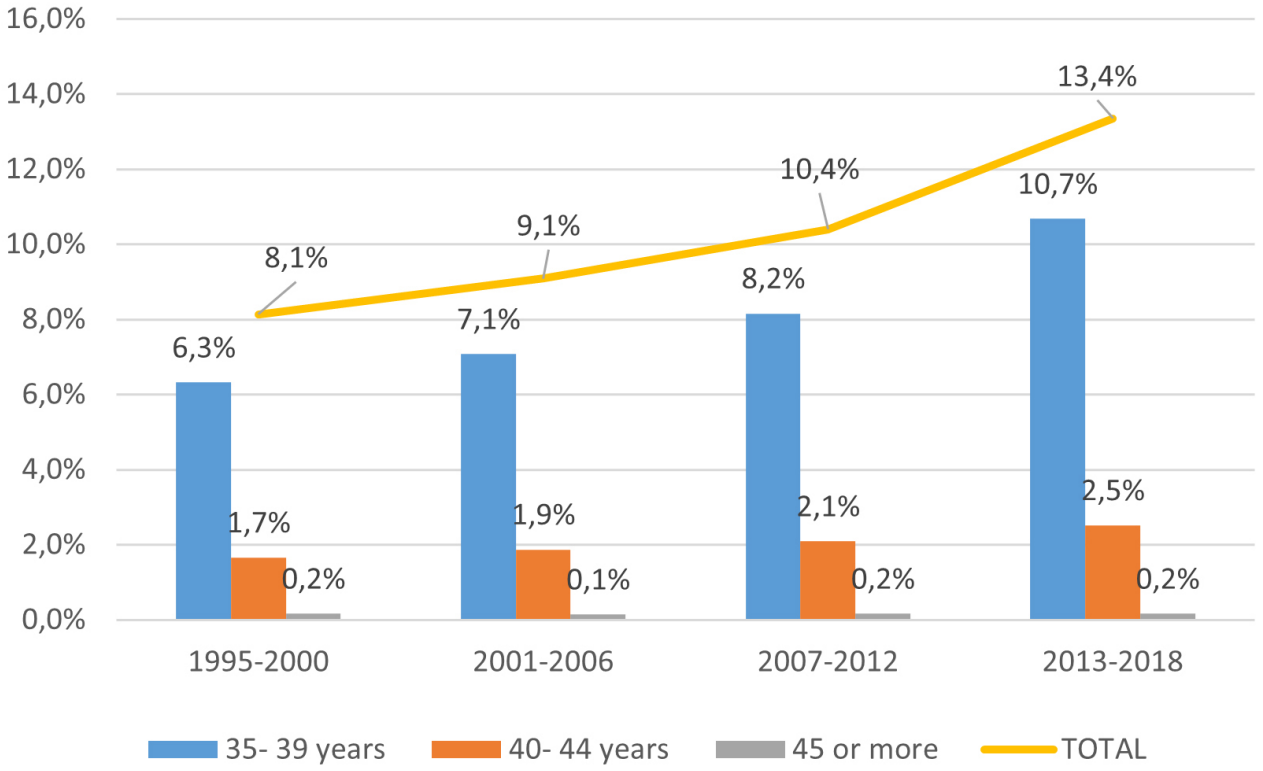
In the central-west region, ASFR increased by 48.9% between 35 and 39 years and by 32.1% between 40 and 44 years. It reduced by 26.6% in the age range of 45–49 years.

In the southeast region, ASFR increased by 26.7% between 35 and 39 years and by 20.1% between 40 and 44 years. For mothers aged between 45 and 49 years, it was reduced by 16.7%.

In the southern region of the country, ASFR/1,000 increased by 6.4% between 35 and 39 years. The other two age groups reduced by 12.2% and 50.9%, respectively (Table 1).

As for the duration of early pregnancy, the number of LB at 22–27 weeks increased by 70.2% between 1995 and 2018. Between 28 and 36 weeks and between 37 and 41 weeks, it increased by 58% and 66.3%, respectively (Table 2). Therefore, there was a higher frequency of pregnancies ≥35 years in all subgroups, which was more pronounced in extremely premature and full-term infants.

As for LBW, there was an increase in all subgroups between 1995 and 2018 in mothers aged ≥35 years. The frequency of LB increased by 68.7% between 500 and 1,499 g and by 57% between 1,500 and 2,499 g.



	1995–2000	2001–2006	2007–2012	2013–2018	Variation in the period (%)
35–39 years	1,162,926 (6.3)	1,288,588 (7.1)	1,418,740 (8,2)	1,881,796 (10.7)	↑69.8
40–44 years	305,340 (1.7)	341,116 (1.9)	363,495 (2.1)	443,609 (2.5)	↑51.7
45 years or above	29,926 (0.2)	25,806 (0.1)	28,343 (0.2)	28,900 (0.2)	↓1.6
Total	1,498,193 (8.1)	1,655,517 (9.1)	1,808,578 (10.4)	2,354,305 (13.4)	↑64.0

The values in the table represent the absolute number of live births in the respective age groups and, between parentheses, the percentage of live births in the period in the respective age groups in relation to the total live births in the period.

