Epidemiological characteristics of live births with esophageal atresia in Sao Paulo State, Brazil, from 2005 to 2018

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ABSTRACT

Background The estimated prevalence of esophageal atresia (EA) is 1 in 2500–4500 live births (LBs). Researchers have already identified risk factors, but the mechanisms are still unknown. The aim of this study is to identify EA prevalence trends and its risk factors in the São Paulo State (SPS) population database.

Methods We conducted a population-based study using all EA cases identified by the Live Births Information System across 14 years (2005–2018) to estimate EA prevalence trends in recent years, stratified by maternal age and SPS geographical clusters. We calculated the prevalence trends, regression coefficient (β), annual percent change (APC), and 95% confidence interval (CI).

Results We found 820 EA cases among 8,536,101 LBs with a prevalence of 1.0/10,000 LBs in SPS, Brazil. There was no significant difference in distribution by sex. Among all the cases, the majority (65%) were Caucasian; 51.8% were born at term; 43% had weight of ≥2500 g; 95.4% were singleton; and 73.4% of births were by cesarean section. From 2005 to 2018, there was an increasing trend of EA prevalence (APC=6.5%) with the highest APC of 12.2%. The highest EA prevalence rate (1.7/10,000 LB) was found in the group with maternal age of ≥35 years. No significant seasonal variation was found based on the conception month (p=0.061).

Conclusions EA had an increasing prevalence trend in SPS, Brazil, in recent years, with the highest prevalence rate in the group with maternal age of ≥35 years. No seasonality was observed. This population-based study is the first to summarize the current epidemiology of EA in SPS LB.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The estimated esophageal atresia (EA) prevalence is 1 in 2500–4500 live births (LBs), with a higher prevalence in lower-income to middle-income countries compared with high-income ones.

WHAT THIS STUDY ADDS

⇒ EA prevalence in São Paulo State increased from 0.5/10,000 LBs to 1.5/10,000 LBs from 2005 to 2018 with an average rate of 6.5% per year,
⇒ It does not show monthly seasonal variation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Prenatal follow-up should be distinguished between mothers <20 years and ≥35 years of age, and ultrasound examination should focus on identifying congenital malformations such as EA.
⇒ High-complexity hospitals with trained medical personnel should be established in areas far away from large urban centers to diagnose and treat congenital malformations such as EA.

INTRODUCTION

Esophageal atresia (EA) is the principal congenital defect affecting the esophagus and requires reconstructive surgery.[1 2] It is a congenital anomaly that occurs between the fourth and fifth weeks of embryological development during anterior intestine formation and separation.[3–5] Generally, EA is associated with other congenital malformations or abnormalities, including sequence of vertebral anomalies, anal atresia, cardiovascular anomalies, tracheosophageal fistula, renal and/or radial anomalies, and limb defects, trisomy 18 or 21, and CHARGE syndrome (coloboma, heart defects, atresia choanae, growth retardation, genital abnormalities, and ear abnormalities).[6–8]

The estimated prevalence of this defect is 1 in 2500–4500 live births (LBs), with a higher prevalence in lower-income to middle-income countries than that in high-income countries.[9–11] The mechanisms or risk factors of EA are still unknown; some researchers have already identified risk factors, such as white race, fetus male (M) sex, multiple gestations, low birth weight (≤2500 g), prematurity (≤36 weeks), maternal age of ≤20 years or ≥35 years, and being born in urban areas.[2 12]

The present study aims to characterize the descriptive epidemiology and to identify EA prevalence trends and its risk factors using the São Paulo State (SPS) population database.

Table 1 Maternal and infant sociodemographic characteristics in São Paulo State, Brazil, from 2005 to 2018

