

Joinpoint Regression Analysis of Pertussis Cases in Brazil from 2007 to 2018

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Abstract. Pertussis is a respiratory infection caused by the bacterium *Bordetella pertussis*. Which the introduction of pertussis vaccines in the 1990s in Brazil, there was a clear reduction in the incidence rate, from 10.6/100 thousand inhabitants to 0.32/100 thousand inhabitants in 2010. However, surveillance was intensified with the increase in cases between 2011 and 2014. The database of the Notifiable Diseases Information System (SINAN) was used to analyse the pertussis historical series between the years 2007 and 2018 in Brazil. The study included all confirmed cases and investigated the incidence rate per 100,000 inhabitants in relation to gender, age, and region variables. The joinpoint regression was used for trend analysis. The annual percentage change (APC) and the average annual percentage change (AAPC) was calculated. The significance level used was 5%. During the period from 2007 to 2018, 36075 cases of whooping cough were recorded in Brazil, 60.9% of which were in babies under 1 year of age. Individuals between 5 and 14 years old also showed an increase in the rate, although much smaller when compared to younger children. From the age of 15, there was no increase in the incidence of pertussis over the analysed period. The female gender corresponded to 55.3% of the cases. We observe an increase in the incidence rate of pertussis from the year 2011 in both genders. As of 2014, there is a drop in the rate. The most affected regions were the Southeast (42%), the Northeast (24%) and the South (20%). The Midwest (7%) and North (7%) regions were the least affected. There was a period of growth in the number of cases in Brazil between 2007 (0.46 cases/100,000 inhab) and 2014 (4.19 cases/100,000 inhab), with an APC of 34.4 (CI95% = (4.8; 72.4)), followed by a stationary period. This behaviour was also observed in the Northeast and Southeast regions. As for age, the rise and fall behaviour was also observed in the range from 0 to 5 years, 5 to 9 years and in adults, and the change in the rate was observed first in 2013 with children under 5 years of age and in 2014 at other ages. In the age groups of 10 to 14 years, 15 to 19 years, and elderly there is a progressive increase in APC of 16.9 (CI95% = (-0.8;37.8)), 13.1 (CI95% = (-7.5;38.3)) and 10.6 (CI95% = (2.1;19.8)), respectively. The present study concludes that the period from 2007 to 2014 was marked by the increase in the number of pertussis cases in Brazil, including in the Southeast and Northeast regions. Such behaviour was also observed in the variables sex and age.

Keywords. Pertussis, Brazil, Joinpoint regression, Time series

1. Introduction

Pertussis is a respiratory infection caused by the bacterium *Bordetella pertussis*, characterized by a paroxysmal cough that ends in a prolonged and strident inspiration (whooping cough). Pertussis is highly transmissible (secretions from the infected

individual) and mainly affects early childhood. [1]

This disease has a universal distribution, does not show preference for climate or individual characteristics (sex, ethnicity, age). However, there is a strong relationship between the presence or absence of immunity and the possibility of having the disease.

In Brazil, there was a clear reduction in the incidence rate with the introduction of pertussis vaccines in the 1990s, from 10.6/100 thousand inhabitants in the 1990s, from 10.6/100 thousand inhabitants to 0.32/100 thousand inhabitants in 2010. [1]

Despite the continuous surveillance data in Brazil, there are no studies analyzing the time trend in recent years. Therefore, the use of the jointpoint in time series analysis becomes more relevant.

In this article, we focus on analyzing the pertussis incidence rate at regional and national levels.

2. Research Methods

A time series ecological study was performed. The database of the Notifiable Diseases Information System (SINAN) was used to analyze the pertussis historical series between the years 2007 and 2018. SINAN is available on DATASUS website[4]. The data used were up to the year 2018 due to the delay in updating the data in the system.

The study included all confirmed cases in the analyzed period and investigated the incidence rate per 100,000 inhabitants stratified by gender, age, and region variables.

For trend analysis, jointpoint regression was used, considering log-transformation and variance of constant errors. Then, the annual percentage change (APC) was calculated, looking for the inflection points that indicate the rate variations with greater significance in the increase of the line to be identified. The average annual percentage change (AAPC) was also calculated, it is a measure that summarizes the period trend, describing the average of the APC. The trend was considered present when zero was not contained within 95% confidence intervals (95% CI). Being 'ascending' when APC or AAPC positive and 'decreasing' when APC or AAPC negative. In variables in which only one APC covers the entire period studied, the AAPC is equal to the APC.

