Heliyon 10 (2024) e35463

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Association between detection rate of norovirus GII and climatic factors in the Northwest Amazon region

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ARTICLE INFO

Keywords:
Viral gastroenteritis
Humidity
Climate
Amazonic region
Norovirus
Weather/epidemiology

ABSTRACT

Worldwide, approximately one fifth of all cases of diarrhea are associated with norovirus, mainly in children, with a defined seasonality in temperate climates, but seasonal dynamics are less known in tropical climates. The objective was to investigate the impact of external clinical, epidemiological, and climatic factors on norovirus detection rates in samples from children under 5 years of age from Roraima, the Amazon region of Brazil. A total of 941 samples were included. According to climatic factors, we observed correlations between external climatic factors and weekly positivity rates, where temperature ($P = 0.002$), relative humidity ($P = 0.0005$), absolute humidity ($P < 0.0001$) and wind speed had the strongest effect ($P = 0.0006$). The Brazilian Amazon region presents a typical and favorable scenario for the persistence, expansion, and distribution of viral gastroenteritis.

Importance: This study is important as it will serve as a basis for studies carried out in Brazil and Latin American countries on the epidemiological importance, seasonality, climate change, antigenic diversity, among other factors in the circulation of gastroenteric virus.

1. Introduction

Viral gastroenteritis is one of the most common causes of morbidity and mortality worldwide in children (especially <5 years old), with major relevance in developing countries [1,2]. According to literature data, the most common and important viral enteropathogenesis are norovirus (NoV) and rotavirus A (RVA), followed by sapoviruses (SaV), enteric adenoviruses (HadV) and, less commonly, bocaviruses (HBoV) [1–4].

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https://doi.org/10.1016/j.heliyon.2024.e35463
Received 3 February 2024; Received in revised form 29 July 2024; Accepted 29 July 2024
Available online 3 August 2024

Norovirus has a high infectious capacity, is environmentally stable for long periods and is one of the main etiological agents for both outbreaks and sporadic cases of acute gastroenteritis (AGE) in adults and children around the world [5]. Approximately one-fifth of all cases of diarrhea worldwide are associated with norovirus [6]. In countries with rotavirus vaccination programs, norovirus is the most common cause of gastroenteritis in children [7].

Noroviruses belong to the Caliciviridae family, and the norovirus genus contains six genogroups (G), of which GI, GII and GIV infect humans, with GII causing the majority of diseases in humans, having greater importance in Brazil and also presenting a pattern more seasonal than other genogroups and are of greater epidemiological importance due to their high evolutionary capacity [8–10]. Although the GI genogroup is responsible for causing epidemic outbreaks in many parts of the world, a low frequency of this genogroup has recently been observed in samples from the Amazon region [11].

Norovirus, like many other gastrointestinal viruses, exhibit seasonality in the autumn and winter periods in temperate climates [12,13], but the seasonal dynamic is less known for tropical climates. Due to irregular epidemic patterns, with incidence peaks change frequently for weeks between seasons [14].

Previous studies in temperate climates have shown that low external temperature and relative humidity are associated with annual epidemics of norovirus and rotavirus [12,13,15,16], but there are also studies that show outbreaks of norovirus during the months with higher temperatures [17,18]. There are few studies in tropical regions and a lack of definition between seasonality and norovirus, as it is difficult to find robust data due to different epidemiological patterns [5,18].

The Amazon region covers territories of Latin American countries, most of which are in Brazil. Due to its great biodiversity, this region has several peculiarities, such as well-defined seasons and periods of rain and drought. The predominant climate is humid equatorial, with an average temperature of 27.9 °C during the season with the lowest humidity, and 25.8 °C during the season with the highest rainfall [19].

Different to other regions of Brazil, In Amazon region has only two climatic periods: dry and rainy. The first runs from October to June and the second from July to September. Although the temperature does not vary greatly, the hottest months are: March, April and May (beginning of autumn), followed by November and December (beginning of summer). The Amazon region is spending a few years under the effect of El Niño, meaning months of drought plus forest fires, forest destruction and higher levels of carbon dioxide (CO^2) emissions. It was like this in 2015 and 2016, with successive negative records. During this same period, the forest was under the influence of a phenomenon so strong that researchers dubbed it "El Niño Godzilla", alluding to its severity [20].

The sky during this period has fewer clouds, less wind and humidity is higher than in the previous season, increasing the sensation of heat, which can be worsened under the influence of El Niño [21].

The objective of the study was to investigate the impact of external clinical, epidemiological and climatic factors on noroviruses detection rates in samples of children <5 years old from Roraima, Amazon region of Brazil.

2. Materials and methods

This is a retrospective, observational and cross-sectional study.

2.1. Study population

A total of 941 samples of convenience of children aged ≤5 years were included in this study, from October 2016 to October 2017 and from May to July 2021. They attended exclusively the emergency care unit of the "Hospital da Criança de Santo Antonio (HCSA)". Inclusion criteria were: ≤5 years, three liquid/semi-liquid bowel movements in 24 h and dehydration. The HCSA is the only hospital located in Boa Vista, in the state of Roraima (RR), that serves children living in the extreme north of Brazil and on the border with Venezuela and Guyana, including those who live in the Amazon. The pediatrician responsible for collecting the samples right after the children's hospitalization attended the HCSA every day. Each child was examined and their parents or guardians were interviewed to collect data and fill out a form containing clinical and epidemiological information about each child.

2.2. Sample processing

All samples were collected from diapers with feces, where the feces were scraped and placed into a collection pote. This is a globally accepted method for detecting viruses that cause gastroenteritis and yields quality samples for detection by molecular methods. Feces were collected from all children with AGE attended in the hospital emergency room.

All samples were sent along with the clinical-epidemiological records to the Regional Reference Laboratory for Rotavirus–Laboratory of Comparative and Environmental Virology (RRRL–LVCA). This laboratory is part of the ongoing national EFA surveillance network and is coordinated by the General Coordination of Public Health Laboratories, Ministry of Health of Brazil. Samples were strictly kept at −20 °C until processing. Then, fecal suspensions were prepared at 10 % in phosphate buffered saline (PBS) pH 7.4.

