

Childhood vaccination coverage of hepatitis A, measles, mumps and rubella, and varicella: temporal trend analysis in Minas Gerais, Brazil

Cobertura vacinal infantil de hepatite A, tríplice viral e varicela: análise de tendência temporal em Minas Gerais, Brasil

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ABSTRACT: *Objective:* To analyze the temporal trend of vaccination coverage for hepatitis A, measles, mumps and rubella, and varicella in a Brazilian state from 2014 to 2020. *Methods:* An ecological, time-series study that considered data from 853 municipalities in the state of Minas Gerais that compose the 14 regions of the state, these being the territorial units of analysis. Records of applied doses of hepatitis A, measles, mumps and rubella, and varicella vaccines registered in the Brazilian Immunization Information System were analyzed. Trends were estimated by Prais-Winsten regression and 95% confidence intervals of measures of variation were calculated. *Results:* Low vaccine coverage of hepatitis A, measles, mumps and rubella, and varicella was identified. Coverages above 95% were observed only in 2015 for the vaccine against hepatitis A (98.8%) and, in 2016, for varicella (98.4%). The measles, mumps and rubella vaccine showed coverage of less than 95% in all analyzed years. Decreases of 13.6 and 4.3% between the years 2019 and 2020 were identified for the measles, mumps and rubella, and hepatitis A vaccines, respectively. There was a decreasing trend in hepatitis A vaccination coverage in the South ($p=0.041$), East ($p=0.030$), and North ($p=0.045$) regions; and for the measles, mumps and rubella in Jequitinhonha Valley ($p=0.002$), East ($p=0.004$), and North ($p=0.024$) regions. Increasing coverage was observed only for varicella in eight regions of the state. *Conclusions:* The data point to heterogeneity in the temporal behavior of vaccination coverage in Minas Gerais. The downward trend in some regions causes concern about the possibility of resurgence of diseases, such as measles, which until then had been controlled.

Keywords: Immunization programs. Vaccination coverage. Health information systems. Health evaluation. Ecological studies.

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RESUMO: *Objetivo:* Analisar a tendência temporal da cobertura vacinal de hepatite A, tríplice viral e varicela em um estado brasileiro no período de 2014 a 2020. *Métodos:* Estudo ecológico de séries temporais, que considerou dados dos 853 municípios de Minas Gerais que compõem as 14 regiões do estado, sendo estas as unidades territoriais de análise. Foram analisados registros de doses aplicadas das vacinas hepatite A, tríplice viral e varicela registrados no Sistema de Informação de Imunização do Brasil. As tendências foram estimadas pela regressão de Prais-Winsten e calculados os intervalos de confiança 95% das medidas de variação. *Resultados:* Identificaram-se baixas coberturas vacinais de hepatite A, tríplice viral e varicela. Coberturas acima de 95% foram observadas somente no ano de 2015 para a vacina contra hepatite A (98,8%) e, em 2016, para a varicela (98,4%). A vacina tríplice viral apresentou cobertura inferior a 95% em todos os anos analisados. Uma queda de 13,6 e 4,3% entre os anos de 2019 e 2020 foi identificada para as vacinas tríplice viral e hepatite A, respectivamente. Observou-se tendência decrescente na cobertura vacinal da hepatite A nas regiões Sul ($p=0,041$), Leste ($p=0,030$) e Norte ($p=0,045$); para a tríplice viral, nas regiões Jequitinhonha ($p=0,002$), Leste ($p=0,004$) e Norte ($p=0,024$). A cobertura crescente foi observada somente para a varicela em oito regiões do estado. *Conclusões:* Os dados apontam heterogeneidade no comportamento temporal das coberturas vacinais em Minas Gerais. A tendência decrescente em algumas regiões desperta preocupação pela possibilidade do recrudescimento de doenças, como o sarampo, até então controladas. *Palavras-chave:* Programas de imunização. Cobertura vacinal. Sistemas de informação em saúde. Avaliação em saúde. Estudos ecológicos.

