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Parental age profile in Espírito Santo, Brazil, and its influence on the incidence of congenital anomalies in newborns

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Abstract

Congenital anomalies constitute an important public health problem, associated with advanced maternal age and possibly paternal age. This retrospective observational study, using data from SINASC/DATASUS (Espírito Santo, 2017–2023; n = 377668), evaluated this association through descriptive analyses, chi-square testing, and adjusted logistic regression, with estimation of odds ratios and 95% confidence intervals. An independent and dose-dependent association was observed between maternal age and congenital anomalies, with a marked increase in risk from the age of 35 onward, particularly for chromosomal abnormalities. In contrast, paternal age did not remain significant after adjustment. Despite the low absolute incidence, the highest relative risks were concentrated in advanced maternal ages, notably for Down syndrome and congenital heart defects. These findings reinforce advanced maternal age as the main determinant of these conditions, consistent with the accumulation of meiotic alterations and oocyte aging. Conversely, the lack of an independent association with paternal age suggests a possible confounding effect by maternal age. The absence of increased risk at younger maternal ages and the integrated population-based approach strengthen the consistency of the results, and help to fill a relevant gap in the national literature. In this context, the importance of targeted counseling and prenatal care for early diagnosis and risk reduction is highlighted.

KEYWORD: Genetic abnormalities, Chromosomal abnormalities, Parental age profile.

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Introduction

Congenital anomalies represent a major global public health concern, affecting approximately 2% to 5% of live births and constituting an important cause of neonatal and infant morbidity and mortality (GONÇALVES et al., 2021). In Brazil, analyses based on health information systems have revealed a heterogeneous distribution of these conditions, both regarding the types of malformations and the associated maternal and neonatal profiles, reflecting the influence of biological, social, and healthcare-related determinants. Furthermore, congenital anomalies rank among the leading causes of perinatal mortality, highlighting their substantial clinical and epidemiological relevance (ZHOU et al., 2024).

The occurrence of these anomalies is determined by a complex set of factors arising from the interaction between genetic, environmental, socioeconomic, lifestyle, and healthcare-related conditions (LEE et al., 2021). National studies have reported associations with maternal characteristics, including age, educational level, clinical conditions, and access to prenatal care, as well as neonatal factors (COSME et al., 2017). However, although these studies contribute to describing the magnitude and distribution of congenital anomalies, they remain limited in their integrated assessment of parental determinants, particularly regarding the interaction between maternal and paternal age.

Over recent decades, a progressive shift in reproductive patterns has been observed, characterized by delayed motherhood and fatherhood across different populations (BEAUJOUAN, 2020). This phenomenon, associated with social and economic changes, has been linked to an increased risk of congenital anomalies, particularly at advanced parental ages. Advanced maternal age is a well-established risk factor, especially for chromosomal abnormalities, due to the increased frequency of meiotic

errors (MIKWAR et al., 2020). More recently, evidence has suggested that paternal age may also influence the occurrence of congenital anomalies, potentially through the accumulation of genetic mutations and epigenetic alterations throughout the male reproductive lifespan (AITKEN, 2024). Recent analyses indicate that the impact of parental age is not restricted to advanced ages and may involve non-linear effects, with distinct risk patterns observed at both extremes of the age spectrum (PETHŐ et al., 2024). Studies based on large population cohorts have suggested that specific combinations of parental ages may influence perinatal outcomes, reinforcing the importance of analytical approaches that simultaneously consider both variables (YU et al., 2024).

Despite these advances, an important gap remains in the Brazilian literature, as most studies have focused on maternal age in isolation, without adequately incorporating paternal age as either an independent variable or an adjustment factor for confounding control (FERNANDES et al., 2025). In addition, investigations based on large and recent population datasets that jointly evaluate the effects of maternal and paternal ages, including potential non-linear patterns and regional variations, remain scarce.

Given this context, an integrated analysis of parental age profiles and their association with congenital anomalies is warranted. Therefore, the present study aimed to evaluate the association between maternal and paternal age and the occurrence of congenital anomalies among live births in the State of Espírito Santo, Brazil, from 2017 to 2023. This study seeks to contribute to the understanding of the epidemiology of congenital anomalies and to support the development of healthcare strategies focused on reproductive counseling and the prevention of adverse outcomes. We hypothesized that maternal age would have a significant effect on the incidence of congenital anomalies, even after adjustment for paternal age, and that this effect

would be dose-dependent, with increasing maternal age associated with a progressively higher risk of congenital anomalies in newborns.