Characteristics	Total births N=8,536,101 (%)	LB with EA N=820 (%)	EA proportional distribution by 10,000 LB (95% CI)	P value
Sex				<0.001
Male	4,372,877 (51.23)	433 (52.80)	0.99 (0.9 to 1.08)	
Female	4,162,047 (48.76)	375 (45.73)	0.90 (0.81 to 0.99)	
Ignored	1177 (0.01)	12 (1.46)	101.95 (44.27 to 159.64)	
Race/color				<0.001
White	5,493,241 (64.35)	533 (65.00)	0.97 (0.89 to 1.05)	
Black	301,973 (3.54)	47 (5.73)	1.56 (1.11 to 2)	
Asian	37,797 (0.44)	3 (0.37)	0.79 (0 to 1.69)	
Pardo	2,346,993 (27.49)	220 (26.83)	0.94 (0.81 to 1.06)	
Indian	10,439 (0.12)	2 (0.24)	1.92 (0 to 4.57)	
Ignored	345,658 (4.05)	15 (1.83)	0.43 (0.21 to 0.65)	
Gestational age (weeks)				<0.001
< 22	3455 (0.04)	0 (0)	0 (0 to 0)	
22–27	40,669 (0.48)	28 (3.41)	6.88 (4.33 to 9.44)	
28–31	78,572 (0.92)	62 (7.56)	7.89 (5.93 to 9.86)	
32–36	7,18,823 (8.42)	296 (36.10)	4.12 (3.65 to 4.59)	
37–41	7,513,372 (88.02)	425 (51.83)	0.57 (0.51 to 0.62)	
≥42	98,102 (1.15)	4 (0.49)	0.41 (0.01 to 0.81)	
Ignored	83,108 (0.97)	5 (0.61)	0.60 (0.07 to 1.13)	
Birth weight (g)				<0.001
≥2500	7,733,807 (90.60)	353 (43.05)	0.46 (0.41 to 0.5)	
2499–1500	658,042 (7.71)	326 (39.76)	4.95 (4.42 to 5.49)	
<1500	121,863 (1.43)	137 (16.71)	11.24 (9.36 to 13.12)	
Ignored	22,389 (0.26)	4 (0.49)	1.79 (0.04 to 3.54)	
Maternal age (years)				<0.001
≤14	45,329 (0.53)	6 (0.73)	30.22 (25.16 to 35.28)	
15–19	1,207,522 (14.15)	105 (12.80)	0.87 (0.7 to 1.04)	
20–24	2,088,715 (24.47)	170 (20.73)	0.81 (0.69 to 0.94)	
25–29	2,172,594 (25.45)	158 (19.27)	0.73 (0.61 to 0.84)	
30–34	1,810,017 (21.20)	180 (21.95)	0.99 (0.85 to 1.14)	
≥35	1,211,232 (14.19)	201 (24.51)	1.66 (1.43 to 1.89)	
Ignored	692 (0.01)	0 (0)	0 (0 to 0)	
Maternal schooling (complete years)				<0.001
0	24,948 (0.29)	6 (0.73)	2.41 (0.48 to 4.33)	
1–3	185,827 (2.18)	12 (1.46)	0.65 (0.28 to 1.01)	
4–7	1,355,478 (15.88)	131 (15.98)	0.97 (0.8 to 1.13)	
8–11	5,092,703 (59.66)	450 (54.88)	0.88 (0.8 to 0.97)	
≥ 12	1,763,411 (20.66)	214 (26.10)	1.21 (1.05 to 1.38)	
Ignored	113,704 (1.33)	7 (0.85)	0.62 (0.16 to 1.07)	
Gestation				<0.001
Singleton	8,332,682 (97.62)	782 (95.37)	0.94 (0.87 to 1)	
Twins	192,483 (2.25)	36 (4.39)	1.87 (1.26 to 2.48)	
Triplet or higher	60,065 (0.70)	2 (0.24)	0.33 (0 to 0.79)	
Ignored	4871 (0.06)	0 (0)	0 (0 to 0)	

Continued

Table 1 Continued

Characteristics	Total births N=8,536,101 (%)	LB with EA N=820 (%)	EA proportional distribution by 10,000 LB (95% CI)	P value
Type of delivery				0.234
Vaginal	3,531,576 (41.37)	218 (26.59)	0.62 (0.54 to 0.7)	
Cesarean section	4,997,600 (58.55)	602 (73.41)	1.20 (1.11 to 1.3)	
Ignored	6925 (0.08)	0 (0)	0 (0 to 0)	
Prenatal care consultations				<0.001
0	93,945 (1.10)	11 (1.34)	1.17 (0.48 to 1.86)	
1–3	319,640 (3.74)	57 (6.95)	1.78 (1.32 to 2.25)	
4–6	1,513,258 (17.73)	200 (24.39)	1.32 (1.14 to 1.5)	
≥7	6,537,270 (76.58)	544 (66.34)	0.83 (0.76 to 0.9)	
Ignored	71,988 (0.84)	8 (0.98)	1.11 (0.34 to 1.88)	

Source: Sistema de Informação Sobre Nascidos Vivos, Dados do Departamento de Informática do Sistema Único de Saúde (www.datasus.gov.br), Ministério da Saúde, Brasil.
CI, Confidence interval; EA, esophageal atresia; LB, live birth.