The exploratory data analysis was performed using R software [5], version 4.0.4 and the jointpoint regressions Statistical analyzes were made using Joinpoint Regression Software version 4.8.0.1 (<https://surveillance.cancer.gov/joinpoint/>) provided by the US National Cancer Institute (NCI).

3. Results

During the period from 2007 to 2018, 36075 cases of whooping cough were recorded in Brazil, 60.9% of which were in babies under 1 year of age. The female gender corresponded to 55.3% of the cases and the most affected regions were the Southeast (42%), the Northeast (24%) and the South (20%). The Midwest (7%) and North (7%) regions were the least affected.

In Fig 1-a, we observe an increase in the incidence rate of pertussis from the year 2011 in both genders. As of 2014, there is a drop in the rate.

In Fig 1-b we notice a behavior like that of Fig 1-a.

The North region is the one with the smallest increase in the incidence rate. The South, Northeast, and Midwest region have the bigger increase in the period.

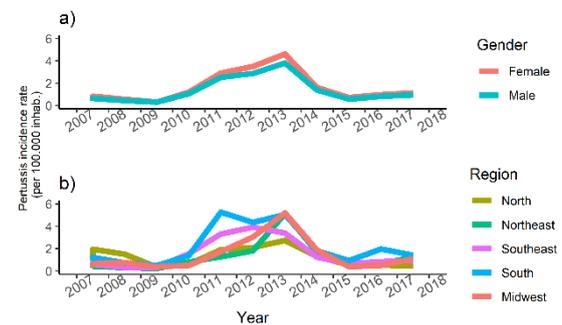


Fig 1 - Pertussis incidence rate/100 thousand inhabitants by gender and region in the period between 2007 and 2018.

In Fig 2 we observe a large increase in the rate in the population between 0 and 5 years of age. Individuals between 5 and 14 years old also showed an increase in the rate, although much smaller when compared to younger children. From the age of 15, there was no increase in the incidence of pertussis over the analyzed period.

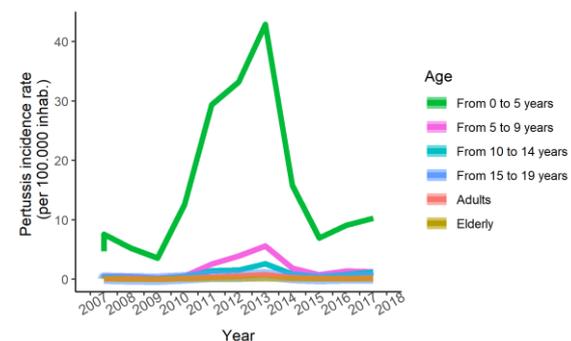


Fig 2 - Pertussis incidence rate/100 thousand inhabitants by age in the period between 2007 and 2018.

The Tab 1 shows that there was a period of growth in the number of cases in Brazil between 2007 (0.46 cases/100,000 inhab) and 2014 (4.19 cases/100,000 inhab), with an APC of 34.4 (CI95% = (4.8; 72.4)), followed by a stationary period. This behavior was also observed in the Northeast and Southeast regions.

The South and Midwest regions showed a small increase in the incidence rate with APC 7.8 (CI95% = (-6.4;24.2)) and 7.5 (CI95% = (-9.0;27.0)), respectively. On the other hand, the North region showed a reduction over the last few years, from 0.92 cases/100 thousand inhabitants in 2007 to 0.44 cases/100 thousand inhabitants in 2018 and a descending APC of -5.4 (CI95% = (-17.3;8.2)).

Tab 1 – Point and interval estimates of the joinpoint regression for pertussis incidence ratio in Brazil stratified by region, 2007-2018.

Region	Incidence rate/100 thousand inhabitants				Segment range	APC (95% CI)	AAPC (95% CI)
	2007 ^a	2013 ^b	2014 ^b	2018 ^c			
North	0.93			0.44	2007-2018	-5.4 (-17.3; 8.2)↓	-5.4(-17.3;8.2)↓
Northeast	0.25		5.13	1.20	2007-2014	44.4 (14.8; 81.7)	12.3(-8.4;37.7)
					2014-2018	-27.7 (-58.0; 24.5)↓	
Southeast	0.40	3.92		0.92	2007-2013	51.3 (5.1; 117.9)	8.3(-15.3;38.4)
					2013-2018	-27.5 (-55.2; 17.5)↓	
South	0.86			1.39	2007-2018	7.8 (-6.4; 24.2)	7.8(-6.4;24.2)
Midwest	0.36			1.08	2007-2018	7.5(-9.0;27.0)	7.5(-9.0;27.0)
Brazil	0.46		4.19	1.03	2007-2014	34.4(4.8;72.4)	5.2(-15.6;31.2)
					2014-2018	-31.4(-61.9; 23.5)↓	

Abbreviations: ^a starting point; ^b joinpoints; ^c period; APC: annual percent change; AAPC: average annual percent change; 95% CI: 95% confidence interval; ↓: decreasing trend.