2.3. Study design and detection of norovirus

Total viral nucleic acid was obtained from 140 μL of each supernatant of 10 % fecal suspension sample that was subjected to an automatic nucleic acid extraction procedure using a QIAamp Viral RNA Mini kit (QIAGEN, CA, USA) and a QIAcube automated system (QIAGEN), according to the manufacturer's instructions, with a final elute sample volume of 60 μL. The total viral nucleic acids isolated were immediately stored at −80 °C until molecular analysis. For molecular detection of norovirus, quantitative duplex

RTqPCR (GI/GII) was performed; this technique already detects both genogroups [22].

Monoplex reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was performed for detection of Rotavirus A [23] and Sapovirus (SaV) [24,25], as previously described. For Enteric Adenovirus 40 and 41 (HAdV), a quantitative polymerase chain reaction (qPCR) assay was carried out according to that recently presented [11].

2.4. Meteorological data

Data on average weekly outdoor temperature maxim and minim (degrees Celsius), vapor pressure (VP; Pa), absolute humidity (AH; gH2O/m^3), relative humidity (RH; %), wind speed (m/s), precipitation (mm)and nebulosity (tenths of cloudy sky) for the study period were obtained from the National Institute of Meteorology (INMT), located at Boa Vista station in Roraima, Brazil (82.35 m above sea level, situated at Latitude: 2.81694443N, Longitude: 60.69083333E). Detection rates (weekly number of positive samples) of viral agents included in the standard of care PCR panel and the weekly means of included meteorological parameters were used to analyze seasonality and correlations. A total of 64 consecutive and paired weekly observations were included. To study meteorological conditions during the slope of norovirus GII epidemics, subsets of weekly data were extracted. The choice to evaluate only GII was due to its epidemiological importance and evolutionary capacity [19]. **Statistical methods**.

We performed the sample calculation using the online calculator "SurveyMonkey", which was based on the global prevalence of Norovirus in Brazil. As this is the minimum number of samples that have been achieved.

We used a generalized linear mixed model (GLMM) as an extension of the generalized linear model as our data has random effects in addition to the usual fixed effects.

After evaluating the data distribution, we used the Poisson distribution, including time series components. When fitting the models, the residuals were autocorrelated, especially for norovirus GII. The modeling was first carried out in a univariate manner in which all variables were entered individually in different periods, (encompassing positive and negative samples for GII – Outcome variable). These variables are not independent and therefore were performed together in the multivariate analyses. From this, we carried out the modeling of multivariate analyzes taking into account more than one variable (previously significant in univariate analysis) in a "group" format with the aim of finding patterns and relationships between several variables, allowing the prediction of effects and changes that one variable will have on the other. As this is modeling between variables, positive and negative samples are considered. The analyzes demonstrate how the positive samples of the outcome variable are correlated with the other variables. For the analysis of risk factors, we used the Mann-Whitney test and binomial logistic regression for univariate analyses. Variables with P value < 0.05 were modeled in multivariate analyzes in which adjusted Odds ratios were estimated.

The function in the "Forecast" R package selected models containing a combination of autoregressive and moving average terms to model the data.

Optimal thresholds were identified by repeated GLMM analyses, delaying climate factors one week at a time until the highest F value (This is a proportion of two variances based on the mean squares ratio, that is, an estimate of the population variance that explains the degrees of freedom used to calculate that estimate.) for each model was determined. For example, the 'lag one' effect represented the effect of the weather factor measured 1 week before, on the current week's positivity rate. Was performed using the Rstudio software package version 4.3.1.

Maps of the study site, case distribution, and spatial analysis were created using QGIS (version 3.32.2), employing computers provided by the Oswaldo Cruz Foundation, Rio de Janeiro, Brazil.

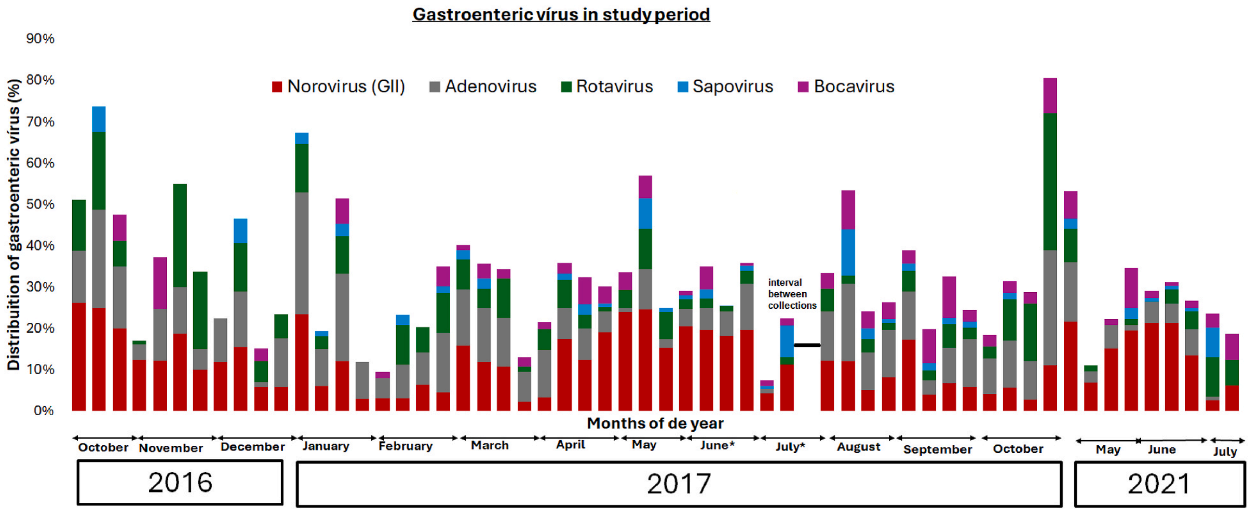

Fig. 1. Weekly (each bar refers to 1 week) incidence of various gastrointestinal viruses, detected with real-time PCR. Total number of samples tested for month: 2016–October and November N = 16 each; December N = 17; 2017–January N = 33, February N = 62, March N = 84, April and August N = 120 each, May N = 93, June N = 20, July N = 53, September N = 70, October N = 36; 2021–May N = 72, June N = 114 and July N = 16.

3. Results

A total of 941 samples were analyzed, of which 618 (65.6 %) were positive for at least one gastroenteric virus investigated viral GE agent. Noroviruses was the most common agent detected, accounting for 302 (48.8 %) of the positive samples, being a total of 281 samples (93 %) belonging to GII genotype even though we tested for GI and GII, only 1.9 % (18/941) of the samples were positive for GI.