METHODS

Study design and participants

This is a population-based study with a time trend,[13] following Strengthening the Reporting of Observational Studies in Epidemiology[14] guidelines. The present study was conducted in SPS, which is the most populous in Brazil, with a population (41,262,199 in 2010)[15] and birth rate (610,000/year)[16] comparable to countries in Europe[17 18] and Latin America[19 20] and where the completeness of public data is more reliable.[21 22] We included all LBs of mothers residing in SPS, Brazil. Official microdata of all EA cases identified by the Live Births Information System (Sistema de Informação sobre Nascidos Vivos) in SPS, Brazil, from January 1, 2005, to December 31, 2018 were used. We extracted data on the maternal city of residence from the Unified Health System Department of Informatics[15] (Departamento de Informática do Sistema Único de Saúde (DATASUS)), a department maintained by the Ministry of Health of Brazil. The 10th Edition of International Classification of Diseases (codes Q39.0, Q39.1, and Q39.2) was used[23] to identify all EA cases, with or without tracheoesophageal fistula (TEF), and TEF alone, at the LB declaration, among all LBs in the period of study.

Variables

Sociodemographic and clinical explanatory variables of LBs such as gender, race/color, gestational age, birth weight, maternal age, maternal schooling, maternal occupation, type of gestation, type of delivery, and the number of prenatal consultations were all collected. We calculated EA prevalence trends according to maternal age range (≤ 14, 15–19, 20–24, 25–29, 30–34, and ≥35 years) and for territorial clusters (São Paulo Metropolitan Region (SPMR), São Paulo City (SPC), Baixada Santista Metropolitan Region (BSMR), Taubaté Administrative Area (TAR), Central South Cluster (CSC), Campinas Region Cluster (CRC), Central North Cluster (CNC), and Northwest Cluster (NWE)) in SPS, following Calderon et al's proposal.[24]
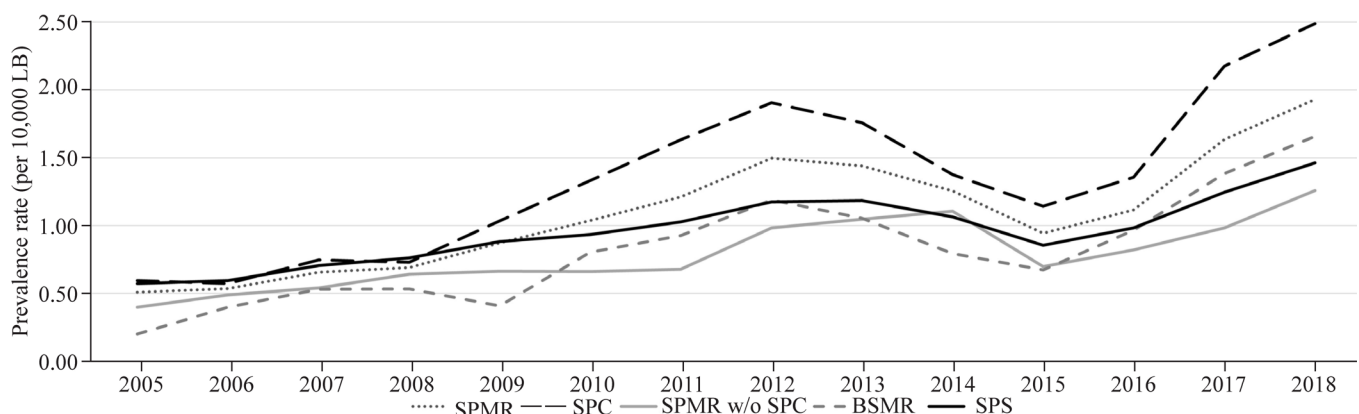

Figure 1 Esophageal atresia prevalence trend (per 10 000 LBs) by clusters in SPS, Brazil, from 2005 to 2018. BSMR, Baixada Santista Metropolitan Region; LB, live birth; SPC, São Paulo City; SPMR w/o, São Paulo Metropolitan Region without SPC; SPS, São Paulo State.