INTRODUCTION

Achieving coverage goals for all vaccines in the national immunization schedule by 2020 was proposed by the Global Vaccine Action Plan 2011-2020. However, less than two-thirds of the countries attained the proposed goal, as illustrated by the third dose of the DTaP (diphtheria, tetanus, and acellular pertussis) vaccine, with 66% coverage¹. In Brazil, a recent study showed temporal trends of reduction in vaccination coverage in the five Brazilian regions in the period from 2006 to 2016². The circulation of fake news about immunobiologicals³, vaccine hesitancy⁴ and, more recently, the pandemic caused by COVID-19⁵ are some of the determinants pointed out in the literature. Nonetheless, the decline in immunization is heterogeneous among Brazilian municipalities² and may reflect social inequalities⁶ and inequities related to access to health services⁷.

Currently, the Immunization Agenda 2030 global strategy envisions a world where people, of all ages and from everywhere, fully benefit from vaccines offered to improve the health and well-being of the population. This intervention proposes to maintain the positive results achieved in vaccination and recover the losses caused by COVID-19⁸.

The most significant impacts of non-vaccination have been morbidity and mortality from serious infections that disproportionately affect children⁹. Among the vaccines offered to this group, there is a concern about the drop in coverage observed in several countries of the vaccination against measles, mumps, rubella, and varicella, highly contagious diseases with several associated clinical complications¹⁰.

The introduction of the live-attenuated vaccine against varicella is a preventive strategy adopted in several countries. The schedules vary in terms of the number of doses, the combination with other vaccines, and the age of immunization¹¹. The efficacy of a single-dose varicella vaccine in preventing infection and moderate/severe disease is estimated to be 81 and 98%, respectively¹². However, its coverage had an estimated average of 78% in 2016 in Brazil, and since then a decrease has been observed, reaching 34.3% in 2019¹³.

Another vaccine that is part of the national schedule is the measles, mumps, and rubella (MMR) vaccine, which prevents the occurrence of these diseases. Estimates of the effectiveness of the MMR vaccine are 99% in preventing measles after a second dose, more than 95% in preventing mumps, and 90% in preventing rubella after a single dose¹⁴. Nevertheless, a reduction of 2.7% per year in its coverage was observed in Brazil in the period from 2006 to 2016².

In addition, the hepatitis A vaccine also had a decrease in coverage in all Brazilian regions after 2015, ranging between 60.0 and 82.0% among Brazilian municipalities¹⁵. Although hepatitis A has mild clinical manifestations in childhood, the World Health Organization (WHO) estimates more than 7,000 deaths per year worldwide¹⁶.

Considering the variations in vaccination coverage between countries and within Brazil, it is opportune to analyze the territory in spatial units with a higher level of spatial disaggregation. The state of Minas Gerais, the second most populous in Brazil¹⁷, has recently faced epidemics and outbreaks of vaccine-preventable diseases¹⁸.

Therefore, considering the low childhood vaccination coverage and its already visible consequences, efforts to propose a strategic planning consistent with the characteristics of each Brazilian region for assertive decision-making are justified. Thus, the objective of this study was to analyze the temporal trend of vaccination coverage for hepatitis A, MMR, and varicella in a Brazilian state from 2014 to 2020.

METHODS

This is an ecological, time-series study whose location is the state of Minas Gerais, the second-most populous state in Brazil and the fourth in territorial extension¹⁷. The 14 regions of the state were used as territorial units of analysis: South, South-Central, Central, Jequitinhonha Valley, West, East, Aço Valley, Southeast, North, Northwest, Leste do Sul, Northeast, Triângulo do Sul, and Triângulo do Norte¹⁷.

The study population consisted of children living in the 853 municipalities of Minas Gerais who had vaccination records for immunobiological agents offered by the National Immunization Program (*Plano Nacional de Imunizações* – PNI) in the PNI Information System (SI-PNI). Data from vaccine doses administered for the prevention of hepatitis A (single dose at 15 months of age), MMR (second dose at 15 months of age), and varicella (first dose at 15 months of age) in the period from 2014 (deadline for implementing the SI-PNI in Brazil) to 2020 were used. The coverage goal recommended by PNI for all these vaccines is 95%¹⁹.