- **Distribution of viral gastroenteritis by seasonality**

Norovirus was the most prevalent 29.8 % (281/941) followed by enteric adenovirus 29 % (272/941), Rotavirus 19.3 % (181/941), bocavirus 13.1 % (123/941) and Sapovirus 7 % (65/941).

Among the samples positive for norovirus when compared to other enteric viruses detected, we observed that: Coinfection between NoV and HaDV was the most prevalent 31.3 % (88/281), followed by RVA 17,4 % (49/281), HBoV 16,3 % (46/281) and SaV 11 % (31/281) respectively. There was statistical significance correlated between norovirus GII and Sapovirus co-infection. Among the total samples positive for Sapovirus (N = 65), 31 of them were positive for Norovirus GII (47.6 %) (Table 3).

Even though they were detected year-round, norovirus, sapovirus, and bocavirus followed a distinct seasonal pattern, with peaks during the driest period (October, May, and June), while adenovirus were detected more continuously throughout the year (Fig. 1).

- **Distribution of norovirus GII by seasonality and climatic factors**

The seasonal patterns of relative and absolute humidity, precipitation and temperature are shown in relation to Norovirus GII in Fig. 2, it can be seen that in drier periods there was an increase in the NoV detection rate. Still according to climatic factors, we observed that after some weekly drops in relative humidity and absolute humidity, there is an increase in the NoV detection rate. This pattern was observed in October 2016, January, May and September 2017 and between May and June 2021 (Fig. 2).Univariate analyzes comparing the weekly detection rate of each virus with meteorological factors showed that low absolute humidity correlated with detection of all viruses, but low relative humidity and low precipitation were correlated with norovirus GII, adenovirus, and rotavirus. Low temperature correlated with high detection rates of norovirus GII. Furthermore, there was a positive correlation between norovirus GII and cloudiness (able 1). Univariate climate factors do not affect each other, due to the inclusion of time series components in statistical analyses, (Table 1). This analysis is carried to better model the multivariate analysis described in Table 2.

In multivariate analysis, infection patterns and correlations with climatic factors were different in between gastroenteric viruses (supplementary table). The strongest correlations between external weather factors and weekly positivity rates were observed for norovirus GII. Temperature, relative humidity, absolute humidity and wind speed had the strongest effect (F value) on norovirus GII (Table 2).

- **Prevalence of norovirus GII in Roraima**

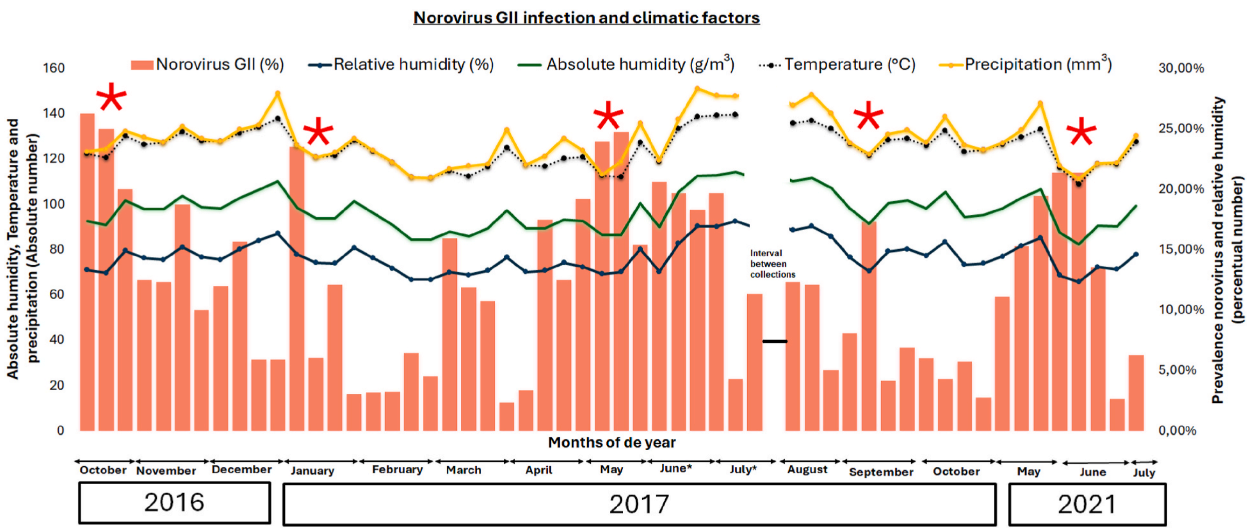

Fig. 2. Weekly positivity rate of norovirus infections (% right axis; red bars) according to weekly average external relative humidity (% right axis; blue line with a point), Absolute humidity (% right axis; green line), weekly average temperature (°C left axis; black line with a point) and Average weekly precipitation (mm^3 left axis yellow line) throughout the study period (2016–2017 and 2021). The red marcation indicate that when there is a drop in relative humidity on a weekly basis, there is an increase in the incidence of norovirus.

Table 1
Correlations between gastrointestinal viruses and weather factors during the study period (Data collected daily, weekly averages calculated throughout the study period 2016–2017 and 2021).

Virus	Temperature		Relative humidity		Absolute humidity		Vapor pressure		Wind speed		Precipitation		Nebulosity	
	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value	Coeff	p value
Norovirus GII	**−0.15**	**0.002**	**−0.06**	**$8x10^{-12}$**	**−0.3**	**$2x\ 10^{-6}$**	−0.01	0.9	**−0.3**	**0.0009**	**−0.02**	**0.04**	**0.09**	**0.005**
Adenovirus	0.08	0.8	**−0.04**	**$1x\ 10^{-6}$**	**−0.14**	**$3x\ 10^{-5}$**	**1.6**	**0.03**	0.1	0.1	**−0.03**	**0.02**	**−0.19**	**$1x10^{-5}$**
Rotavirus	0.04	0.4	**−0.07**	**$4\ x\ 10^{-8}$**	**−0.2**	**$2x\ 10^{-8}$**	0.2	0.9	0.16	0.2	**−0.06**	**0.009**	−0.02	0.6
Sapovirus	−0.4	0.02	0.01	0.9	**−0.2**	**0.001**	0.1	0.8	**−0.8**	**0.003**	**0.10**	**0.001**	0.18	0.07
Bocavirus	−0.12	0.1	−0.01	0.2	**−0.12**	**0.01**	**0.01**	**0.03**	**−0.5**	**0.002**	0.02	0.3	−0.01	0.8

References for average temperature variation: 27.6 °C (±1.15 °C); Relative air humidity: 77.3 % (±7.04 %); Absolute air humidity: 20.6 g/m^3 (±1.68 g/m^3); Precipitation: 3.69 mm^3 (±3.86 mm^3); vapor pressure: 1001.3 nPa (±4.2 nPa); wind speed: 1.56 (±1.08 m/s) and nebulosity: 4.6 tenths (±3.4 tenths).In bold, results with statistical significance (P value $<$ 0.05)Coeff – Coefficient.