Table 2 Prais-Winsten regression model for trends in EA prevalence by clusters in SPS, Brazil, from 2005 to 2018

Clusters	β (95% CI) 2005–2011	APC (%) (95% CI) 2005–2011	Reading	β (95% CI) 2012–2018	APC (%) (95% CI) 2012–2018	Reading	β (95% CI) 2005–2018	APC (%) (95% CI) 2005–2018	Reading
SPMR	0.074 (0.054 to 0.093)	18.5 (13.3 to 23.9)	Increasing	0.029 (−0.081 to 0.138)	6.8 (−17.0 to 37.4)	Stationary	0.045 (0.017 to 0.074)	11.0 (3.9 to 18.6)	Increasing
SPC	0.092 (0.057 to 0.128)	23.7 (14.0 to 34.2)	Increasing	0.029 (−0.109 to 0.168)	7.0 (−22.3 to 47.3)	Stationary	0.050 (0.014 to 0.086)	12.2 (3.3 to 21.8)	Increasing
SPMR without SPC	0.038 (0.000 to 0.075)	9.0 (0.1 to 18.8)	Increasing	0.005 (−0.087 to 0.098)	1.2 (−18.2 to 25.3)	Stationary	0.028 (0.008 to −0.048)	6.7 (1.9 to 11.8)	Increasing
BSMR	0.063 (−0.103 to 0.229)	15.6 (−21.1 to 69.4)	Stationary	0.034 (−0.020 to 0.088)	8.1 (−4.5 to 22.4)	Stationary	0.048 (0.022 to 0.073)	11.6 (5.3 to 18.3)	Increasing
TAR	0.173 (−0.120 to 0.466)	49.1 (−24.1 to 192.7)	Stationary	0.049 (−0.088 to 0.186)	12.0 (−18.2 to 53.6)	Stationary	0.015 (−0.051 to 0.081)	3.6 (−11.0 to 20.5)	Stationary
CSC	0.012 (−0.082 to 0.107)	2.8 (−17.3 to 27.8)	Stationary	−0.082 (−0.208 to 0.043)	−17.2 (−38.0 to 10.5)	Stationary	−0.011 (−0.059 to 0.036)	−2.6 (−12.7 to 8.7)	Stationary
CRC	0.018 (−0.072 to 0.108)	4.2 (−15.3 to 28.3)	Stationary	0.019 (−0.028 to 0.066)	4.4 (−6.3 to 16.4)	Stationary	0.009 (−0.011 to 0.028)	2.0 (−2.4 to 6.6)	Stationary
CNC	−0.022 (−0.064 to 0.020)	−4.9 (−13.7 to 4.8)	Stationary	0.018 (−0.018 to 0.054)	4.2 (−4.1 to 13.2)	Stationary	−0.007 (−0.019 to 0.004)	−1.7 (−4.3 to 1.0)	Stationary
NWE	0.038 (−0.042 to 0.118)	9.2 (−9.2 to 31.3)	Stationary	−0.034 (−0.103 to 0.036)	−7.4 (−21.2 to 8.7)	Stationary	0.006 (−0.020 to 0.033)	1.4 (−4.6 to 7.8)	Stationary
SPS	0.049 (0.042 to 0.056)	12.0 (10.3 to 13.7)	Increasing	0.016 (−0.063 to 0.095)	3.8 (−13.5 to 24.5)	Stationary	0.027 (0.008 to 0.047)	6.5 (1.8 to 11.4)	Increasing

520 LBs with unknown cluster.

Source: Sistema de Informação sobre Nascidos Vivos, Dados do Departamento de Informática do Sistema Único de Saúde (www.datasus.gov.br), Ministério da Saúde, Brasil.