Methods

An observational, longitudinal, and ecological study with a retrospective analytical design was conducted using data from the Live Birth Information System (SINASC), publicly available through the DATASUS platform of the Brazilian Ministry of Health. Data on maternal and paternal age, maternal education, geographic region, year of birth, newborn sex, prenatal care, and ethnicity were extracted. The study was conducted in the State of Espírito Santo, Brazil, covering the period from 2017 to 2023 and comprising a total of 377,668 live birth records. Records presenting evident inconsistencies, including missing values for the main exposure variables, were excluded prior to analysis.

The primary outcome was the presence of a congenital anomaly (yes/no) recorded in the Live Birth Certificate and classified according to ICD-10 codes Q00–Q99. As a secondary outcome, congenital anomalies were categorized as chromosomal or non-chromosomal (WORLD HEALTH ORGANIZATION, 2016). Maternal and paternal ages were analyzed both as continuous variables (absolute age in years) and categorical variables (age groups) to assess trends and investigate potential non-linear effects. The age groups considered were: <14, 14–18, 18–24, 25–29, 30–34, 35–39, 40–44, 45–49, and ≥50 years, following classifications adopted in previous studies (GREEN et al., 2010; PETHŐ et al., 2024).

Descriptive analyses were performed using absolute and relative frequencies for all variables, and the prevalence of congenital anomalies was estimated according to maternal and paternal age groups. Associations

between maternal and paternal age categories were assessed using contingency tables, and Pearson's chi-square test was applied to evaluate statistical significance ($p < 0.05$).

To estimate the association between parental age and congenital anomalies while controlling for the age of the opposite parent, two binomial logistic regression models were fitted to calculate odds ratios (ORs). In both models, the presence or absence of congenital anomalies was used as the dependent variable. In the first model, maternal age was included as a covariate and paternal age group as the main factor. In the second model, paternal age was included as a covariate and maternal age group as the main factor. Additionally, maternal education, geographic region, year of birth, newborn sex, prenatal care, and ethnicity were included as covariates in both models after assessment of multicollinearity (Spearman's rho < 0.8 and variance inflation factor [VIF] < 3). Measures of association were reported with 95% confidence intervals and a significance level of 5%. Furthermore, the ten most frequent congenital anomalies identified during the study period were selected for calculation of relative risk (risk ratio) according to maternal age group.

This study used publicly available, anonymized data and therefore did not require approval by the Brazilian Research Ethics Committee System (CEP/CONEP).

Results

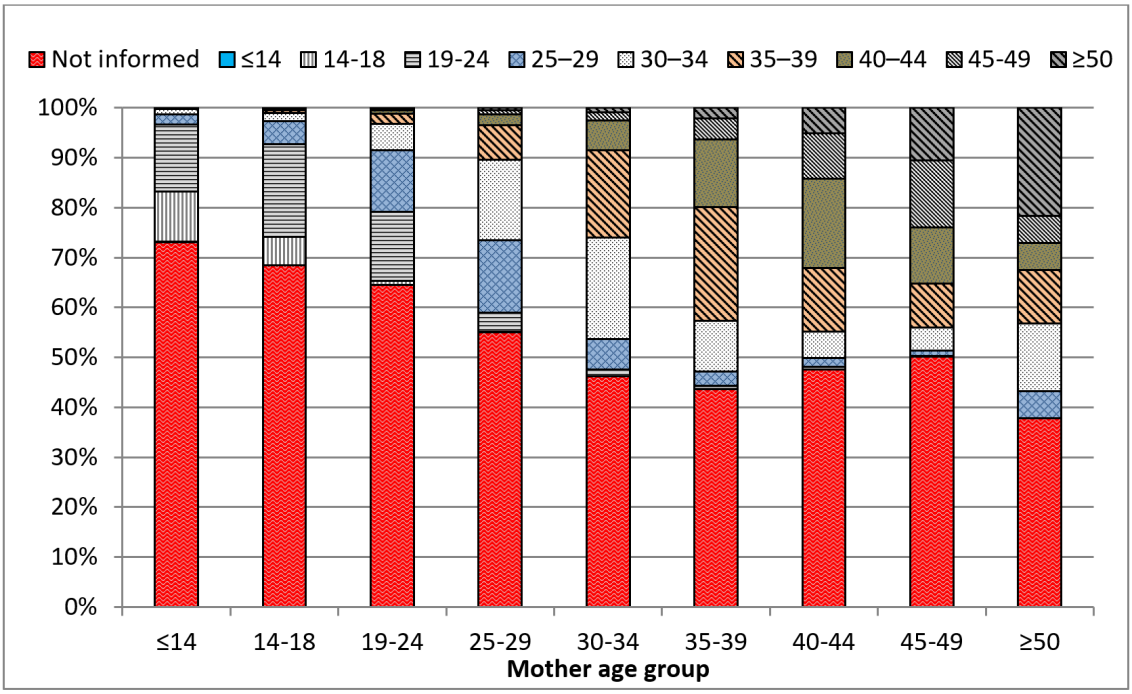
A consistent age-related pattern was observed from adolescence onward. In general, maternal age groups were most frequently associated with the corresponding paternal age group, while the second most frequent paternal category tended to be one age group younger than the

