Artigo Original

Analysis of the incidence of trisomy of chromosome 21 in pregnancies across different age groups between 2000 and 2020

Análise da incidência da trissomia do cromossomo 21 nas gestações em diferentes faixas etárias entre 2000 e 2020

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Abstract

Objective: This study investigated the relationship between maternal age and the risk of trisomy 21 (T21) in mothers over 35 years old by analyzing the incidence of T21 in Brazil from 2000 to 2020. Methods: A descriptive quantitative and cross-sectional methodology was employed, with data collected from the DATASUS database and the Integrated Health Surveillance Platform. IBM SPSS Statistics v23 software was used for statistical analysis. Results: A decrease in pregnancies among younger mothers (15-24 years) and stable numbers for mothers over 35 were observed. There was a significant increase in births of children with T21 from mothers over 35 in the last decade. Conclusion: Data suggest the influence of biopsychosocial factors on the significant increase in births of children with T21 from mothers over 35, as the total number of pregnancies in this age group did not vary significantly over the two decades analyzed.

Keywords: Maternal age; Trisomy 21; Down syndrome; Pregnancy; Incidence.

Resumo

Objetivo: Este estudo investigou a relação entre idade materna e o risco de trissomia 21 (T21) em mães com mais de 35 anos analisando a incidência de T21 no Brasil no período do ano 2000 ao ano de 2020. Métodos: Foi utilizada uma metodologia descritiva quantitativa e transversal onde os dados foram coletados na base de dados DATASUS e na Plataforma Integrada de Vigilância em Saúde. A análise estatística foi feita com o software IBM SPSS Statistics v23. Resultados: Observou-se uma queda no número de gestações entre mães jovens (15-24 anos) enquanto o número de gestações entre mães com mais de 35 anos permaneceu estável. Houve um aumento significativo no número de nascimentos de crianças com T21 de mães com mais de 35 anos na última década analisada. Conclusão: Os dados sugerem a influência de fatores biopsicossociais no aumento significativo de nascimentos de crianças com T21 de mães com mais de 35 anos, dado que o número total de gestações nesta faixa etária não variou significativamente nas duas décadas analisadas.

Palavras-chave: Idade maternal; Trissomia 21; Síndrome de Down; Gravidez; Incidência.

INTRODUCTION

Down Syndrome (DS), or Trisomy 21 (T21), is a genetic condition resulting in intellectual disability due to an extra chromosome in chromosome pair 21. Individuals with Down syndrome exhibit a delay in neuropsychomotor development, which is associated with low muscle tone and challenges in maintaining posture and balance. DS may also manifest distinctive physical characteristics, such as a flat face, almond-shaped eyes, and a single crease in the palm. These characteristics can vary in severity from person to person. Although DS may present significant challenges, many individuals with this syndrome lead fulfilling lives, achieving various developmental milestones and positively contributing to their communities (Knychala *et al.,* 2018). In Trisomy 21 (T21), the genetic origin lies in an additional chromosome 21, resulting in 47 chromosomes instead of the usual 46. This extra chromosome can occur during the formation of reproductive cells, eggs, or sperm in a nondisjunction process. Nondisjunction happens when chromosomes fail to separate properly during cell division, leading to an unequal distribution of chromosomes in the resulting cells. As a result, when an egg or sperm with an extra chromosome 21 combines with a normal egg or sperm during fertilization, the resulting embryo ends up with three copies of chromosome 21 instead of the usual two. This genetic anomaly leads to the characteristic features and health challenges associated with Down syndrome (Ferreira *et al.*, 2019).

One of the primary features of Down syndrome (DS) is a delay in intellectual development, as well as physical characteristics such as folds in the eyelids, a flat facial profile, upward-slanting eyes, hypotonia, and small hands, among others. Individuals with DS may also experience additional health issues, including heart disease, hearing and vision problems, obesity, premature aging, and neurological difficulties. Research has identified maternal parental origin as the cause of chromosome 21 in 95% of cases (Ferreira *et al.*, 2019).