APC, annual percent change; BSMR, Baixada Santista Metropolitan Region; CI, Confidence interval; CNC, Central North Cluster; CRC, Campina Region Cluster; CSC, Central South Cluster; NWE, Northwest Cluster; SPC, São Paulo City; SPMR, São Paulo Metropolitan Region; SPS, São Paulo State; TAR, Taubaté Administrative Area; β, regression coefficient.
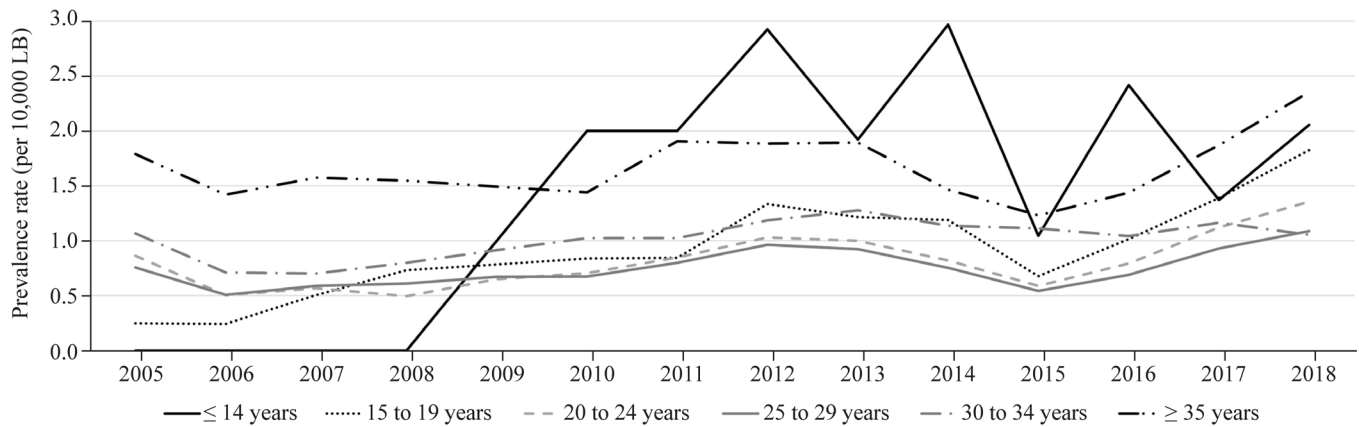
Figure 2 Esophageal atresia prevalence trend (per 10,000 LBs) by maternal age group in São Paulo State, Brazil, from 2005 to 2018. LB, live birth.

Data sources

We extracted the microdata from the file transfer service provided by DATASUS. The TABNET and TABWIN programs were used to extract the data. These tabs were developed to perform fast tabulations on DBF files, and then we expanded the files to the XLS version and classified the variables selected for this study in Excel. To minimize possible discrepancies, two researchers collected data independently.

DATASUS developed the Live Birth Information System to gather epidemiological information on births reported throughout the country to subsidize interventions related to women's and children's health for all levels of the Unified Health System (Sistema Único de Saúde). This database has been validated and previously used for public health and perinatal epidemiological research and surveillance.[24–26]

Statistical analysis

We used only the population of LBs to obtain the prevalence rates to remove age bias. Therefore, it is unnecessary to standardize the rates since all the studied populations (LB) had the same age. With this, the result obtained by the analysis can be used for comparison with other studies. EA prevalence rates were calculated for 10,000 LBs by territorial clusters and maternal age group in a global period (2005–2018) and two time intervals of 7 consecutive years (2005–2011 and 2012–2018).

We used the Prais-Winsten regression model for trend analysis, following Antunes and Cardoso's[13] methodological indications. The dependent variable was the logarithm of the rates, and the independent variable was the years of the historical series. The annual percent change (APC) of the rates was also calculated, as suggested by Antunes et al.[27]

The data modeling process includes transforming the standardized rates into a base 10 logarithmic function using the Durbin-Watson test to measure the existence of first-order autocorrelation of the time series composed of the annual coefficients and to verify if the correlation was compatible with the random regression residuals hypothesis. According to geographical clusters and maternal age groups, annual rates of increase or decrease APC with the respective 95% confidence interval (CI) were then calculated. This procedure makes it possible to classify the EA trend as increasing, decreasing, or stationary, considering to be stationary the trend whose coefficient was not significantly different from 0 ($p > 0.05$).[13] To facilitate graphical visualization, we performed the third-order centered moving averages technique for trends and seasonality.[27 28]

To model seasonality, we used monthly measures for births (84 months). The calendar months were numbered sequentially for monthly measurements; for the seasonality hypothesis test, Antunes et al's[27] methodological indications were used. For seasonality analysis, we used the month of the conception date; in this case, the available data were from April 2011 to April 2018. We considered the seasonal variation significant if one or more of the coefficients of the seasonal term ($B3$ and $B5$ for Seno and $B2$ and $B4$ for Cosseno) were significantly different from 0 ($p < 0.05$).[13] We used Stata V.15.1 for all statistical analyses.