maternal category. Among mothers younger than 14 years and those aged 14–18 years, fathers aged 19–24 years were the most frequently reported, indicating a more pronounced age asymmetry within these groups.

In addition to this pattern, the predominant category across all maternal age groups was missing paternal age information. The proportion of records with unreported paternal age showed a decreasing trend as maternal age increased, reaching relative stability among mothers aged 35–39 years and remaining largely constant until a further decline was observed among mothers aged 50 years or older. Among mothers aged ≤14 years, 452 births were identified during the study period, of which 330 (73.0%) had no recorded information on paternal age (Figure 1).

Figure 1. Percentage distribution of paternal age groups within each maternal age group (horizontal axis) among live births recorded in the State of Espírito Santo, Brazil, from 2017 to 2023.

Analysis of variance revealed a statistically significant association

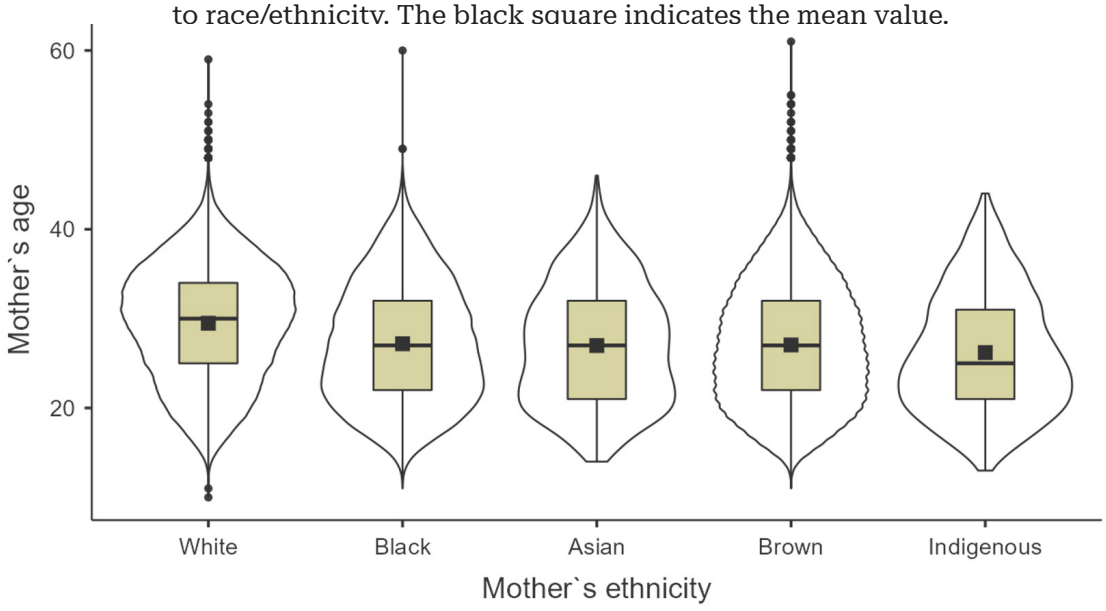


between maternal age (continuous variable) and maternal race/ethnicity (categorical variable) (Figure 2). Descriptively, White mothers had a mean age of approximately 29.5 years at delivery (median = 30 years), whereas Indigenous mothers had a mean age of approximately 26.2 years (median = 25 years) (Figure 2).