Maternal age is a critical factor in pregnancy, with research indicating that the ideal reproductive age range is typically considered to be between 18 and 35 years old. Beyond this age range, particularly after the age of 35, women may face increased risks during pregnancy. This is primarily due to the natural decline in the quantity and quality of a woman's eggs as she ages. With advancing maternal age, there is a heightened likelihood of chromosomal abnormalities occurring in the developing fetus, including Trisomy 21, the chromosomal anomaly associated with Down syndrome (Franasiak *et al.*, 2014).

The risk of chromosomal abnormalities, such as Trisomy 21, tends to rise exponentially with maternal age, especially after the age of 35. This is because older eggs are more prone to errors during cell division, increasing the chance of an extra chromosome 21 in the resulting embryo. Therefore, maternal age is a crucial factor to consider in prenatal care, and women over the age of 35 are often offered additional screening and diagnostic tests to assess the risk of chromosomal abnormalities in their pregnancies (Ferreira *et al.*, 2019).

At the end of the reproductive age, pregnancy has significantly increased worldwide (Veiga *et al.* 2019). Due to various social transformations, such as increased levels of education influencing the economic and cultural spheres, women are giving birth later in life. Therefore, this puts them at a higher risk for developing complications during pregnancy, thereby making their pregnancy high-risk (Aldrighi *et al.*, 2016). The likelihood of developing genetic syndromes, such as Edwards syndrome, Patau syndrome, and Down syndrome, is lower in women who are pregnant at the optimal age (Ferreira *et al.* 2022).

In Brazil, the percentage of births to mothers of advanced maternal age increased from 7.6% in 1994 to 15.5% in 2018. Despite awareness of the potential maternal-fetal complications due to advanced age, the rate of such cases continues to rise (Brasil, 2022).

In diagnosing Down syndrome (DS), various methods are available to assess the likelihood of a chromosomal abnormality such as Trisomy 21. One common method is prenatal screening, which involves non-invasive tests such as maternal serum screening and ultrasound examinations. These tests can provide an indication of the likelihood of Down syndrome in the fetus, allowing parents to make informed decisions about further diagnostic testing for a definitive diagnosis; diagnostic tests such as chorionic villus sampling (CVS) or amniocentesis may be performed. These procedures involve sampling fetal cells or amniotic fluid to directly analyze fetal chromosomes. While these tests carry a small risk of miscarriage, they provide a highly accurate diagnosis of Down syndrome. In recent years, non-invasive prenatal testing (NIPT) has also become available, which

involves analyzing cell-free fetal DNA circulating in the mother's blood. NIPT offers a highly accurate screening option with a lower risk of miscarriage compared to invasive diagnostic tests. Overall, the availability of these diagnostic methods allows healthcare providers to offer comprehensive prenatal care and support to families facing the possibility of a child with Down syndrome. Additionally, early diagnosis enables families to access appropriate medical care and support services, facilitating better outcomes for the child and their family (Schettini *et al.*, 2022).

Health professionals must provide them with all pregnant women and provide them with vital information throughout the gestational period, which facilitates proper emotional growth in women during pregnancy. Nurses are instrumental in offering guidance on healthcare during pregnancy and postpartum care and supporting the woman's future necessities. Therefore, competent and experienced professionals who offer guidance and support to these women, promoting improved outcomes for late-term pregnancies, can be game changers throughout gestation (Aldrighi *et al.*, 2016).

This study was based on the following guiding question: What is the statistical significance of advanced maternal age in the birth of children with Down syndrome? Sample tests were conducted to confirm the hypothesis's significance.

This study aims to examine the incidence of trisomy 21 (T21) cases among mothers in pregnancies in different age groups in Brazil between 2000 and 2020. Its primary objective is to investigate the variation in the number of births with T21.

