

Población y Salud en Mesoamérica

Statistical control charts to assess the incidence of presumably infectious diarrhea reported between 2009 and 2019 in children under 4 years of age in the macro regions of Araçatuba, Marília and Presidente Prudente, São Paulo, Brazil.

Suelen Navas-Úbida y Rogério Giuffrida

Como citar este artículo:

Navas-Úbida, S. y Giuffrida, R. (2021). Statistical control charts to assess the incidence of presumably infectious diarrhea reported between 2009 and 2019 in children under 4 years of age in the macro regions of Araçatuba, Marília and Presidente Prudente, São Paulo, Brazil. *Población y Salud en Mesoamérica, 19*(1). Doi: 10.15517/psm.v19i2.47011



ISSN-1659-0201 http://ccp.ucr.ac.cr/revista/

Revista electrónica semestral <u>Centro Centroamericano de Población</u> <u>Universidad de Costa Rica</u>

Statistical control charts to assess the incidence of presumably infectious diarrhea reported between 2009 and 2019 in children under 4 years of age in the macro regions of Araçatuba, Marília and Presidente Prudente, São Paulo, Brazil.

Gráficos de control estadístico para evaluar la incidencia de diarrea presumiblemente infecciosa notificada entre 2009 y 2019 en niños menores de 4 años en las macro regiones de Araçatuba, Marília y Presidente Prudente, São Paulo, Brasil.

Suelen Navas-Úbida¹ y Rogério Giuffrida²

Resumen: Objective. To evaluate the monthly rates of hospitalizations for childhood diarrhea in macroregions of Araçatuba, Marília and Presidente Prudente, SP, between 2019 -June Between June 2009. **Methods.** The average rates and their standard deviations for admission of diarrhea in the target population were obtained from DATASUS and standardized for cases x 100,000 inhabitants. Confidence limits were established, occurrences above confidence limits were considered epidemic events. The normality of the data and serial autocorrelation were tested using the Shapiro-Wilk and Durbin-Watson method. **Results.** All methods detected epidemic occurrences in the three regions. Araçatuba and Marília, the peaks were concentrated in the first half of the decade and Presidente Prudente, close to the middle. The CUSUM method was more sensitive to detect epidemic periods, however the normality data and assumptions have been violated by serial autocorrelation in a few months. The EWMA method was considered the most appropriate. **Conclusions**. Statistical process control charts can be used to monitor and compare disease incidence between different regions.

Keywords: diarrheal diseases, sanitation, children, temporal analysis.

Resumen: Objetivo. Evaluar las tasas mensuales de hospitalizaciones por diarrea infantil en las macrorregiones de Araçatuba, Marília y Presidente Prudente, SP, entre entre Junio 2009 -Junio 2019. **Métodos**. Las tasas medias y sus desviaciones estándar de ingreso de diarrea en la población diana se obtuvieron de DATASUS y se estandarizaron para casos x 100.000 habitantes. Se establecieron límites de confianza, las ocurrencias por encima de los límites de confianza se consideraron eventos epidémicos. La normalidad de los datos y la autocorrelación en serie se probaron utilizando el método de Shapiro-Wilk y Durbin-Watson. **Resultados**. Todos los métodos detectaron ocurrencias epidémicas en las tres regiones. Araçatuba y Marília, los picos se concentraron en la primera mitad de la década y Presidente Prudente, cerca de la mitad. El método CUSUM fue más sensible para detectar períodos epidémicos, sin embargo, los datos de normalidad y los supuestos han sido violados por la autocorrelación en serie en unos pocos meses. El

¹ Universidade do Oeste Paulista (UNOESTE), Limoeiro, Presidente Prudente, BRASIL. Correo electrónico: <u>suellen ubida@hotmail.com</u>. ORCID: https://orcid.org/0000-0002-7483-1486

²Universidade do Oeste Paulista (UNOESTE), Limoeiro, Presidente Prudente, BRASIL. Correo electrónico: <u>rgiuffrida@unoeste.br.</u> ORCID: https://orcid.org/0000-0002-2380-4349

método EWMA se consideró el más apropiado. **Conclusiones**. Los gráficos de control de procesos estadísticos se pueden utilizar para monitorear y comparar la incidencia de enfermedades entre diferentes regiones.

Palabras clave: enfermedades diarreicas, saneamiento, ninõs, análisis temporal.

Recibido: 01 oct, 2020 | Corregido: 30 abr, 2021 | Aceptado: 07 may, 2021

1. Introduction

Diarrheal diseases are highly prevalent in the human population. It is estimated that approximately 1.4 million people worldwide are killed by diarrheal diseases, including 500,000 children under five years old (Troeger et al., 2017). In children, the disease can trigger important consequences, such as poor weight development and cognitive deficits (Troeger et al., 2018).