RESULTS

Sociodemographic distributions of LBs with EA in SPS, Brazil, from 2005 to 2018 are summarized in table 1, including data on total births, type of birth, maternal and infant characteristics, with the respective p values for each variable. We identified a higher proportion of EA (52.8%) in men than in women and a greater proportion of white births (65%). The highest proportional prevalence was in preterm infants from 28 to 31 weeks (7.89/10,000 LBs, 95% CI 5.93 to 9.86). The highest proportion of EA LB had weight of ≥2500 g (43%). The highest proportional prevalence group was <1500 g (11.24/10,000 LBs, 95% CI 9.36 to 13.12). EA prevalence was found to be higher in mothers aged younger than 14 years (30.22/10,000 LBs, 95% CI 25.16 to 35.28) and more than 35 years (1.66/10,000 LBs, 95% CI 1.43 to 1.89) compared with the other maternal age groups,

Table 3 Prais-Winsten regression model for trends in esophageal atresia prevalence, by maternal age group in São Paulo State, Brazil, from 2005 to 2018

Maternal age (years)	β (95% CI) 2005–2011	APC (%) (95% CI) 2005–2011	Reading	β (95% CI) 2012–2018	APC (%) (95% CI) 2012–2018	Reading	β (95% CI) 2005–2018	APC (%) (95% CI) 2005–2018	Reading
< 14	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	Stationary	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	Stationary	0.004 (0.004 to 0.004)	1.0 (1.0 to 1.0)	Increasing
15–19	0.146 (0.028 to 0.264)	40.0 (6.6 to 83.7)	Increasing	0.029 (−0.097 to 0.155)	6.9 (−20 to 42.9)	Stationary	0.063 (0.016 to 0.109)	15.5 (3.7 to 28.6)	Increasing
20–24	0.033 (−0.014 to 0.080)	7.9 (−3.1 to 20.1)	Stationary	0.021 (−0.112 to 0.155)	5.0 (−22.8 to 42.8)	Stationary	0.025 (−0.003 to 0.053)	5.9 (−0.7 to 12.9)	Stationary
25–29	0.037 (0.000 to 0.074)	8.9 (−0.1 to 18.7)	Stationary	0.008 (−0.115 to 0.132)	1.9 (−23.3 to 35.4)	Stationary	0.017 (−0.009 to 0.044)	4.0 (−2.2 to 10.6)	Stationary
30–34	0.032 (−0.011 to 0.074)	7.5 (−2.4 to 18.5)	Stationary	−0.015 (−0.048 to 0.018)	−3.4 (−10.4 to 4.1)	Stationary	0.018 (0.004 to 0.033)	4.3 (0.9 to 7.8)	Increasing
> 35	0.013 (−0.024 to 0.049)	2.9 (−5.3 to 11.9)	Stationary	0.001 (−0.110 to 0.111)	0.1 (−22.4 to 29.2)	Stationary	0.011 (−0.011 to 0.032)	2.5 (−2.4 to 7.7)	Stationary

Source: Live Births Information System. Data: Unified Health System Department of Informatics (www.datasus.saude.gov.br%7D), Ministry of Health, Brazil.
APC, annual percent change; CI, Confidence interval; β, regression coefficient.

and in these age groups, we found the lowest and the highest proportion of cases (0.7% and 24.5%, respectively). The vast majority of cases occurred in single pregnancy (95.4%), but there was a higher proportional prevalence in twin pregnancy (1.87/10,000 LBs, 95% CI 1.26 to 2.48). Cesarean delivery was the most frequent (73.4%) and prevalent (1.2/10,000 LBs, 95% CI 1.11 to 1.3) compared with vaginal delivery in EA LBs.

The annual proportions and prevalence trends of EA cases in LBs in all SPS clusters from 2005 to 2018 are summarized in online supplemental table 1 and figure 1. During this period, SPS presented the highest number of cases (91) and the highest prevalence rate (1.5/10,000 LBs) in 2018. From 2005 to 2018, SPC presented the highest annual prevalence rate (2018: 3.0/10,000 LBs) and total prevalence (1.3/10,000 LBs), while TAR presented the lowest total prevalence (0.6/10,000 LBs). There was an increasing EA prevalence trend in SPMR, SPC, SPMR without SPC, BSMR, and SPS from 2005 to 2018. Their increasing APC rates were 11.0%, 12.2%, 6.7%, 11.6%, and 6.5%, respectively, while the other cluster's tendencies were stationary. In the first period (2005–2011), an increasing EA prevalence trend was observed in SPMR, SPC, SPMR without SPC, and SPS, presenting the following APCs: 18.5%, 23.7%, 9%, and 12%, respectively. In the second period (2012–2018), the EA prevalence trend was stationary in all clusters. We noticed that the TAR, CSC, CRC, CNC, and NWE clusters showed a stationary prevalence trend from 2005 to 2018 and during the two-interval periods (table 2).