It is observed in Tab 2 that was an upward and downward movement in the rate considering the gender variable. The change point being in 2013 for males (2.86 cases/100 thousand inhabitants) and 2014 for females (4.60 cases/100 thousand inhabitants). Thus, the APC was upward in the first years of the series and decreases after the peak.

As for age, the rise and fall behavior was also observed in the range from 0 to 5 years, 5 to 9 years

and in adults, and the change in the rate was observed first in 2013 with children under 5 years of age and in 2014 at other ages.

In the age groups of 10 to 14 years, 15 to 19 years, and elderly there is a progressive increase in APC of 16.9 (CI95% = (-0.8;37.8)), 13.1 (CI95% = (-7.5;38.3)) and 10.6(CI95% = (2.1;19.8)), respectively.

Tab 2 - Point and interval estimates of the joinpoint regression for pertussis incidence ratio in Brazil stratified by gender and age, 2007-2018.

Gender	Incidence rate/100 thousand inhabitants				Segment range	APC (95% CI)	AAPC (95% CI)
	2007 ^a	2013 ^b	2014 ^b	2018 ^c			
Male	0.48	2.86		0.94	2007-2013	42.8 (1.6;100.9)	7.7(-14.4;35.4)
					2013-2018	-23.3(-51.1;20.4)↓	
Female	0.48		4.60	1.13	2007-2014	35.0(4.1;75.2)	5.7(-16.1;33.2)
					2014-2018	-31.1(-62.8;27.5)↓	
Age							
From 0 to 5 years	4.66	33.20		10.24	2007-2013	43.6(3.3;99.6)	7.4(-14.0;34.0)
					2013-2018	-24.2(-51.0;17.2)↓	
From 5 to 9 years	0.27	5.60		1.25	2007-2014	49.7(7.6;108.1)	14.3(-14.7;53.2)
					2014-2018	-28.6(-67.3;55.8)↓	
From 10 to 14 years	0.22			1.15	2007-2018	16.9(-0.8;37.8)	16.9(-0.8;37.8)
From 15 to 19 years	0.08			0.24	2007-2018	13.1(-7.5;38.3)	13.1(-7.5;38.3)
Adults	0.03		0.71	0.18	2007-2014	49.2(8.3;105.4)	13.1(-14.8;50.3)
					2014-2018	-30.3(-67.3;48.8)↓	
Elderly	0.02			0.08	2007-2018	10.6(2.1;19.8)	10.6(2.1;19.8)

Abbreviations: ^a starting point; ^b joinpoints; ^c period; APC: annual percent change; AAPC: average annual

percent change; 95% CI: 95% confidence interval; ↓: decreasing trend.

4. Discussion

The present study identified that between 2013 and 2014 there was an increase of whooping cough in the country, mainly affecting early childhood, which reached a rate of 33.20 cases/100 thousand inhabitants in 2013.

It is not yet known what reasons led to the increase in the number of cases, but, there are some hypotheses such as the increased sensitivity of epidemiological surveillance and the network assistance, failures in the population's immune protection, loss of immunity, cyclicity of the disease (intervals of three to five years) and improvement in laboratory diagnosis with the introduction of biomolecular techniques. [2]

In 2015, there was a drop in the number of notifications, possibly due to the introduction of the adsorbed diphtheria, tetanus, and acellular pertussis vaccine for pregnant women from the 20th week and health professionals in November 2014 in the country. [3]

Joinpoint regression analysis has been used in other contexts to identify increases and even outbreaks of other public health issues such as suicide [6], chickenpox [7] and *Clostridium difficile* [8].

Among the limitations of the study, we have the Brazilian territorial extension, the heterogeneity of the surveillance system and the system's sensitivity to notifications.

5. Conclusions

The present study identified that the period from 2007 to 2014 was marked by the increase in the number of pertussis cases in Brazil, including in the Southeast and Northeast regions. Such behaviour was also observed in the stratified gender and age. In the analysed period we have stationary time series.

Additionally, the use of the joinpoint regression in temporal trend analyses of epidemiological indicators is a very useful tool to identify changes in the disease situation. This tool has a greater statistical precision in identify the time point(s) of follow-up at which the trend significantly changes.

6. References

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