METHOD

This study utilized primary data from the Department of Informatics of the Brazilian Unified Health System (DATASUS) and the Integrated Health Surveillance Platform between 2000 and 2020. Ethical evaluation was not required as per the National Health Council's Resolution 510/16, which waives ethical appraisal in the sole paragraph of Article 1.

This is a descriptive quantitative cross-sectional study. The Department of Informatics of the Brazilian Unified Health System (DATASUS) provided data on the number of children born between 2000 and 2020. The Integrated Health Surveillance Platform collected information on the total number of children born with Trisomy 21 (Down Syndrome).

Data from women aged 15 to 40 years and older during pregnancy were analyzed to determine the total number of births and children born with Trisomy 21 from 2000 to 2020. Data on total births and births of children diagnosed with Trisomy 21 were sourced from the government websites DATASUS and Plataforma Integrada em Saúde, collected in August 2022. The data were collated and organized in Microsoft Office Excel 2019 spreadsheets for descriptive analysis and subsequent statistical testing.

IBM SPSS Statistics version 23 was utilized for data analysis. Initially, assumptions for univariate analysis, including normal distribution, extreme data, missing data, and homogeneity of variance, were tested. The mean and standard deviation were used to describe the data. The collected years were segregated into decade periods (first decade: 2000-2010, second decade: 2011-2020). The number of children with Trisomy 21 was normalized by the total number of births and then multiplied by 1000 (PT21). An unpaired t-test was utilized to compare the decades. An age group comparison was conducted using a one-way ANOVA, followed by the Bonferroni post hoc test. A two-way ANOVA was performed to evaluate the interaction between the decade and age groups for the total number of births and percentage variables. Statistical significance was considered at $p < 0.05$ for all tests.

RESULTS

Two comparisons were made: the first was between the decades and the percentage of births of children with Trisomy 21(PT21), and the other was between the decades with the total number of births. In the first comparison, it was verified that there was an increase in the number of births with T21 in the age groups between 35 to 39 years and over 40 years, while in the other age groups, there was no significant increase. In the second comparison, there was only a decrease in total births in relation to the 15 to 24 age groups, while in the other age groups there were few significant differences.

No significant differences were identified for the total number of births when the decades were compared [$t(82) = 0.181$; $p = 0.856$], as well as the percentage of births with Trisomy 21 (PT21) [$t(82) = 1.484$; $p = 0.142$] (Table 1).

Table 1 - Analysis of the percentage of births of children with T21

| Variable	Decades		Total	p-value
	2000-2010	**2011-2020**		
	Mean ± sd	**Mean ± sd**	**Mean ± sd**	
Total number of births /10^6	7,41± 6,27	7,18 ± 5,39	7,30± 5,83	0,856
Percentage of births of children with T21 x 10^3	2,57± 3,60	4,06 ± 5,47	3,28 ± 4,62	0,142

Source: The authors

When the age groups were compared, significant differences were identified in total births [$F(3.80) = 799.01$; $p < 0.001$]; Post hoc analysis showed that there are significant differences ($p < 0.001$) in the comparison between all age groups and the younger the age group, greater is the number of births. With regard to PT21, a significant difference was also found [$F(3.80) = 49.40$; $p < 0.001$]. The age group 15 to 24 years old (mean = $0.29 ± 0.15$) had a lower percentage when comparing the age groups 35 to 39 years old (mean = $2.79 ± 1.56$; $p < 0.001$); 0.029) and over 40 years old (mean = $9.48 ± 5.34$; $p < 0.001$). The age group over 40 years old also had a higher percentage in the comparison between the age groups 25 to 34 years old (mean = 0. $58 ± 0.29$; $p < 0.001$) and 35 to 39 years old ($p < 0.001$) (Table 2).