The annual EA prevalence trends in different maternal age group were also analyzed. The group with maternal age of ≤14 years had the highest EA prevalence in 2013 (5.8/10,000 LBs), while the group with maternal age of 15–19 years had the lowest EA prevalence in 2006 (0.1/10,000 LBs) (figure 2 and online supplemental table 2). From 2005 to 2018, the maternal age group of 15–19 years had the highest APC (APC=15.5%, 95% CI 3.7% to 28.6%). When separated by period, only the maternal age group of 15–19 years presented an increasing prevalence trend (APC=40.0%, 95% CI 6.6% to 83.7%) from 2005 to 2011, and all other maternal age groups presented a stationary prevalence trend. In the second period (2012–2018), all maternal age groups presented a stationary prevalence trend (table 3).

From 2011 to 2018, no significant seasonal variation in EA monthly prevalence rate was found based on the month of conception (95% CI −0.047 to 1.972, p=0.061) (figure 3).

DISCUSSION

To the best of our knowledge, this is the first population-based study to describe the recent epidemiology of LBs with EA, its seasonality, and prevalence in SPS, Brazil, in a recent period of 14 years (2005–2018). Furthermore, this study adds essential information on EA to the limited
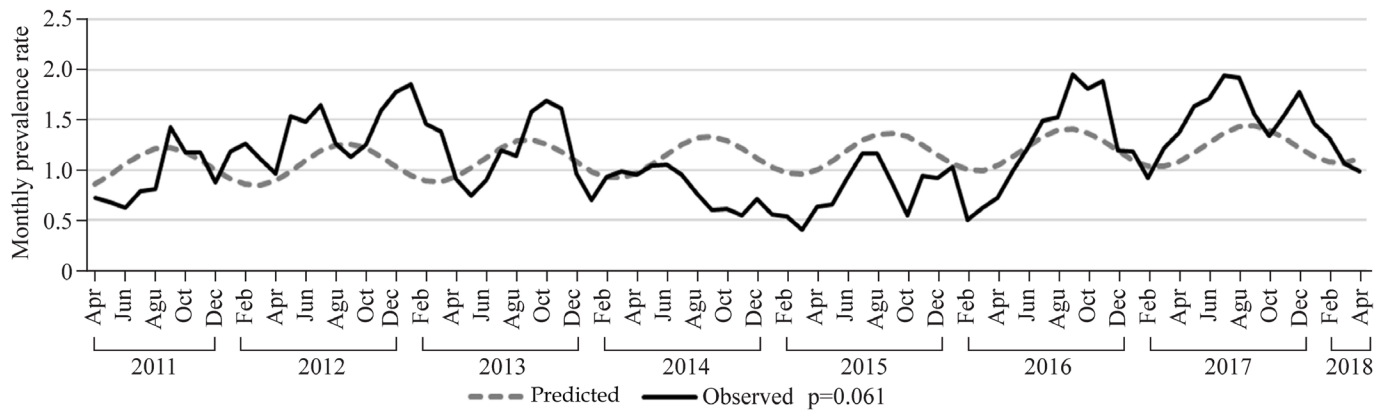
Figure 3 Esophageal atresia monthly prevalence rate (per 10,000 live births) in São Paulo State, Brazil, from 2011 to 2018.

data in Brazil since this population has not been previously evaluated in detail concerning this pathology.

The EA prevalence found in SPS of 0.96/10,000 LBs was lower than that found in many previous studies with a range of 1.8–11.98/10,000 LBs.[2 29–35] We found only one study with the EA prevalence similar to ours, carried out by Rankin et al,[36] in five British regions between 1991 and 1999, where only the Oxford region had a low EA prevalence of 0.7/10,000 LB. According to the EUROCAT[37] data, the only region with a low EA prevalence from 2005 to 2018 similar to that in our study was Southeast Ireland (0.71/10,000 LBs).

The present study found no significant difference of EA proportion in different sex groups, which differs from that in other studies with a higher prevalence in men (M:female (F) sex ratio of 1.3:4.1).[1 9 10 38] Although some studies have already shown a higher risk of EA occurrence in white women,[1 2] we did not find significant results when considering race/ethnicity as a risk factor.