Figure 1. Frequency of pregnancy in women aged ≥35 years or more in Brazil (1995–2018).

The chances of premature delivery and LBW were analyzed based on data from 2018. The prevalence of premature delivery in the control group (20–34 years) was 10.3%. These rates increase proportionally to maternal age, being 12.9% between 35 and 39 years, 15.0% between 40 and 44 years, and 19.7% in ≥45 years. Pregnant women aged 35–39 years have a 29% higher chance of premature delivery than those aged 20–34 years [p<0.001, OR=1.29 (95%CI 1.27–1.30)]. At 40–44 years, the chance increases to 54% [p<0.001, OR=1.54 (95%CI 1.51–1.57)], and at ≥45 years, the chance of preterm delivery doubles in relation to 20–34 years [p<0.001, OR=2.14 (95%CI 1.99–2.30)].

The prevalence of LBW was 7.9% in the control group. Between 35 and 39 years, it increased to 9.8, 11.7% at 40–44 years, and 18.3% at ≥45 years. The chance of LBW between 35 and 39 years was 28% higher than that between 20 and 34 years [p<0.001, OR=1.28 (95%CI 1.26–1.30)]. At 40–44 years, the chance of NB with LBW increases to 56% [p<0.001, OR=1.56 (95%CI 1.53–1.59)] and 139% at ≥45 years [p<0.001, OR=2.39 (95%CI 2.23–2.57)] (Table 2).

DISCUSSION

The last decades of the 20th century showed increased participation of women in the labor market. This includes a process of continuous expansion, political and economic changes, and movement to seek equity between men and women[7]. This movement followed a decreased birth rate that reflected

Table 1. Age-specific fertility rate/1,000 women aged ≥35 years in the regions of Brazil (1995–2018).

North region													
Maternal age (years)	1995–2000			2001–2006			2007–2012			2013–2018			Variation 2013–2018 to 1995–2000
	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	
35–39	2,019,196	64,013	31.7	2,512,602	79,561	31.7	3,119,241	97,624	31.3	3,984,599	132,498	33.3	4.9%
40–44	1,590,054	1,9250	12.1	2,040,078	22,423	11.0	2,626,489	25,694	9.8	3,312,505	32,224	9.7	-19.6%
45–49	1,212,189	2,293	1.9	1,742,507	2,608	1.5	2,194,995	2,471	1.1	2,680,054	2,375	0.9	-53.2%
Total	8,612,299	85,556	9.9	10,555,205	104,592	9.9	14,082,620	125,789	8.9	9,977,158	167,097	16.7	68.6%
Northeast region													
Maternal age (years)	1995–2000			2001–2006			2007–2012			2013–2018			Variation 2013–2018 to 1995–2000
	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	
35–39	8,407,568	290,313	34.5	9,863,931	329,563	33.4	11,048,258	345,828	31.3	13,234,508	441,184	33.3	-3.5%
40–44	7,043,303	92,026	13.1	8,162,943	98,462	12.1	10,206,393	95,591	9.4	11,529,569	107,354	9.3	-28.7%
45–49	26,515,402	11,463	0.4	30,959,251	9,120	0.3	39,417,304	7,820	0.2	24,764,077	7,106	0.3	-33.6%
Total	42,247,527	394,329	9.3	48,986,125	437,374	8.9	60,671,955	449,822	7.4	49,528,154	556,289	11.2	20.3%
Central-west region													
Maternal age (years)	1995–2000			2001–2006			2007–2012			2013–2018			Variation 2013–2018 to 1995–2000
	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1,.000	
35–39	2,333,033	57,883	24.8	2,880,175	72,237	25.1	3,335,263	95,671	28.7	3,934,303	145,312	36.9	48.9%
40–44	1,880,647	12,956	6.9	2,344,215	15,807	6.7	3,007,460	21,139	7.0	3,486,192	31,722	9.1	32.1%
45–49	1,444,370	1,167	0.8	2,047,978	990	0.5	2,611,653	1,304	0.5	3,075,702	1,823	0.6	-26.6%
Total	9,589,369	72,006	7.5	12,061,893	89,034	7.4	16,313,916	118,114	7.2	10,496,197	178,857	17.0	126.9%

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Table 1. Continuation.