According to Tukey's post hoc test, no statistically significant differences were observed among Black, Asian, and Mixed-race mothers. However, the age distribution of White mothers was significantly higher than that of all other ethnic groups, whereas the age distribution of Indigenous mothers was significantly lower than that of all other ethnic groups at the time of delivery (ANOVA, $p < 0.05$; Figure 2).

In the multivariable binomial logistic regression, with maternal and paternal ages included as continuous covariates, maternal age remained significantly associated with the risk of both congenital anomalies and chromosomal abnormalities. In contrast, paternal age was significantly associated with these outcomes only when analyzed separately, losing statistical significance after adjustment for maternal age (Table 1).

Figure 2. Box plot and violin plots showing the distribution of maternal age according to race/ethnicity. The black square indicates the mean value.



For congenital anomalies overall, maternal age was significantly associated with risk (Z = 7.83; p < 0.001), with an OR of 1.05 (95% CI: 1.04–1.06), indicating an approximately 5% increase in the odds of occurrence for each additional year of maternal age. For chromosomal abnormalities, the association with maternal age was stronger (Z = 11.274; p < 0.001), with an OR of 1.22 (95% CI: 1.18–1.27), corresponding to an approximately 22% increase in the odds for each additional year of maternal age (Table 1).

When maternal age group was analyzed as an ordinal categorical variable (reference category = 19–24 years), adjusted for paternal age as a continuous covariate, a gradual dose-dependent increase in risk was observed with advancing maternal age, particularly from 30 years onward for congenital anomalies overall and from 35 years onward for chromosomal abnormalities.

For congenital anomalies overall, no statistically significant increase in odds was observed among mothers aged ≤14 years (OR = 1.87; p = 0.534), 14–18 years (OR = 1.11; p = 0.505), or 25–29 years (OR = 1.22; p = 0.064) compared with mothers aged 19–24 years. From 30–34 years onward, a significant and progressive increase in risk was detected, with an OR of 1.46 (95% CI: 1.18–1.80; p < 0.001; AR = 0.8%), increasing to 1.75 (95% CI: 1.39–2.20; p < 0.001; AR = 0.9%) among mothers aged 35–39 years, 3.10 (95% CI: 2.32–4.14; p < 0.001; AR = 1.7%) among those aged 40–44 years, and 5.62 (95% CI: 2.79–11.33; p < 0.001; AR = 3.6%) among those aged 45–49 years (Table 2).

For chromosomal abnormalities, the increase in risk was more pronounced and became statistically significant from 35 years of age onward. A progressive increase in odds was observed with advancing maternal age. Compared with mothers aged 19–24 years, the 30–34-year age group did not show a statistically significant association with risk (OR = 0.88; 95% CI: 0.85–4.17; p = 0.12; AR = 0.1%). From 35–39 years onward, a significant increase in risk was detected (OR = 7.06; 95% CI: 3.31–15.06; p < 0.001; AR =

0.2%), which intensified among mothers aged 40–44 years (OR = 17.61; 95% CI: 7.77–39.91; p < 0.001; AR = 0.5%) and reached its highest magnitude in the 45–49-year age group (OR = 56.59; 95% CI: 18.31–174.87; p < 0.001; AR = 1.7%) (Table 2).

In contrast, paternal age, when analyzed as a continuous covariate while controlling for maternal age group, was not significantly associated with either congenital anomalies overall (p = 0.691) or chromosomal abnormalities (p = 0.39) (Table 2).

Table 3 presents the relative risk analysis by maternal age group for the ten most frequent congenital anomalies recorded in Espírito Santo between 2017 and 2023 (Table 3). The overall association test (chi-square) was significant (p < 0.001), indicating an association between maternal age group and the distribution of relative risks across the evaluated anomalies.

The ten most frequent anomalies identified in the dataset were: (1) polydactyly of the hand, (2) Down syndrome, (3) unspecified polydactyly, (4) gastroschisis, (5) other congenital deformities of the feet, (6) unspecified congenital heart malformation, (7) unspecified hypospadias, (8) congenital talipes equinovarus, (9) anencephaly, and (10) unspecified congenital malformations (Table 3).