The results of EA prevalence in different gestational age groups is consistent with those in other literature concerning the relationship between tracheoesophageal anomalies and gestational age, indicating similar findings already described by other authors.[2 29–31] Even though we are aware of the importance of prenatal consultations,[39] we did not observe significant differences regarding the number of consultations carried out in pregnant women with fetuses with EA. Cesarean section is the most frequent type of delivery and has the highest prevalence compared with vaginal delivery, which may be due to the suggestive characteristics of EA found in prenatal ultrasonography, such as polyhydramnios and the association of the absence of a gastric bubble with the dilatation of the cervical esophagus (Pouch sign).[40 41] These alterations, when present, often lead obstetricians to opt for cesarean delivery due to the greater possibility of malformation of the digestive tract.

Our results show that EA occurs more frequently in singleton pregnancies but is more prevalent in twin pregnancies. Nazer et al[31] showed similar results in Chile, with EA being two to three times more common in twins; Torfs et al[29] described that twins, especially homozygous twins, were considered a risk factor for the occurrence of EA.

In SPS, we identified a growing prevalence both in the global period (2005–2018) and in the first subperiod (2005–2011). A similar situation occurs throughout the predominantly urban area of the state (SPC and SPMR) and has 58.4% of all identified cases. The other predominantly urban cluster, which presented a slightly different behavior, was BSMR, which also presents an increasing trend in prevalence in the full period, with stationary trends when analyzed by subperiods. These clusters are the most developed and urbanized in the entire state, which leads us to believe that this increase in prevalence is related to better access to diagnostic methods and high-complexity hospitals.[29] Remote regions with a lower population density and low birth rate may have less access to highly differentiated resources and thus a lower number of prenatal diagnoses for EA.

The highest EA prevalence and number of EA cases were found in the group with a maternal age of ≥35 years old compared with other maternal age groups. Among adolescent mothers with age of 15–19 years, we found a low number of cases; however, it is the one with the highest APC in the global period, even with a significant LB number decrease from the first to the last year. These results allow us to consider that maternal ages of <20 and ≥35 years are risk factors for the development of EA. Takahashi et al[32] also identified maternal ages of ≤20 and ≥35 years as risk factors for EA. Depaepe et al,[30] in Europe, also identified a higher prevalence of EA in mothers aged ≤20 and ≥35 years and a more significant prevalence rate increase in mothers aged 25–29 years. However, Nazer et al[31] did not find significant differences of EA prevalence among the maternal age groups, and the average maternal age was 29.7 years old.

A possible explanation that maternal age of ≥35 years is considered a risk factor for EA occurrence is the susceptibility to fetal pathological alterations, such as congenital malformations and chromosomal alterations more frequently occurring in this age group. In addition, there is also a higher incidence of miscarriages, maternal mortality, gestational diabetes, and pre-eclampsia. Thus, advanced maternal age can be associated with the identification of several birth defects, not just EA.[1 29 32 42]

We performed a seasonality analysis as described by other authors.[1 29 43] Although we did not find a significant monthly seasonal variation based on the conception date over a 7-year study (April 2011– April 2018), the result suggests a trend of higher EA prevalence in the period in which conceptions occurred in the middle of the year, which corresponds to the winter season in the southern hemisphere.

The strengths of this study are the high EA number of cases (n=820) and the 14-year studied period. The main limitation of this study was the presence of incomplete fields or ignored content in the Live Birth Declaration, which was made available by the information system and could be resolved with adequate training of professionals who complete the document or by establishing a dedicated birth defect surveillance system; also, we have no data about fetal deaths. However, we made statistically relevant observations that provide data that can be combined with other future investigations for meta-analyses, both in periods before and after the COVID-19 pandemic.

In conclusion, there is an increasing prevalence trend in SPS, Brazil, from 2005 to 2018 at an average rate of 6.5% per year with no monthly seasonal variation. The increasing prevalence in urban areas indicates improved diagnosis. The lower prevalence from less urbanized areas indicates the need to strengthen diagnostic and treatment facilities in other regions or improve referral systems to facilities with advanced capabilities. The EA risk factors identified are urban area residence, maternal age of <20 and ≥35 years, twins, and prematurity. Although many results of this study were similar to those reported in the literature, there were some differences, mainly regarding the increasing EA prevalence trend.

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