It is worth highlighting that the measles, mumps, rubella, and varicella vaccine (MMRV) was not analyzed, considering that, according to information from the PNI Coordination of Minas Gerais, there were gaps in its supply to the municipal health service during the study period.

Data on routine childhood vaccinations were extracted from the SI-PNI provided by the Minas Gerais State Department of Health, and data on vaccine target populations per municipality were obtained through access to the Brazilian Health Informatics Department, of the Brazilian Unified Health System (SUS)/Live Birth Information System. Microsoft Office Excel software (2016) was used to structure the vaccination coverage indicator. This indicator presents, in the numerator, the number of children vaccinated considering the complete vaccination schedule and, in the denominator, the target population for the vaccine. Multiplication factor: 100¹⁹.

For trend analysis, the Stata software (version 12) and the Prais-Winsten linear regression model were used, in which the independent variable (x) was the year (2014 to 2020) and the dependent variable (y), the vaccination coverage. This model is indicated to correct serial correlation in time series and it allows analyzing trends with seven or more points²⁰.

Initially, the logarithmic transformation of the y values was performed to reduce the heterogeneity of the variance of the residuals of the regression analysis. Subsequently, the application of the Prais-Winsten model was carried out. To identify the average annual percent change (APC), the values of the b1 coefficient corresponding to each of the indicators were applied to the following formula: $APC = -1 + 10 [b1] * 100\%$. Finally, the 95% confidence intervals (CI) of the variation measures were calculated by applying the following formulas: Minimum 95%CI = $-1 + 10 [b1 - t * e] * 100\%$; maximum 95%CI = $-1 + 10 [b1 + t * e] * 100\%$.

The values of the b1 coefficient (beta) and e (standard error) were generated by the statistical analysis program. The t refers to the Student's t-test and corresponds to six degrees of freedom (2.447), which indicates the seven years of analysis (2014-2020), with a confidence level of 95%. The interpretation of the results was performed as follows: upward trend, when the average annual percent change was significantly positive; downward trend, when the average annual percent change was significantly negative; and stationary, when accepting the null hypothesis that there is no significant difference between the value of the variation and zero²⁰.

The present study uses data from the public domain of open access, for which there is no identification of the individuals participating in the investigation; therefore, there is no need for consideration on the part of the Research Ethics Committee.

RESULTS

Throughout the analyzed period, the state of Minas Gerais presented fluctuations in the vaccination coverage of hepatitis A, MMR, and varicella. Coverages above 95% were observed only in 2015 for the vaccine against hepatitis A (98.8%) and, in 2016, for varicella

(98.4%). The MMR vaccine had coverage of less than 95% in all years. Decreases of 13.6 and 4.3% between the years 2019 and 2020 were identified for the MMR and hepatitis A vaccines, respectively (Figure 1).

The graph was the first step in understanding the processes underlying temporally ordered measures. Subsequently, the values, established for each region of the state, demonstrate an even more emblematic result. In Table 1 the predominance of the stationary trend, by region, for hepatitis A and MMR vaccines can be observed. The downward trend in hepatitis A vaccination coverage stands out in the South ($p=0.041$), East ($p=0.030$), and North ($p=0.045$) regions; and for the MMR vaccine, in Jequitinhonha Valley ($p=0.002$), East ($p=0.004$), and North ($p=0.024$) regions. The annual percentage change in the downward trend of vaccination coverage was between -5.21 and -8.43% in the period from 2014 to 2020. Conversely, the upward trend was only observed for the varicella vaccine in most regions, with an annual percentage change from 29.15 to 49.57%.

DISCUSSION

The average vaccination coverage in Minas Gerais, for the three analyzed vaccines, did not achieve the 95% coverage goal as recommended by PNI¹⁹. The study findings corroborate records of recent low coverage in other countries^{21,22}.