Table 2
Correlations between norovirus genogroup II and weather factors during period of the study (2016–2017 and 2021). **References for average temperature variation**: 27.6 °C (±1.15 °C); Relative air humidity: 77.3 % (±7.04 %); Absolute air humidity: 20.6 g/m^3 (±1.68 g/m^3); Precipitation: 3.69 mm^3 (±3.86 mm^3); vapor pressure: 1001.3 nPa (±4.2 nPa); wind speed: 1.56 (±1.08 m/s) and nebulosity: 4.6 tenths (±3.4 tenths).I

Norovirus			
Weather factor (weekly mean)	Fixed effects F	Coefficient	*P* value
Temperature	**10**	**−0.32**	**0.002**
Vapor pressure	0.2	0.45	0.9
Relative humidity	**30**	**−0.06**	**0.0005**
Absolute humidity	**18**	**−0.36**	**3x10^{-9}**
Wind speed	**8**	**−0.72**	**0.0006**
Nebulosity	0.9	0.10	0.06
Precipitation	0.6	−0.004	0.8

In bold, results with statistical significance (P value < 0.05).

Table 3
In the univariate analysis column, these data were evaluated in a stratified and separate manner, and consequently these data were not evaluated jointly. Clinical factors associated with the detection rate of norovirus GII and risk factors associated.OR – Odds ratio for univariate analysis ORa – Odds ratio adjusted in variables with P Value a <0.05 in multivariate analysis.

Total sample (%)	N° of Fecal Samples–Positive/Tested (%)							
	Total GII (%)	2016–2017	2021	OR	P value	ORa (IC95 %)	P value (a)	
Samples distribution (%)	941 (100)	281 (29.8)	220 (78.2)	61 (21.8)	0.9 (0.5–2.1)	0.3	1.2 (0.5–1.8)	0.9
Region								
Boa Vista (state's capital)	504 (53.5)	157 (56.1)	104 (47.2)	53 (86.8)	1		1	
Others	437 (46.5)	124 (43.9)	116 (52.8)	8 (13.2)	0.3 (0.2–1.8)	0.8	0.9 (0.4–1.5)	0.9
Gender								
Female	386 [41]	123 (43.7)	92 (41.8)	31 (50.8)	1		1	
Male	555 (59)	158 (56.3)	128 (58.2)	30 (48.2)	0.5 (0.3–1.9)	0.5	0.7 (0.3–1.8)	0.9
Diarrhea/days								
0	244 (25.9)	46 (16.3)	46 (20.9)	0	1		1	
1	**564 (59.9)**	**221 (78.6)**	**171 (77.7)**	**50 (81.9)**	**1.8 (1.1–2.3)**	**0.02**	**1.1 (1.0–2.7)**	**0.03**
2	**18** [2]	**13 (4.8)**	**3 (1.4)**	**10 (16.5)**	**2.0**	**0.001**	**1.3 (1.0–3.2)**	**0.003**
3 or more	115 (12.2)	1 (0.3)	0	1 (1.6)	0.3 (0.1–1.1)	0.5		
Fever (>38°C)								
No	173 (18.4)	37 (13.1)	32 (14.5)	5 (8.2)	1		1	
Yes	768 (81.6)	244 (86.9)	188 (85.5)	56 (91.8)	**1.9 (1.3–2.4)**	**0.01**	**1.5 (1.3–2.8)**	**0.03**
Vomit								
No	595 (63.2)	163 (58)	138 (62.7)	25 (40.9)	1		1	
Yes	**346 (36.8)**	**118** [42]	**82 (37.3)**	**36 (59.1)**	**0.001**	**0.001**	**1.8 (1.2–4.1)**	**0.003**
Abdominal pain								
No	206 (21.9)	41 (14.6)	34 (15.4)	7 (11.5)	1		1	
Yes	735 (78.1)	240 (85.4)	186 (84.6)	54 (88.5)	1.8 (0.3–1.4)	0.2	1.2 (0.5–2.1)	0.1
Dehydration								
No	863 (91.7)	263 (93.5)	207 (94)	56 (91.8)	1			
Yes	**78 (8.3)**	**18 (6.5)**	**13** [6]	**5 (8.2)**	**1.7 (1.2–3.8)**	**0.01**	**1.6 (1.3–3.1)**	**0.02**
Antibiotic use (days)								
No	93 (9.8)	23 (8.1)	20 [9]	3 (4.9)	1		1	
1	815 (86.6)	248 (88.2)	193 (87.7)	55 (90.2)	0.9 (0.5–3.9)	0.2	1.2 (0.7–1.8)	0.2
2	11 (1.3)	3 (1.2)	1 (0.5)	2 (3.3)	1.1 (0.4–3.5)	0.2	1.3 (0.7–1.7)	0.1
3 or more	**22 (2.3)**	**7 (2.5)**	**6 (2.8)**	**1 (1.6)**	**2.9 (1.5–4.2)**	**0.01**	**2.1 (2.0–5.2)**	**0.02**
Rotavirus								
Negative	760 (80.7)	232 (82.5)	173 (78.6)	59 (96.7)	1		1	
Positive	181 (19.3)	49 (17.5)	47 (21.4)	2 (3.3)	**1.1 (1.08–2.5)**	**0.05**	0.8 (0.6–1.2)	0.09
Adenovirus								
Negative	669 (71)	193 (68.6)	134 (60.9)	59 (96.7)	1		1	
Positive	272 [29]	88 (31.4)	86 (39.1)	2 (3.3)	0.6 (0.2–1.5)	0.1	0.9 (0.5–1.8)	0.1
Sapovirus								
Negative	876 (93)	250 (88.9)	194 (88.1)	56 (91.8)	1		1	
Positive	**65** [7]	**31 (11.1)**	**26 (11.9)**	**5 (8.2)**	**2.1 (1.3–4.8)**	**0.01**	**1.8 (1.3–3.2)**	**0.03**
Bocavirus								
Negative	818 (86.9)	235 (83.6)	181 (82.2)	54 (88.5)	1		1	
Positive	123 (13.1)	46 (16.4)	39 (17.8	7 (11.5)	1.8 (0.7–3.2)	0.5	1.3 (0.7–1.9)	0.7

The prevalence of norovirus GII found in our study was 29.8 % (281/941), this was distributed throughout almost the entire territory of Roraima, with the highest found in the Capital (Boa Vista) being 56.1 % (Fig. 3).