North region													
Southeast region													
Maternal age (years)	1995–2000			2001–2006			2007–2012			2013–2018			Variation 2013–2018 to 1995–2000
	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	
35–39	16,060,684	527,001	32.8	18,278,641	590,144	32.3	18,539,827	660,988	35.7	21,046,815	875,035	41.6	26.7%
40–44	13,754,946	123,286	9.0	16,264,584	146,153	9.0	17,807,649	164,219	9.2	19,052,960	205,111	10.8	20.1%
45–49	10,986,161	8,886	0.8	14,665,077	8,632	0.6	16,744,024	9,623	0.6	17,542,724	11,814	0.7	-16.7%
Total	76,884,903	659,173	8.6	91,095,225	744,929	8.2	111,158,805	834,830	7.5	57,642,499	1,091,960	18.9	121.0%
South region													
Maternal age (years)	1995–2000			2001–2006			2007–2012			2013–2018			Variation 2013–2018 to 1995–2000
	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	Fem. pop.	Nº LB	ASFR/1,000	
35–39	5,519,462	223,716	40.5	6,379,145	217,083	34.0	6,121,427	218,629	35.7	6,674,118	287,767	43.1	6.4%
40–44	4,701,741	57,822	12.3	5,526,089	58,271	10.5	6,157,495	56,852	9.2	6,220,413	67,198	10.8	-12.2%
45–49	3,806,339	4,697	1.2	5,005,921	3,735	0.7	5,867,858	3,426	0.6	6,027,612	3,652	0.6	-50.9%
Total	26,305,429	286,235	10.9	31,199,313	279,089	8.9	37,957,265	278,907	7.3	44,120,618	358,617	8.1	-25.3%
Brazil													
Maternal age (years)	1995–2000			2001–2006			2007–2012			2013–2018			Variation 2013–2018 to 1995–2000
	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1.000	Fem. pop.	Nº LB	ASFR/1.000	
35–39	34,339,943	1,162,926	33.9	39,914,494	1,288,588	32.3	42,164,016	1,418,740	33.6	48,874,343	1,881,796	38.5	13.7%
40–44	28,970,691	305,340	10.5	34,337,909	341,116	9.9	39,805,486	363,495	9.1	43,601,639	443,609	10.2	-3.5%
45–49	24,492,362	109,069	4.5	31,624,426	114,427	3.6	37,624,923	112,415	3.0	40,855,661	127,018	3.1	-30.2%
Total	87,802,996	1,577,335	18.0	105,876,829	1,744,131	16.5	119,594,425	1,894,650	15.8	133,331,643	2,452,423	18.4	2.4%

Source: SINASC/IBGE; Fem. pop.: female population; ASFR: age-specific fertility rate; Nº: number; LB: live born.

Table 2. Total number of live births of mothers ≥35 years by gestational age and birth weight, and association with prematurity and low birth weight.

	1995–2000		2001–2006		2007–2012		2013–2018		Variation in the period 1995–2018 (%)
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	
Gestational age (weeks)									
22–27	7,178	8.4	6,170	9.9	8,291	11.4	12,362	14.3	70.2
28–36	32,828	10.0	127,307	11.5	176,266	13.1	294,299	15.8	58.0
37–41	1,209,895	8.0	1,483,394	8.9	1,567,948	10.2	1,955,544	13.3	66.3
≥42	40,873	7.7	17,807	8.3	21,882	7.7	43,633	8.4	9.1
Total	1,290,774	8.1	1,634,678	9.1	1,774,387	10.4	2,305,838	13.4	65.4
NB weight (g)									
Less than 500	247	1.0	547	12.1	1,525	11.1	2,445	13.5	1,200.2
500–1,499	8,945	10.5	22,906	12.3	27,865	14.2	36,628	17.7	68.7
1,500–2,499	90,200	10.2	142,155	11.4	154,775	12.8	196,437	16.1	57.0
2,500–3,999	1,069,815	7.7	1,349,170	8.7	1,633,763	11.1	1,931,823	13.0	69.3
4,000 or more	106,274	10.9	108,288	11.5	108,812	12.5	137,914	15.7	44.3
Total	1,275,481	8.1	1,623,066	9.1	1,926,740	11.3	2,305,247	13.4	67.2
Association between maternal age and prematurity (Brazil, 2018)									
Maternal age (years)	Freq	%	p-value	OR (95%CI)					
20–34	205,831	10.3							
35–39	46,451	12.9	<0.001	1.29 (1.27–1.30)					
40–44	12,707	15.0	<0.001	1.54 (1.51–1.57)					
>45	954	19.7	<0.001	2.14 (1.99–2.30)					
Association between maternal age and low birth weight (Brazil, 2018)									
Maternal age (years)	Freq.	%	p-value	OR (95%CI)					
20–34	159,564	7.9		c					
35–39	36,004	9.8	<0.001	1.28 (1.26–1.30)					
40–44	10,076	11.7	<0.001	1.56 (1.53–1.59)					
≥45	900	18.3	<0.001	2.39 (2.23–2.57)					

Freq.: frequency; c: denotes comparative group.

the behavior of a significant part of the Brazilian population, with the demographic profile changing to a lower number of children per family unit due to pregnancy postponement, among other factors[1].