Around 14 million children worldwide did not receive vital vaccines, such as the measles vaccine, which resulted in outbreaks recorded in Venezuela, in 2017; Madagascar, the Philippines, and Brazil between 2018 and 2019^{23,24}. In Ukraine, in 2016, only 42% of newborns and 31% of children up to six years of age were vaccinated against measles²⁵. In England,

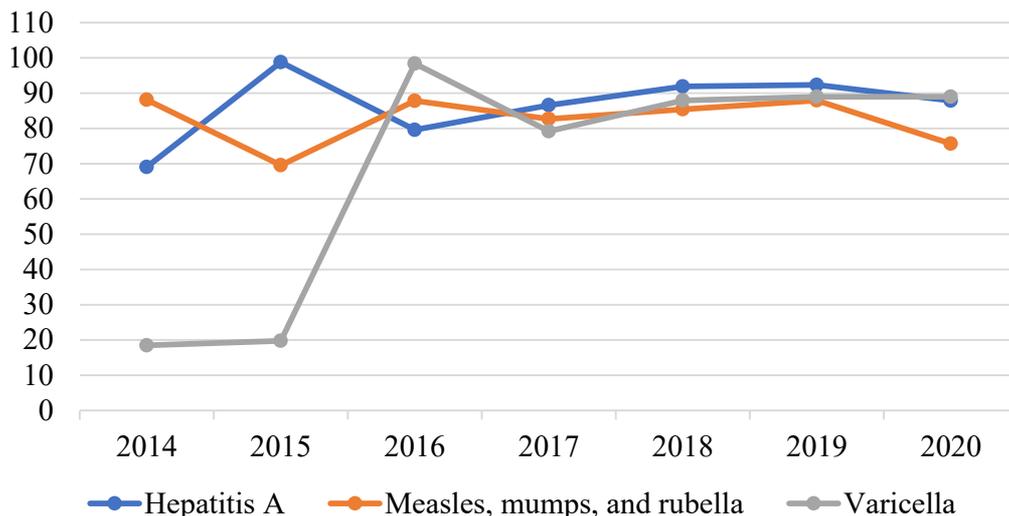


Figure 1. Vaccination coverage in the state of Minas Gerais, Brazil, from 2014 to 2020, for hepatitis A, measles, mumps and rubella, and varicella vaccines.

Table 1. Trend of vaccination coverage in the state of Minas Gerais, Brazil, from 2014 to 2020, for hepatitis A, measles, mumps and rubella, and varicella vaccines.

Vaccines/Regions	Annual change (%)	95%CI	p	Trend
Hepatitis A				
South	-6.72	(-12.33; -0.74)	0.041	Downward
South-Central	-4.73	(-11.77; 2.88)	0.184	Stationary
Central	-0.10	(-8.71; 0.33)	0.980	Stationary
Jequitinhonha Valley	-2.75	(-9.55; 4.56)	0.390	Stationary
West	-4.20	(-12.85; 5.31)	0.318	Stationary
East	-5.83	(-10.34; -1.09)	0.030	Downward
Southeast	-5.66	(8.79; -18.18)	0.058	Stationary
North	-8.25	(-15.25; -0.67)	0.045	Downward
Northwest	-4.38	(-10.85; 2.57)	0.179	Stationary
Leste do Sul	-1.66	(-11.80; 9.65)	0.722	Stationary
Northeast	-3.41	(-7.84; 1.24)	0.131	Stationary
Triângulo do Sul	-4.03	(-11.46; 4.02)	0.267	Stationary
Triângulo do Norte	-6.14	(-14.49; 3.02)	0.157	Stationary
Aço Valley	-1.93	(-12.67; 10.14)	0.699	Stationary
Measles, mumps, and rubella				
South	-5.34	(-13.36; 3.42)	0.190	Stationary
South-Central	-6.12	(13.55; 1.95)	0.120	Stationary
Central	-2.93	(-7.30; 1.65)	0.175	Stationary
Jequitinhonha Valley	-5.21	(-7.35; -3.02)	0.002	Downward
West	-5.46	(-13.56; 3.40)	0.186	Stationary
East	-7.31	(-10.68; -3.82)	0.004	Downward
Southeast	-5.49	(-11.13; 0.51)	0.075	Stationary
North	-8.43	(-14.37; -2.08)	0.024	Downward
Northwest	-4.34	(-11.83; 3.77)	0.240	Stationary
Leste do Sul	-3.29	(-12.35; 6.71)	0.443	Stationary
Northeast	-2.18	(-8.56; 4.64)	0.460	Stationary
Triângulo do Sul	-2.94	(-10.61; 5.39)	0.416	Stationary
Triângulo do Norte	-6.07	(-14.08; 2.68)	0.146	Stationary
Aço Valley	-3.24	(-12.63; 7.15)	0.465	Stationary