4. Clinical factors associated with the detection rate of norovirus GII

The table below presents data stratified by collection periods for better observation, however, univariate (OR) and multivariate (ORaj) analyzes were carried out together in both periods. These were carried out to assess which risk factors (clinical/epidemiological) were associated with the prevalence of GII norovirus. Climatic factors were not included in this analysis, as the statistical model used is different, as they rely on external factors and were evaluated weekly.

In Multivariate Analysis. The detection of norovirus GII was associated with the following clinical factors: Children <5 years old who had diarrhea in the first and two days, fever, vomiting and dehydration, 3 or more days duration of antibiotic use and even though viral co-infection rates were high, only in co-infection with sapovirus was significant (Table 3).

5. Discussion

Our study is of great importance as it helps in the correlation between the dynamics of norovirus infection and climatic factors in the tropical region, specifically in the Northwest of Amazon region of Brazil. From the data collected from the medical documentation, on average, the samples were collected on the second day of diarrhea.

It was demonstrated that the drop in temperature, humidity and wind speed were significantly correlated with the increase in norovirus GII throughout the study period. The drop in temperature and humidity were represented in Fig. 1, but although figures can be useful for visualizing data, in this case it was not visually applicable for wind speed.

The results of our study corroborate others around the world, which state the correlation between norovirus infection and climate variations. This indicates that changes, whether simple or more drastic, can change the dynamics of norovirus infection. Studies have already indicated that increased humidity relative can potentially facilitate virus transmission through aerosols [26]. One of the

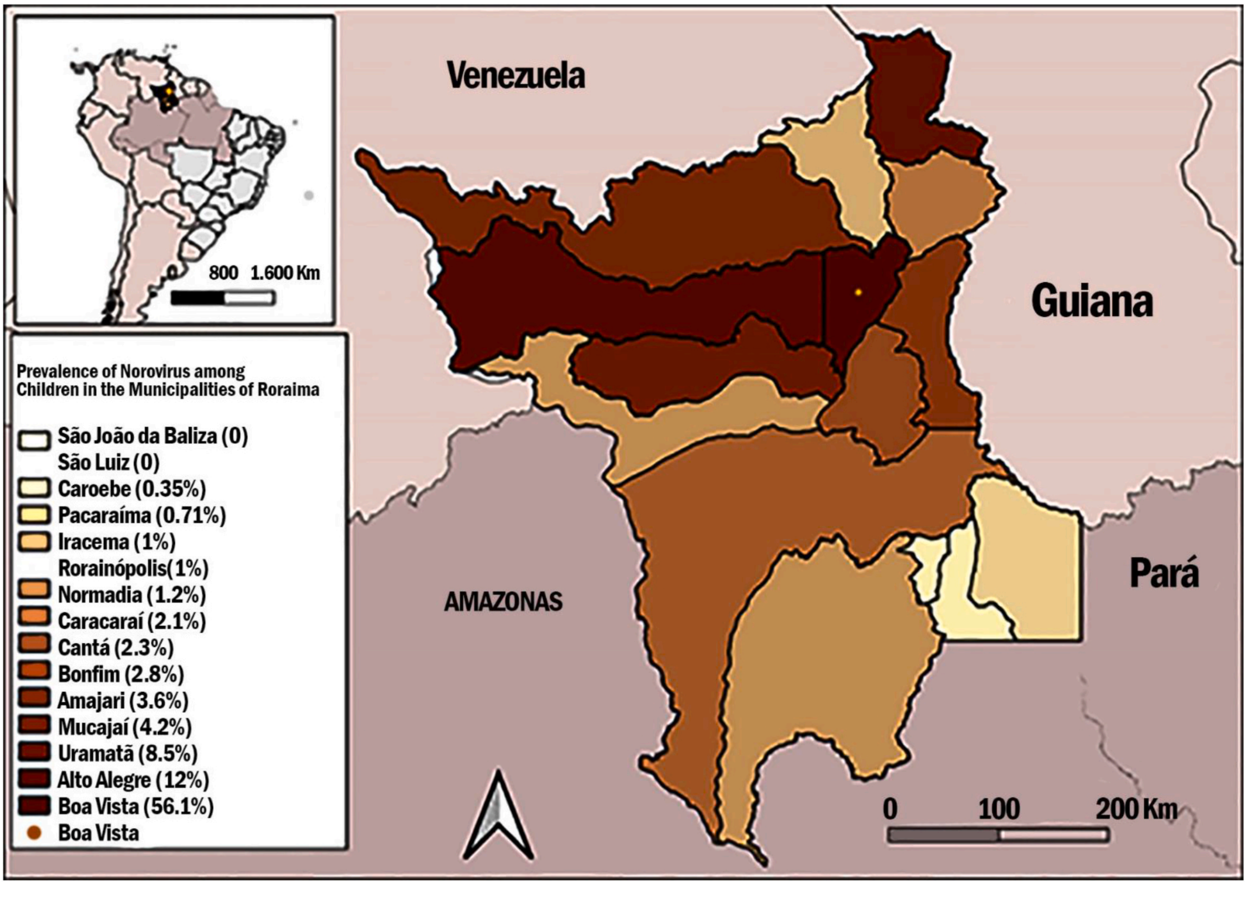

Fig. 3. Distribution of nororvirus prevalence in Municipalities in the Roraima (RR), Brazil. The prevalence of Norovirus is represented by the color changes on the map, where it goes from lighter to darker (higher prevalence) and the borders of the state of Roraima encompass other South American countries.

hypotheses is: During this period of greater humidity, transmission of the infection occurs and when there is a drop in the relative/absolute humidity of the air, this is when signs and symptoms appear (24/48 h after infection).Furthermore, there is evidence that cases in children may begin to rise earlier in the norovirus season than cases in adults [27]. Therefore, cases in children could provide an early warning of seasonal norovirus [28].