Table 2 - Analysis of the difference between age groups

| Variables	Age group				Total	p-Value
	15 to 24 years old	**25 to 34 years old**	**35 to 39 years old**	**over 40 years old**		
	Mean ± sd	**Mean ± sd**	**Mean ± sd**	**Mean ± sd**	**Mean ± sd**	
Total number of births /10^6	13,74± 1,95	12,14 ± 0,65	2,62 ± 0,55	0,70 ± 0,12	7,30 ± 5,83	> 0,001
Percentage of births of children with T21 x 10^3	0,29 ± 0,14	0,57 ± 0,29	2,78 ± 1,56	9,47 ± 5,34	3,28 ± 4,62	> 0,001

Source: The authors

The two-way ANOVA identified the interaction between decade and age group [$F(3.76) = 53.747$; $p < 0.001$; $np2 = 0.680$]. When the two decades were compared, a decrease in births of children with mothers aged between 15 and 25 years ($p < 0.001$) was found, and an increase was observed for the age groups between 25 and 34 years ($p < 0.01$) and 35 to 39 years old ($p < 0.05$) (Graph 1).
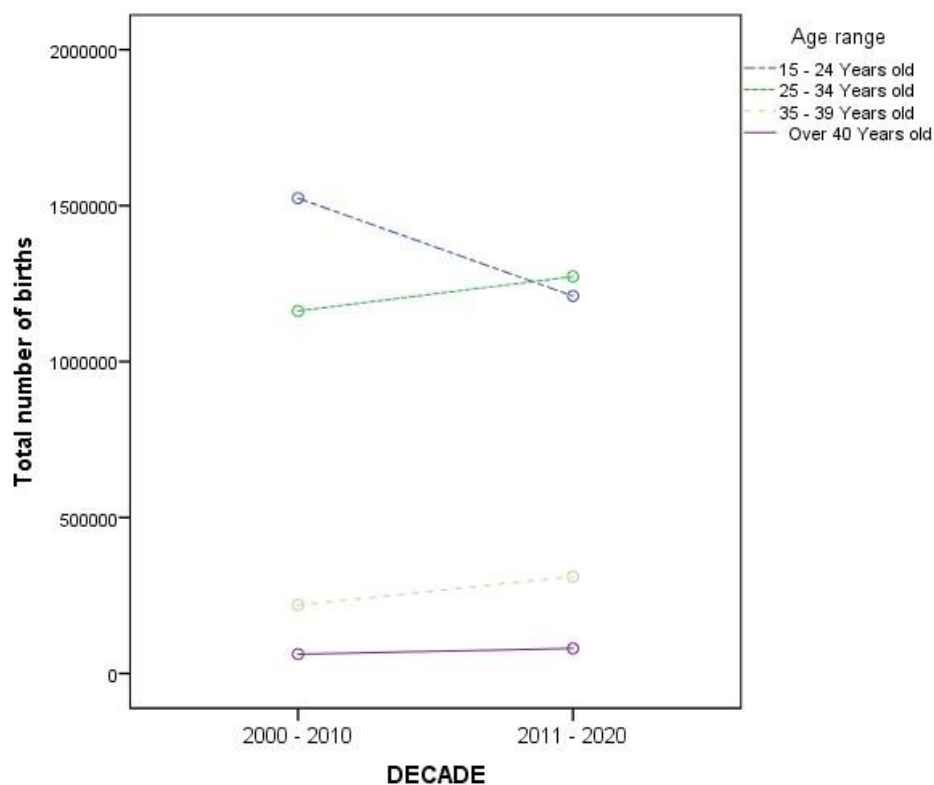
Graph 1 - Data on the total number of births in the last two decades by age groups.
Source: The authors
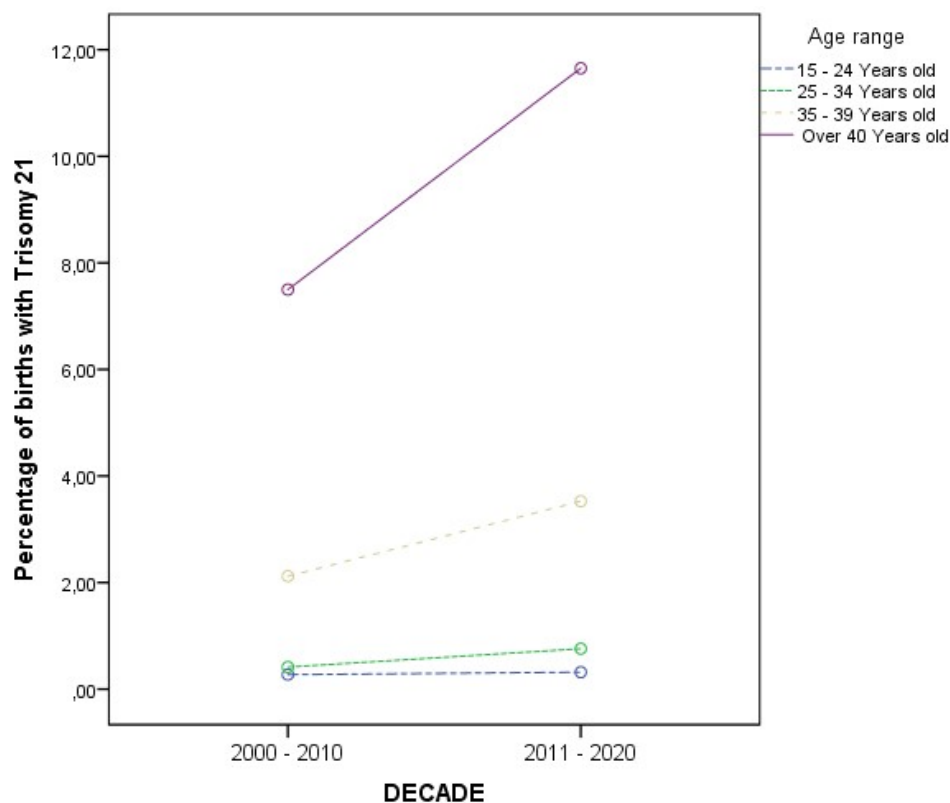
Graph 2 - Percentage of births with trisomy 21 in the last two decades by age groups.
Source: The authors