The maternal age group with the highest relative risk was 40–44 years, in which four of the ten most frequent anomalies showed statistically significant relative risks, consistent with the progressive increase in risk observed from 35 years onward in the previous analyses. In this age group, the most notable findings were Down syndrome (RR = 2.62), unspecified polydactyly (RR = 2.52), unspecified congenital heart malformation (RR = 4.26), and congenital talipes equinovarus (RR = 2.41) (Table 3).

Table 1. Binomial logistic regression analysis of the risk of congenital anomalies and chromosomal abnormalities in offspring. Models were fitted using maternal age as a continuous independent variable with paternal age included as a continuous covariate, and paternal age as a continuous independent variable with maternal age included as a continuous covariate. OR = Odds ratio.

	GENETIC ABNORMALITIES			CHROMOSOMAL ABNORMALITIES		
Predictor	**Z**	**p**	**OR (95% IC)**	**Z**	**p**	**OR (95% IC)**
Mother's age	7,83	<,001	1,05 (1,04-1,06)	11,274	<,001	1,22 (1,18-1,27)
Father's age	-0,474	0,636	0,99 (0,98-1,01)	0,062	0,951	1,00 (0,97-1,03)

Table 2. Binomial logistic regression analysis of the risk of congenital anomalies and chromosomal abnormalities in offspring according to maternal age group, with paternal age included as a continuous covariate. The reference category for all maternal age groups was mothers aged 19–24 years. MAG = Maternal age group; FAG = Father's age group; AR = Absolute risk (%) relative to the maternal age group of 19–24 years; OR = Odds ratio.

		GENETIC ABNORMALITIES				CHROMOSOMAL ABNORMALITIES			
	Comparison	**AR**	**Z**	**p**	**OR (95% IC)**	**AR**	**Z**	**p**	**OR (95% IC)**
MAG	**≤14** – 19-24	0,2	0,62	0,534	1,87 (0,26-13,50)	0,0	-0,02	0,979	0,00 (0,00-0,00)
	14-18 – 19-24	0,8	0,67	0,505	1,11 (0,81-1,53)	0,0	-0,30	0,765	0,80 (0,17-3,68)
	19-25 – 19-24	0,7	--	--	--	0,0	--	--	--
	25-29 – 19-24	0,7	1,85	0,064	1,22 (0,99-1,50)	0,0	-0,41	0,68	0,82 (0,32-2,09)
	30-34 – 19-24	0,8	3,56	<,001	1,46 (1,18-1,80)	0,1	1,57	0,12	1,88 (0,85-4,17)
	35-39 – 19-24	0,9	4,74	<,001	1,75 (1,39-2,20)	0,2	5,06	<,001	7,06 (3,31-15,06)
	40-44 – 19-24	1,7	7,64	<,001	3,10 (2,32-4,14)	0,5	6,87	<,001	17,61 (7,77-39,91)
	45-49 – 19-24	3,6	4,82	<,001	5,62 (2,79-11,33)	1,7	7,01	<,001	56,59 (18,31-174,87)
	FAG	--	0,40	0,691	1,00 (0,99-1,01)	--	0,86	0,39	1,01 (0,98-1,04)

Among mothers aged 45–49 years, the highest relative risk values were observed for unspecified congenital heart malformation (RR = 6.15) and unspecified congenital malformations (RR = 10.92). In the 25–29 and

30–34-year age groups, relative risks generally remained close to 1, whereas among adolescent mothers (≤14 and 14–18 years), risk estimates were predominantly equal to or below unity.

However, these risks should be interpreted in the context of the actual incidence rates within each maternal age group, which ranged from 0.0000% to 0.0162%, the highest value observed in the dataset. The highest incidence rates were recorded among mothers aged 19–24 and 25–29 years, reflecting the fact that these were the most prevalent maternal age groups at delivery within the study population. The most frequent congenital anomalies were polydactyly of the hand, Down syndrome, and polydactyly of the foot, with frequencies of 0.05%, 0.05%, and 0.04%, respectively (Table 4).