The other hypothesis is behavioral of the population: In Brazil, culturally, individuals tend to prioritize seeking health care after the rainy season (even if they already have symptoms), therefore the largest number of norovirus cases were detected during the drier period, this could be due to the difficulty in traveling in these more economically vulnerable regions.

The results demonstrated that the temperature limit for detecting norovirus was a maximum of 31.3 °C, as in this region the temperature does not vary as it occurs in temperate countries, the most observed climatic variation is the relative and absolute humidity of the air. Our data corroborate other studies around the world; a study showed that norovirus outbreaks had inverse linear associations with relative humidity [13]. According to a study carried out in Japan, a rapid decrease in humidity could be the cause of the increase in the incidence rate of norovirus [29]. Two studies conducted in South Korea also statistically reconfirmed the finding of strong negative correlations of humidity with norovirus outbreaks [30,31]. Another study in France tested this correlation experimentally [32].

One of the environmental factors most commonly cited as associated with rates of norovirus infection is temperature. Our study verified a negative correlation (the lower the temperature, the higher detection rate), indicating a possibly favorable physical environment for "virions". Similar results have already been verified in temperate climates [32–36], but more studies are needed to evaluate this association in tropical climates, since Roraima's thermal amplitude is small between the hot and colder seasons [19].

Another correlated climatic factor was wind speed, with a negative correlation, that is, the greater presence of smaller wind was the detection of NoV in this study. This data is interesting to discuss, however, it is not possible to state to a certain extent that wind speed is an independent factor (and not related to temperature or humidity, etc.), more studies are needed to confirm this over a longer period of time, as the external factors mentioned above in this case can influence. What we know is that norovirus transmission is considered common in closed environments, with crowds and poor ventilation, which in this case corroborates our negative correlation results. Furthermore, it is more common to find these viruses on contaminated surfaces, food or water [5,37].

In investigation of clinical factors with the prevalence of norovirus, individuals who had more than 1 day of diarrhea, fever, vomiting and dehydration, longer duration of antibiotic use and coinfection with sapovirus were more likely to have norovirus.

In Brazil, according to the Management of Patients with Diarrhea, treatment with antibiotics should only be reserved for cases with the presence of blood or mucus in the stool (dysentery) and compromised general condition or severe dehydration, always with medical supervision [38], however, it is common in several countries that antibiotics have been administered or prescribed for the majority of non-dysenteric cases [39]. In this study we observed that longer use of antibiotics was an associated with higher prevalence of norovirus. This data is relevant as little is discussed about the misuse of antibiotics for viral infections. It is known that there is an increasing rapid emergence of multi-resistant and pan-resistant bacteria, making it necessary to implement clearer protocols and recommendations in case of viral infection [39,40].

The Brazilian Amazon region presents a typical and favorable scenario for the persistence, expansion and distribution of viral gastroenteritis. Advances have been made in relation to the coverage of drinking water supply and sanitation in the country; however, many children still die as a result of viral gastroenteritis [41]. This is mainly due to socioeconomic disparities found in the Amazonian region that are noticeable in some municipalities in Roraima. Despite the various studies conducted in the Amazon region [42] there is still much to learning partially the relationship between man, health and the environment, as the occurrence of childhood diarrheal diseases is partly associated with socioeconomic conditions, coverage of basic sanitation services, infrastructure and health.

Describing that the results presented, despite preliminary and limitations, provide important evidence about the prevalence of gastroenteric viruses in a region with a tropical climate, but with particularities due to being located in a region with unique characteristics such as the Amazon region and serve as a basis for future expanded studies in this region, Brazil and in Latin American countries about the epidemiological importance, seasonality, climate change, antigenic diversity among other factors in the circulation of gastroenteric viruses, mainly in relation to vaccination coverage for rotavirus A and the eventual and potential introduction of new vaccines, such as for norovirus. According to data from the "Brazilian National Immunization Program Information System", the vaccination coverage rate for rotavirus in the studied region was 84.6 %, 96.5 % and 59.2 % in 2016, 2017 and 2021 respectively. This decrease in the vaccination coverage rate occurred generally in Brazil after the COVID 19 pandemic [43].

Implications and limitations

Studies on climate variables and health have become increasingly important, as climate risks are correlated with infectious diseases through issues such as: warming, precipitation, floods, droughts, storms, land cover change, oceanic climate change, fires, waves of heat and sea level that cause the high number of pathogenic diseases and different possibilities of transmission to increase or change is known behavior. Extreme events introduce considerable fluctuation that can affect the dynamics of waterborne diseases, such as noroviruses.

The samples in this study were collected in these periods, according to the availability of collections in a region of difficult access in the Amazon region, later (between 2018 and 2020) access was even more restricted due to the pandemic caused by the new coronavirus (COVID19), interrupting the collection period. We carried out analyzes separately before combining the two periods in univariate analysis, but there was no difference in the multivariate results However, we found it important to include the 2021 results in the article even with a more restricted period.

Our study had some limitations such as: Short collection period, and few genotyped samples (~30 % of positive samples). Despite these limitations and the importance of environmental variables for the control of viral gastroenteritis, there is a lack of comprehensive investigation in tropical regions which complicates the identification of environmental indicators for norovirus outbreaks.

Ethical statement

This study was approved by the Research Ethics Committee of the Federal University of Roraima (CEP nº: 1,333,480 of November 23, 2015). After an informed consent, the form was filled out and signed by the parents or guardians. Explicitly state information consent obtained from the participants was written.

Data availability statement

The information used in the analysis, such as personal, socioeconomic and epidemiological data combines confidential information in accordance with the Informed Consent Form signed by the research participants (as described in the article). The use of data obtained in the research will only be used for the linked study, which must be kept confidential, in accordance with the terms of resolution 466/12 of the National Health Council of Brazil. The data is physically stored in a confidential database and, due to security considerations, the data cannot be transferred to researchers not linked to this study.

The public data from this research are already published from this research and are the sequences of the amplified genomes. All consequences involved in this work were deposited on the genbank platform. Search for Pimenta Y (author).