The PT21 variable showed no significant interaction [$F(3.76) = 2.678$; $p = 0.053$; $np2 = 0.096$] (Table 2) despite indicating a trend and an average effect magnitude. There was no increase in PT21 in the comparison between decades for the age group between 15 and 25. However, the most significant increase occurred in the age groups of more than 40 and 35 to 39 (Graph 2).

DISCUSSION

Throughout the studied decades, there has been an increase in the birth rate of T21 children related to maternal age groups between 35 and over 40 years, confirming the hypothesis that late pregnancy can lead to chromosomal abnormalities, one of which is T21. Studies indicate that in Brazil, there has been a rise in pregnancies in women above 35 years old, especially in middle-class layers. There was a significant representation in the South and Southeast regions in 2015, with an increase in mothers aged 30 to 39 (Martins & Menezes, 2022).

In contemporary society, women are increasingly delaying pregnancy due to a myriad of interconnected factors that reflect shifts in social norms, economic structures, and personal aspirations. One prominent reason for postponing pregnancy is the pursuit of career advancement and professional fulfillment. With more women pursuing higher education and entering the workforce, many delay starting a family to focus on building their careers and achieving financial stability. The changing dynamics of modern relationships also contribute to delayed pregnancies, as individuals may prioritize finding the right partner and establishing a strong emotional bond before starting a family. Furthermore, fertility awareness and family planning have evolved significantly, allowing women greater control over their reproductive choices. The widespread availability of contraception and reproductive technologies has empowered women to make informed decisions about when to conceive, leading to a trend of delayed childbearing. Moreover, societal attitudes towards motherhood have shifted, with many women opting to postpone pregnancy until they feel emotionally and psychologically prepared to take on the responsibilities of parenthood.