Continue...

Table 1. Continuation.

Vaccines/Regions	Annual change (%)	95%CI	p	Trend
Varicella				
South	28.33	(0.66; 63.61)	0.054	Stationary
Central	24.46	(0.62; 53.96)	0.053	Stationary
South-Central	30.38	(2.46; 65.92)	0.043	Upward
Jequitinhonha Valley	47.69	(5.64; 106.49)	0.036	Upward
West	31.67	(6.01; 63.55)	0.027	Upward
East	26.18	(1.01; 57.63)	0.051	Stationary
Southeast	28.31	(-0.18; 64.94)	0.059	Stationary
North	34.31	(4.31; 72.93)	0.036	Upward
Northwest	29.15	(3.23; 61.58)	0.038	Upward
Leste do Sul	34.36	(1.98; 77.02)	0.047	Upward
Northeast	36.77	(2.40; 82.06)	0.046	Upward
Triângulo do Sul	33.08	(1.07; 75.24)	0.052	Stationary
Triângulo do Norte	37.51	(1.14; 86.96)	0.052	Stationary
Aço Valley	49.57	(2.45; 118.36)	0.048	Upward

CI: Confidence interval; significantly different from zero ($p < 0.05$)

there was a 19.8% drop in the applied doses of the MMR vaccine between 2019 and 2020. In the United States of America, coverage for hepatitis A was below the Healthy People 2020 goal of 85%, reaching about 76.6% among children born in 2015-2016²⁷.

According to official records from the Brazilian Ministry of Health, the decrease in vaccination coverage in Brazil was demarcated from 2016 onwards, with about 10 to 20 percentage points²⁸. A reduction was also observed in the present investigation for MMR and hepatitis A coverage in 2020.

With the COVID-19 pandemic, it is estimated that the probability of a child up to five years of age receiving all vaccines is 20%²⁹. Attendance at health centers dramatically decreased this year, including for childhood vaccinations, due to social distancing measures to mitigate the transmission of the Sars-CoV-2 virus³⁰.

Moreover, the growing anti-vaccine movement, intensified with the vaccination against COVID-19, the circulation of fake news about immunobiological agents, and vaccine hesitancy are some of the determinants pointed out in the literature that accentuate the drops in vaccination coverage, already verified since 2016^{3,31,32}.

However, this decline was not observed for the varicella vaccine, applied together with the MMR vaccine at 15 months of age (replacing the MMRV one), considering that this

vaccine has not been available in the state of Minas Gerais since 2017³³. It is assumed that some professionals are registering the second dose of the MMR vaccine instead of the MMRV vaccine. This assumption points to underestimated coverage of this vaccine, which is consistent with the findings of the present study, in which the MMR vaccine was the one with the greatest decrease in vaccination coverage.

Furthermore, it is worth mentioning the change in the SI-PNI that took place in 2014. The system, which used to be fed according to the applied doses, changed to the nominal record. This change posed difficulties because, in addition to the equipment and all the necessary logistics, it was necessary to have trained personnel to feed the system^{34,35}. Currently, the registration of administered doses is made in the Citizen's Electronic Health Record (*Prontuário Eletrônico do Cidadão*), a software developed based on the e-SUS Primary Care strategy³⁶. These factors may have resulted in lower registration of the administered doses, making data on vaccination coverage inaccurate in some places¹⁵.