CRediT authorship contribution statement

Nathália Alves Araujo de Almeida: Writing – review & editing, Writing – original draft, Validation, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Yan Cardoso Pimenta:** Writing – review & editing, Methodology, Data curation. **Flavia Freitas de Oliveira Bonfim:** Writing – review & editing, Methodology. **Nicole Carolina Araujo de Almeida:** Methodology. **José Paulo Gagliardi Leite:** Writing – review & editing, Validation, Methodology, Conceptualization. **Alberto Ignacio Olivares Olivares:** Methodology, Data curation. **Johan Nordgren:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology. **Marcia Terezinha Baroni de Moraes:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors have no conflicts of interest to declare.

Acknowledgments

We are grateful for financial support from the Coordination for the Improvement of Higher Education Personnel (CAPES) "Programa de Professor Visitante no Exterior-Edital no.01/2019-Processo 88881.337140/2019-01"; The National Council for Scientific and Technological Development–CNPq number 424376/2016-4 and CNPq/Decit/SCTIE/MS nº 49/2022; Foundation for Research Support of the State of Rio de Janeiro-FAPERJ "Edital Carlos Chagas Filho" and Oswaldo Cruz Institute-IOC (PAEF). To Thiago Rios for the graphic treatment of the figures. The authors acknowledge all children and their parents for making this study possible. To Isabelle Baroni de Moraes e Souza and Professor Johan Nordgren for the English revision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35463.

References

[1] K. Bányai, M.K. Estes, V. Martella, U.D. Parashar, Viral gastroenteritis, Lancet 392 (10142) (2018 Jul) 175–186.
[2] A.K. Leung, K.L. Hon, Paediatrics: how to manage viral gastroenteritis, Drugs Context 10 (2021 Mar 26) 1–11.
[3] C.M. Chow, Acute gastroenteritis: from guidelines to real life, Clin. Exp. Gastroenterol. 97 (2010 Jul).
[4] K.B. Carlson, A. Dilley, T. O'Grady, J.A. Johnson, B. Lopman, E. Viscidi, A narrative review of norovirus epidemiology, biology, and challenges to vaccine development, NPJ Vaccines 9 (1) (2024 May 29) 94.
[5] S.M. Ahmed, A.J. Hall, A.E. Robinson, L. Verhoef, P. Premkumar, U.D. Parashar, et al., Global prevalence of norovirus in cases of gastroenteritis: a systematic review and meta-analysis, Lancet Infect. Dis. 14 (8) (2014 Aug) 725–730.
[6] B.A. Lopman, D. Steele, C.D. Kirkwood, U.D. Parashar, The vast and varied global burden of norovirus: prospects for prevention and control, PLoS Med. 13 (4) (2016 Apr 26) e1001999.
[7] G. Capece, E. Gignac, Norovirus, 2023.
[8] M. de Graaf, J. van Beek, M.P.G. Koopmans, Human norovirus transmission and evolution in a changing world, Nat. Rev. Microbiol. 14 (7) (2016 Jul 23) 421–433.
[9] Genus: Norovirus | ICTV [Internet]. [cited 2023 Dec 5]. Available from: https://ictv.global/report/chapter/caliciviridae/caliciviridae/norovirus.
[10] ICTV, International Committee on Taxonomy of Viruses, 2022.

[11] A.I.O. Olivares, G.A.A. Leitão, Y.C. Pimenta, C.P. Cantelli, T.M. Fumian, A.M. Fialho, et al., Epidemiology of enteric virus infections in children living in the Amazon region, Int. J. Infect. Dis. 108 (2021 Jul) 494–502.

[12] A.W. Mounts, T. Ando, M. Koopmans, J.S. Bresee, J. Noel, R.I. Glass, Cold weather seasonality of gastroenteritis associated with norwalk-like viruses, J. Infect. Dis. 181 (s2) (2000 May) S284–S287.

[13] B. Lopman, B. Armstrong, C. Atchison, J.J. Gray, Host, weather and virological factors drive norovirus epidemiology: time-series analysis of laboratory surveillance data in england and wales, PLoS One 4 (8) (2009 Aug 24) e6671.

[14] J.M. Hernandez, L.D. Silva, E.C.S. Junior, R.S. Bandeira, E.A.M. Rodrigues, M.S.S. Lucena, et al., Molecular epidemiology and temporal evolution of norovirus associated with acute gastroenteritis in Amazonas state, Brazil, BMC Infect. Dis. 18 (1) (2018 Dec 2) 147.

[15] R.D. van Gaalen, J. van de Kassteele, S.J.M. Hahné, P. Bruijning-Verhagen, J. Wallinga, Determinants of rotavirus transmission: a lag nonlinear time series analysis, Epidemiology 28 (4) (2017 Jul) 503–513.

[16] T. Beck-Friis, N. Sundell, L. Gustavsson, M. Lindh, J. Westin, L.M. Andersson, Outdoor absolute humidity predicts the start of norovirus GII epidemics, Microbiol. Spectr. 11 (2) (2023 Apr 13).

[17] A. Dimitriadis, J.A. Marshall, Evaluation of a commercial enzyme immunoassay for detection of norovirus in outbreak specimens, Eur. J. Clin. Microbiol. Infect. Dis. 24 (9) (2005 Sep 23) 615–618.

[18] L.D. Bruggink, J.A. Marshall, Molecular and epidemiological features of GIIb norovirus outbreaks in Victoria, Australia, 2002–2005, J. Med. Virol. 81 (9) (2009 Sep 22) 1652–1660.

[19] Instituto Nacional de Meteorologia - INMET [Internet]. [cited 2023 Dec 5]. Available from: https://portal.inmet.gov.br/normais.

[20] Brazil - State Foundation for the Environment and Water Resources. El Niño Phenomenon, Which Reduces Rainfall and Intensifies Heat, Also Facilitating the Spread of Fires, State Foundation for the Environment and Water Resources, 2016.

[21] Brazil - Climatology | Climate Change Knowledge Portal [Internet]. [cited 2023 Dec 5]. Available from: https://climateknowledgeportal.worldbank.org/country/brazil/climate-data-historical.