Table 3. Relative risk of the ten most frequent congenital anomalies recorded in the State of Espírito Santo, Brazil, between 2017 and 2023. Bold values highlighted in red indicate statistically significant relative risks. 1 = Polydactyly of the hand; 2 = Down syndrome; 3 = Unspecified polydactyly; 4 = Gastroschisis; 5 = Other congenital foot deformities; 6 = Unspecified congenital heart malformation; 7 = Unspecified hypospadias; 8 = Congenital talipes equinovarus; 9 = Anencephaly; 10 = Unspecified congenital malformations.

Mother's age group	1	2	3	4	5	6	7	8	9	10
≤14	0,00	0,00	5,12	0,00	0,00	0,00	0,00	0,00	0,00	0,00
14-18	0,71	0,39	0,75	0,66	0,66	1,33	0,47	0,54	1,62	0,21
19-24	1,10	**1,29**	1,25	1,04	0,41	0,57	**1,78**	1,35	1,35	0,69
25-29	1,16	1,02	0,88	1,08	**1,90**	0,99	1,47	0,22	0,49	0,60
30-34	1,11	0,90	0,86	1,03	1,38	0,49	0,72	1,12	1,14	1,20
35-39	0,73	0,71	0,70	0,89	0,82	1,56	0,37	**1,81**	1,11	**2,13**
40-44	0,82	**2,62**	**2,52**	1,46	0,83	**4,26**	0,40	**2,41**	0,00	2,35
45-49	0,00	0,00	3,29	0,00	0,00	6,15	0,00	0,00	0,00	**10,92**

Table 4. Incidence (%) of the ten most frequent congenital anomalies recorded in the State of Espírito Santo, Brazil, between 2017 and 2023. 1 = Polydactyly of the hand; 2 = Down syndrome; 3 = Unspecified polydactyly; 4 = Gastroschisis; 5 = Other congenital foot deformities; 6 = Unspecified congenital heart malformation; 7 = Unspecified hypospadias; 8 = Congenital talipes equinovarus; 9 = Anencephaly; 10 = Unspecified congenital malformations.

Mother's age group	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)	6 (%)	7 (%)	8 (%)	9 (%)	10 (%)
≤14	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
14-18	0,0034	0,0019	0,0029	0,0019	0,0016	0,0026	0,0008	0,0008	0,0019	0,0003
19-24	0,0154	0,0162	0,0135	0,0085	0,0034	0,0040	0,0071	0,0053	0,0045	0,0026
25-29	0,0146	0,0124	0,0095	0,0079	0,0101	0,0056	0,0058	0,0011	0,0019	0,0021
30-34	0,0132	0,0106	0,0087	0,0071	0,0077	0,0029	0,0032	0,0040	0,0034	0,0034
35-39	0,0058	0,0053	0,0045	0,0040	0,0032	0,0048	0,0011	0,0037	0,0021	0,0034
40-44	0,0016	0,0045	0,0037	0,0016	0,0008	0,0032	0,0003	0,0013	0,0000	0,0011
45-49	0,0000	0,0000	0,0003	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0003
≥50	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
TOTAL	**0,0540**	**0,0508**	**0,0434**	**0,0310**	**0,0267**	**0,0233**	**0,0183**	**0,0162**	**0,0138**	**0,0132**

Discussion

The results of the present study consistently demonstrate that maternal age plays a central role in the occurrence of congenital anomalies, including both congenital anomalies overall and chromosomal abnormalities, showing a strong, independent, and clearly dose-dependent association. A progressive increase in risk was observed from 30 years of age onward for congenital anomalies overall and, more markedly, from 35 years onward for chromosomal abnormalities, with an exponential increase in the oldest maternal age groups. However, these findings should be interpreted in the context of the natural occurrence frequencies of the main congenital anomalies evaluated, as none of them exceeded a prevalence of 0.05% among the 377,668 live births recorded in the State of Espírito Santo between 2017 and 2023.