This study showed an increase of 64% in the frequency of advanced-age pregnancies between 1995 and 2018 in Brazil. Those with ages of 35–39 years represented the largest portion of pregnancies in all periods, but the frequency increased by 51% between 40 and 44 years. This information corroborates the data presented in 2005[3], showing an increased proportion of births in mothers aged ≥40 years, from 1.75% to 1.95%, between 1996 and 2002[3,8].

The contribution of women to the household income increased relatively regularly from 15.7% in 1981 to 23.8% in 2002, which is a leap that reflects economic, social, and political changes in this period[7]. More specifically, in the last decade, late pregnancy increased by 84% in the United States due to behavioral changes in the family. Some studies also show that the proportion of deliveries after 40 years of age varies from 2% to 5%[8,9].

The number and quality of oocytes decrease at advanced ages, with a higher decline after 35 years[10]. Nevertheless, the increased frequency of pregnancies of >50% in the age group ≥40 years indicates the influence of other factors, such as the search for assisted reproduction techniques (ART).

The risk of placenta previa, cesarean section, preterm delivery, and LBW is higher in the ART group, but advanced age also poses a risk for these outcomes regardless of the form of

conception[11]. After 40 years of age, with 18.2% of births by ART, a significant increase in preeclampsia and prematurity was observed in the ART group. At ≥45 years, the risk was significantly higher among women who conceived naturally[5].

The ASFR increased between 35 and 44 years in 1995–2018 in Brazil. This increase was related to a higher frequency of late pregnancies between 2013 and 2018. The south, southeast, and center-west regions comprised approximately 65% of the Brazilian female population between 35 and 39 years in 2018. Therefore, the national standard reflects these three regions[6]. They are economically more developed and populous regions, have reference centers in assisted reproduction, higher levels of education, and access to contraception, which is probably related to the increasing participation of women in the workforce leading to the postponement of pregnancy[1,7].

This study showed that prematurity increases proportionally with maternal age, doubling the chance at ≥45 years of age. This result corroborates the results of several previous studies. A meta-analysis of pregnant women aged ≥45 years showed twice the chance (OR=1.96) of premature birth and four times the chance of cesarean delivery[12]. Another meta-analysis evaluated pregnant women aged 35–40 and >40 years with a greater propensity to overweight, hypertension, and gestational diabetes, as well as adverse perinatal results such as premature delivery, LBW, higher perinatal mortality, and stillbirth[13]. Bouzaglou et al. also found a significant increase in gestational hypertension (3.1×1.1%, p<0.001), premature delivery (10.4×6.5%, p<0.001), and intrauterine fetal death (2.1×0.5%, p<0.001) at ≥40 years[4]. Ogawa et al. reported a higher risk of severe preeclampsia, placenta previa, and premature delivery in pregnant women ≥45 years[5].

LBW is directly associated with premature birth. Gravena et al.[14] reported a prevalence of 12.5% and a 24% higher chance of LBW at >35 years, similar to the 12.8% in NB between 1,500 and 2,499 g between 2007 and 2012 obtained in this study.

The proportion of NB with weight <500 and >4,000 g in women of advanced age increased between 1995 and 2018. Although LBW is the focus of this study, due to its close relationship with unfavorable perinatal outcomes, it is worth reflecting on maternal factors involved in the increased number of macrosomic complications at advanced maternal age, such as gestational diabetes[15].

One of the limitations of an observational study is that the formulated hypotheses cannot be tested and proven as an association of cause and effect. Women who became pregnant later are not necessarily the same women who postponed pregnancy due to greater participation in the labor market, among other reasons. However, this phenomenon is observed worldwide, leading to a reflection on the historical and economic contexts in which the period studied is inserted. In addition, it is worth emphasizing the insufficient filling of official data and the obtention of the real number of pregnancies since fetal deaths and abortions were not included.

CONCLUSIONS

There was an increased frequency of LB and ASFR for ages ≥34 years between 1995 and 2018. The chances of prematurity and LBW were higher with increased maternal age. Advanced maternal age is a factor of gestational risk; therefore, adequate access and quality of care are important in the pre-, peri-, and postnatal periods for these women who, by chance or by choice, become pregnant in the late end of their reproductive life.

AUTHORS' CONTRIBUTIONS

LKSS: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **DLMM:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **CRS:** Investigation, Project administration, Visualization. **FEFM:** Formal analysis, Project administration, Resources, Software. **FMS:** Formal analysis, Methodology, Supervision, Validation, Visualization. **NCPR:** Conceptualization, Formal analysis, Resources, Software.

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