[22] T. Kageyama, S. Kojima, M. Shinohara, K. Uchida, S. Fukushi, F.B. Hoshino, et al., Broadly reactive and highly sensitive assay for norwalk-like viruses based on real-time quantitative reverse transcription-PCR, J. Clin. Microbiol. 41 (4) (2003 Apr) 1548–1557.

[23] S.Q. Zeng, A. Halkosalo, M. Salminen, E.D. Szakal, L. Puustinen, T. Vesikari, One-step quantitative RT-PCR for the detection of rotavirus in acute gastroenteritis, J Virol Methods 153 (2) (2008 Nov) 238–240.

[24] J.M. Fioretti, M.S. Rocha, T.M. Fumian, A. Ginuino, T.P. da Silva, M.R. de Assis, et al., Occurrence of human sapoviruses in wastewater and stool samples in Rio De Janeiro, Brazil, J. Appl. Microbiol. 121 (3) (2016 Sep) 855–862.

[25] T. Oka, K. Katayama, G.S. Hansman, T. Kageyama, S. Ogawa, F. Wu, et al., Detection of human sapovirus by real-time reverse transcription-polymerase chain reaction, J. Med. Virol. 78 (10) (2006 Oct 22) 1347–1353.

[26] J. Rohayem, Norovirus seasonality and the potential impact of climate change, Clin. Microbiol. Infection 15 (6) (2009 Jun) 524–527.

[27] H. Bernard, M. Höhne, S. Niendorf, D. Altmann, K. Stark, Epidemiology of norovirus gastroenteritis in Germany 2001–2009: eight seasons of routine surveillance, Epidemiol. Infect. 142 (1) (2014 Jan 21) 63–74.

[28] A.L. Donaldson, J.P. Harris, R. Vivancos, S.J. O'Brien, Can cases and outbreaks of norovirus in children provide an early warning of seasonal norovirus infection: an analysis of nine seasons of surveillance data in England UK, BMC Publ. Health 22 (1) (2022 Dec 20) 1393.

[29] S. Inaida, Y. Shobugawa, S. Matsuno, R. Saito, H. Suzuki, The South to north variation of norovirus epidemics from 2006–07 to 2008–09 in Japan, PLoS One 8 (8) (2013 Aug 19) e71696.

[30] Y.S. Kim, K.H. Park, H.S. Chun, C. Choi, G.J. Bahk, Correlations between climatic conditions and foodborne disease, Food Res. Int. 68 (2015 Feb) 24–30.

[31] J.H. Kim, D.H. Lee, Y. Joo, K.D. Zoh, G. Ko, J.H. Kang, Identification of environmental determinants for spatio-temporal patterns of norovirus outbreaks in Korea using a geographic information system and binary response models, Sci. Total Environ. 569–570 (2016 Nov) 291–299.

[32] A. Colas de la Noue, M. Estienney, S. Aho, J.M. Perrier-Cornet, A. de Rougemont, P. Pothier, et al., Absolute humidity influences the seasonal persistence and infectivity of human norovirus, Appl. Environ. Microbiol. 80 (23) (2014 Dec) 7196–7205.

[33] S.J. Kim, J. Si, J.E. Lee, G. Ko, Temperature and humidity influences on inactivation kinetics of enteric viruses on surfaces, Environ. Sci. Technol. 46 (24) (2012 Dec 18) 13303–13310.

[34] S.J. Lee, J. Si, H.S. Yun, G. Ko, Effect of temperature and relative humidity on the survival of foodborne viruses during food storage, Appl. Environ. Microbiol. 81 (6) (2015 Mar 15) 2075–2081.

[35] L. Yang, S. Shi, C. Na, B. Li, Z. Zhao, T. Yang, et al., Rotavirus and norovirus infections in children under 5 Years old with acute gastroenteritis in southwestern China, 2018–2020, J Epidemiol Glob Health 12 (3) (2022 Jul 20) 292–303.

[36] T. Beck-Friis, N. Sundell, L. Gustavsson, M. Lindh, J. Westin, L.M. Andersson, Outdoor absolute humidity predicts the start of norovirus GII epidemics, Microbiol. Spectr. 11 (2) (2023 Apr 13).

[37] S. Duret, R. Pouillot, W. Fanaselle, E. Papafragkou, G. Liggans, L. Williams, et al., Quantitative risk assessment of norovirus transmission in food establishments: evaluating the impact of intervention strategies and food employee behavior on the risk associated with norovirus in foods, Risk Anal. 37 (11) (2017 Nov) 2080–2106.

[38] Manejo do paciente com diarreia: avaliação do estado de hidratação do paciente (arquivo com marcas de corte) — Ministério da Saúde [Internet]. [cited 2023 Dec 5]. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/svsa/doencas-diarreicas-agudas/manejo-do-paciente-com-diarreia-avaliacao-do-estado-de-hidratacao-do-paciente-arquivo-com-marcas-de-corte/view.

[39] J.A. Lewnard, McQuade Rogawski Et, J.A. Platts-Mills, K.L. Kotloff, R. Laxminarayan, Incidence and etiology of clinically-attended, antibiotic-treated diarrhea among children under five years of age in low- and middle-income countries: evidence from the Global Enteric Multicenter Study, PLoS Negl Trop Dis 14 (8) (2020 Aug 10) e0008520.

[40] N. Khardori, C. Stevaux, K. Ripley, Antibiotics: from the beginning to the future: Part 2, Indian J. Pediatr. 87 (1) (2020 Jan 5) 43–47.

[41] J.L. Duarte, F.A. Diaz-Quijano, A.C. Batista, A.F. Duarte, L.A.K. Melchior, L.L. Giatti, Climate variability and hospitalizations for infectious diarrheal diseases in a municipality in the Brazilian Western Amazon, Cien Saude Colet 24 (8) (2019 Aug) 2959–2970.

[42] K.S. Imada, TS de Araújo, P.T. Muniz, VL de Pádua, Socioeconomic, hygienic, and sanitation factors in reducing diarrhea in the Amazon, Rev. Saude Publica 50 (0) (2016).

[43] Brazil, National immunization program information system (SI-PNI/CGPNI/DEIDT/SVS/MS). Brazil, https://infoms.saude.gov.br/extensions/SEIDIGI_DEMAS_VACINACAO_CALENDARIO_NACIONAL_MENU_COBERTURA/SEIDIGI_DEMAS_VACINACAO_CALENDARIO_NACIONAL_MENU_COBERTURA.html, 2024.