Economic factors also play a significant role in the decision to delay pregnancy, as rising living costs and economic uncertainties may deter couples from starting a family until they feel financially secure. Additionally, cultural and societal pressures, such as the idealization of youth and beauty, can contribute to women feeling compelled to postpone pregnancy to maintain their perceived attractiveness and vitality. The decision to delay pregnancy is multifaceted and reflects

the complex interplay of individual aspirations, societal expectations, and economic realities in the contemporary world (Fernandes & Martins, 2018).

As a result, late female reproduction is more prone to complications during pregnancy and childbirth, considering it a high-risk pregnancy. There is no public policy specifically aimed at this group of women with advanced maternal age; therefore, specialized care for these women falls within the general guidelines and manuals of the Ministry of Health, focused on managing high-risk pregnancy and prenatal care (Viellas *et al.*,2021).

Pregnant women over 35 years old are predisposed to diseases such as diabetes and hypertension, for example, and may have a higher likelihood of experiencing perinatal complications, including abortions, congenital anomalies, pre-eclampsia, eclampsia, and premature births. Hence, they fall into the classification of high-risk pregnancies, requiring monitoring by specialists and acquiring more knowledge. Studies show that Down Syndrome is one of the chromosomal abnormalities most relevant to maternal age and associated factors (Cosme *et al.* 2017).

It is essential to emphasize to mothers that the motor development of individuals with Down Syndrome is influenced by multiple factors, including biological, psychological, social, and environmental characteristics. Therefore, the environment in which these individuals are placed can play a facilitating role in their development. The home environment offers numerous opportunities for stimuli that can serve as potential for action, learning, and skill development (Ferreira *et al.*,2019).

As a limitation of the study, we acknowledge the absence of current data from the Integrated Health Platform for the past two years (2021-2022), confining our analysis to the past 20 years.

The results of this study can benefit nursing practice regarding the communication of a DS diagnosis. Healthcare professionals must possess appropriate communication skills. Nurses caring for families and children are integral to the maternal experience and play a crucial role during pregnancy by providing information, support, and a welcoming environment (Souza *et al.*,2023).

When informing parents of a diagnosis, nurses should possess knowledge of DS and communicate fundamental care to facilitate their child's integration into society and ensure lifelong respect for the child. They should avoid making subjective evaluations, use clear and concise language, and adhere to formal language principles (Gadonski *et al.*, 2022).

It can be inferred that the total number of births to mothers aged between 15 and 24 decreased significantly between the first and second decades analyzed. This suggests that the

female population avoids pregnancies in the early reproductive years or chooses to have children during the middle reproductive years (25 to 34 years).

The total number of pregnancies among women of advanced reproductive age exhibited a slight increase during the second decade analyzed, reinforcing the perception of the desire of women to delay motherhood. Conversely, the total number of births to mothers over 40 years old remained stable during the two decades analyzed.

The proportion of children born with T21 in pregnancies to mothers in their early reproductive years remained stable over the two analyzed decades. However, among pregnancies to mothers of intermediate reproductive age, the percentage increased slightly, indicating that external factors may have contributed to the rise in T21 incidence in this age group in the second decade (2011-2020). The proportion of births of children with T21 to mothers of advanced reproductive age, compared to the total number of births to mothers over 40, saw a significant increase in the second decade analyzed. This supports the hypothesis that possible external biopsychosocial factors may increase T21 in later pregnancies.

CONCLUSION

This study reveals a trend of women delaying childbirth. Nonetheless, late pregnancies pose a significant risk of high-risk pregnancies and the potential birth of children with Trisomy 21. In the second decade under examination, there was a notable escalation in the ratio of T21 births among mothers of advanced reproductive age relative to the overall birth count and specifically to mothers over 40. This bolsters the conjecture that potential external biopsychosocial influences might contribute to the rise of T21 incidence in later gestations. Therefore, nurses serve as support for mothers and families with a child diagnosed with DS, offering attentive listening and information about the syndrome.

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