The parental age profile observed in Espírito Santo indicates that most couples have children with partners belonging to the same age group, followed by women whose partners are in the immediately older age category. This pattern is consistent with reports from different regions of the world, where men are, on average, approximately four years older than their partners (ASUBEL et al., 2022). Beyond records containing paternal and maternal age information, the high prevalence of missing paternal data deserves attention, as it was the dominant category across all maternal age groups. Furthermore, the proportion of missing paternal records was highest among the youngest mothers. The predominance of unreported paternal information among younger maternal age groups suggests paternal absence beyond what would be expected from random underreporting alone. Among adolescent and very young mothers, paternal involvement tends to be more variable, and some studies have reported higher frequencies of paternal absence or non-participation in childcare (FONTOURA-MATIAS et al., 2024), which may contribute to the pattern observed in the present study. This pattern was particularly pronounced among mothers younger than 14 years (PINTO et al., 2024). Under Brazilian law, any sexual relationship involving an individual younger than 14 years is classified as statutory rape (Article 217-A of the Brazilian Penal Code), which may partially explain the absence of paternal information in official records.

Advanced maternal age is widely recognized as the primary risk factor for aneuploidies, mainly due to the increased likelihood of chromosomal segregation errors during meiosis (MIKWAR et al., 2020). The progressive increase in odds observed with advancing maternal age reinforces the biological plausibility of this association and suggests a cumulative effect related to oocyte aging. Previous studies have reported a similar pattern, with a marked acceleration in risk after 35 years of age (PETHŐ et al., 2024), con-

sistent with the findings of the present study, particularly in the 40–44 and 45–49-year age groups, where the highest risk estimates were observed.

The lack of an independent association between advanced paternal age and congenital anomalies identified in the present study partially contrasts with findings from some international studies reporting associations between advanced paternal age and increased risk of specific conditions, including congenital heart defects and certain genetic syndromes (FENG et al., 2020). Systematic reviews have suggested that paternal age ≥35 years may be associated with a modest increase in the risk of congenital anomalies, potentially related to the accumulation of de novo mutations throughout the male reproductive lifespan (AITKEN, 2024). Methodological differences among studies, including sample size, outcome definitions, and adjustment for confounding variables such as maternal age, may account for these discrepancies. Therefore, the apparent risk associated with paternal age may largely reflect the effect of maternal age, given that parental ages tend to be highly correlated, especially after 30 years of age. This pattern was demonstrated in the present study and has also been reported in international studies showing that older mothers generally have smaller age differences relative to their partners than younger mothers (DUDEL et al., 2023).

Another relevant finding concerns the pattern observed among younger maternal age groups. No increase in the risk of congenital anomalies was detected among mothers younger than 18 years, contrasting with some studies suggesting elevated risks among mothers younger than 20 years (PETHŐ et al., 2024). This result may reflect population-specific differences, as well as potential confounding factors related to socioeconomic conditions and access to prenatal care, which are not always fully captured in secondary databases. It may also reflect risks associated with genetic conditions not specifically addressed in the present analysis. Nevertheless, most studies support an increased risk associated with advan-

ced maternal age, particularly above 35 or 40 years (AHN et al., 2022), corroborating the findings reported here.

The analysis of the most frequent congenital anomalies revealed that specific conditions, such as Down syndrome and congenital heart malformations, were more strongly associated with advanced maternal age, particularly among mothers older than 40 years. These findings further support the role of maternal aging in the development of chromosomal and structural abnormalities and have direct clinical relevance, as these conditions are among the leading causes of neonatal morbidity and mortality (FERNANDES et al., 2025).

From an epidemiological perspective, this study helps address an important gap in the Brazilian literature by simultaneously evaluating maternal and paternal age using a large population-based dataset covering the entire State of Espírito Santo. In addition, the analysis was based on a recent database encompassing a long time series of seven years. This approach provides a broader understanding of the determinants of congenital anomalies in the Brazilian context and overcomes limitations of previous studies that were primarily descriptive or focused exclusively on maternal age.

Conclusions

The implications of these findings are relevant for both clinical practice and public health. The identification of advanced maternal age as the primary risk factor reinforces the importance of preconception counseling, particularly in populations experiencing delayed childbearing due to social and economic factors. In addition, prenatal screening and epidemiological surveillance strategies can be more effectively targeted toward

higher-risk groups, contributing to earlier diagnosis and improved management of these conditions.

Finally, although this study is based on a robust and representative population database, limitations inherent to the use of secondary data should be acknowledged, including potential underreporting and the lack of detailed clinical information. Nevertheless, the findings demonstrate strong internal consistency and are in agreement with the existing literature, supporting their validity and relevance.

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