Seeking to reduce the distortions of analysis of places with great territorial extension, the analyses of this study were carried out per region, which allowed the identification of important heterogeneities within the state of Minas Gerais. In addition, more than delimiting geographic differences, it was possible to diagnose the rate of increase, decrease, or stabilization of the coverage of an area over time through regression models.

The North, East, South, and Jequitinhonha Valley regions stand out, which had downward trends for MMR and/or hepatitis A vaccines. These areas should be considered the most at risk for the transmission of measles, mumps, rubella, and hepatitis A, precisely because of the low vaccination coverage.

Despite the decrease in the incidence of hepatitis A, vaccination coverage in the year of its implementation was low across the country, suggesting the impact of improvements in health conditions³⁷ or even underreporting of the disease¹⁵. Moreover, the lack of the hepatitis A vaccine, which occurred from the beginning of 2016 to the end of 2017, also contributed to the reduction of vaccination coverage¹⁵. Nevertheless, the shortage of hepatitis A vaccine does not seem to be associated with the low vaccination coverage in the state of Minas Gerais, as the downward trend was only restricted to three regions of the state, and the lack of the vaccine affected the entire national territory.

The childhood vaccines recommended worldwide are based on the scientific principle of their preventive effect³⁸. Measles, mumps, and rubella are other highly contagious vaccine-preventable childhood diseases. Although not always serious, these diseases can cause disabilities (such as deafness), complications, and death¹⁰.

In Minas Gerais, the North, East, and Jequitinhonha Valley regions have high levels of poverty³⁹, which could explain the drops in vaccination coverage for MMR and/or hepatitis A. However, this phenomenon should be cautiously analyzed. Low coverage is also verified among the population strata with greater purchasing power⁴⁰.

Other important elements for the low vaccination coverage are the shortage of vaccines³³ and the difficulty in accessing healthcare services (distance between the residence and the health center, lack of public transport, reduced service hours of the health center, deficiency in the continuing education of healthcare professionals)⁷.

Thus, promoting intersectoral involvement, such as awareness-raising actions in churches and schools⁴⁰, monitoring coverage through periodic household surveys, and expanding the supply of vaccines to bring them closer to communities⁴¹, are some key interventions.

The low vaccination coverage in some regions of Minas Gerais is of great concern, considering the possibility of the resurgence of diseases hitherto eliminated or controlled. This scenario can be well illustrated by recalling the measles outbreak that occurred in 2018 in the states of Roraima and Amazonas⁴².

In this sense, it is worth mentioning that, even in countries with effective immunization programs, such as Brazil, the advances achieved in previous years can be easily lost without constant monitoring². Access to immunization must be universal, regardless of geographic location; hence, policies and programs should take more effective measures to reduce inequities in vaccination. Equity must remain as a strong motivator aspect to ensure that everyone enjoys the benefits of immunization, including the most disadvantaged and marginalized populations⁸.

Among the limitations of this study, it is noteworthy that the use of secondary data can often result in inconsistencies in the estimated indicator (vaccination coverage), but, despite this, the choice of this type of source reduces operational costs and does not make the performance of analyses unfeasible. To minimize this limitation, a database consistency analysis was conducted.

The study presents evidence on reduction in the vaccination coverage of hepatitis A in the South, East, and North regions; and of MMR in the Jequitinhonha Valley, East, and North regions of the state of Minas Gerais. Conversely, increasing coverage was observed only for varicella in eight regions of the state. Therefore, it was verified that the heterogeneity in the temporal behavior of vaccination coverage requires strategic planning consistent with the characteristics of each location.

For future studies, it would be opportune to understand the factors associated with the temporal behaviors identified, including the development of field research. In addition, the vaccination records of the SI-PNI require attention and must be continuously monitored to improve the quality of the information used in services and research.

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