In Brazil, childhood diarrhea is related to several infectious viruses, among those we highlight Norovirus GII Adenovirus and Rotavirus. In addition to viruses, colibacillary syndromes are common due to enteropathogenic, verotoxygenic, enteropathogenic and enteroaggregative Escherichia coli virotypes (Lima et al., 2019). Despite the multiplicity of agents, this infection has shown a significant decrease in Latin America and Brazil in recent decades, mainly because of systematic vaccination campaigns against Rotavirus in children under 5 years old (Baker & Alonso, 2018). However, the incidence is still high in vulnerable populations of some regions in Brazil (Fontoura et al., 2018).

The most cases of childhood diarrhea are closely related to environmental sanitary conditions. In Brazil, the disease presents peaks in the rainy season when the humidity and warm climate favor the dispersion of infectious and parasitic agents (Fonseca, Hacon, Reis, Costa, & Brown, 2016). In vulnerable populations, the disease is associated to the lack of food security, polluted water and poor hygiene in vulnerable populations (Mbuya & Humphrey, 2016).

Among the bacterial agents commonly seen in children, the one from the genus Salmonella have been increasing over time in Brazil. For instance, the non tifoidais species that are multidrug resistance to antibiotics (Reis et al., 2018). Children in socially vulnerable situations are more susceptible to colonization by Salmonella sp (Mello et al., 2018). In some regions of Brazil, Salmonella and the Enteretidis serotype (Assis et al., 2014) have been identified as the cause for diarrhea in children and commonly associated with intake of poultry products. Pathogens associated with childhood diarrheal diseases can occur in relatively stable annual or biannual cycles (Chao, Roose, Roh, Kotloff, & Proctor, 2019). However, approaches supported by temporal models to predict disease outbreaks are poorly studied. Among the tools potentially employed for the prediction of outbreaks, the control diagrams stand out. These diagrams are based on the statistical control of industrial processes, a methodology that works with the periodic recording of events, establishing upper and lower limits to classify an event within the normal range.

This process has been adapted to the epidemiology, so that when an event exceeds the upper or lower limit, it is considered an occurrence outside of expected patterns. In the case of epidemiological events, the upper limits are recognized as cutoffs to consider the existence of an anomaly, such as an outbreak or epidemic (Woodall, 2006). Once the cutoff is established, the diagram must have high sensitivity to reduce the rate of false-positive alarms. Similarly, it must be specific enough to do not mislead the detection of disease outbreaks (false positive) (Gandy & Lau, 2013).

The three main methods for the preparation of control charts are the cumulative tabular sum (CUSUM), the Shewhart method and the exponentially weighted moving average (EWMA) (Gomes, Mingoti, & Oliveira, 2011). Here, we aimed to evaluate the performance of the three methods on detecting diarrheal hospital outbreaks in children under four years old.

2. Methodology

2.1 Focus and study population

An analytical and descriptive study was conducted with secondary data on childhood diarrhea reported between June 2009 and June 2019 in the macroregions of Araçatuba, Marília and Presidente Prudente, São Paulo. These macroregions was selected in order to similar physical, climatic, economic and social characteristics, spatial continuity between them and high infant mortality rates, in comparison to the other mesoregions (Mendes, 2009).

The study population consisted of children aged no more than four years old hospitalized with presumably infectious diarrhea (viral or bacterial etiology) and paratyphoids (salmonellosis). Considering that are secondary and collective data notifications, compiled the DATASUS database (Brasil-Ministério da Saúde), 2019), it was not necessary consent or confidentiality term.

2.2 Data collect and analysis.

Raw data were obtained with the TabWin Program for local analysis by Notification System database DATASUS diseases. The TabWin allows the import of tabs that can be compiled and analyzed in other programs. Datasets about hospital morbidity due to presumably infectious diarrhea and paratyphoids (salmonellosis) were selected in the age group of up to 4 years of age in the three macroregions of the study. Because presumably infectious diarrhea can include unconfirmed cases of salmonellosis, we use the sum of reported cases to analyze a single index.

The data were standardized per 100 thousand inhabitants using the direct method. The average rate, median, minimum and maximum values were estimated for each mesoregion and the data were submitted to Kolmogorov-Smirnov test for normality. Serial autocorrelation between data was assessed by the Durbin-Watson test, for each mesoregion. Standardized rates of childhood diarrhea were modeled in a time series based on the generalized linear model using a scale factor (quasi-Poisson) to control data overdispersion.

We used control charts as statistical tools to study and control sequential processes. In the case of epidemiology, these graphs are used to control epidemic adverse events that are included in so-called control limits. These limits define a normal region for the events (or their average) in which are considered under control (Woodall, 2006).

The Shewhart control chart is the simplest and most common of the methods studied. However, it presents low sensitivity to detect subtle changes. In this study, this graph was built using the complete series of observations to estimate the limits, assuming a normal distribution of the variable of interest (Abujiya, Riaz, & Lee, 2013). In the Shewhart chart, the lower limits (LCL), central line (CL) and upper limit (UCL) are calculated by:

$$LCL = \bar{x} - z_{\alpha/2} \frac{\overline{MR}}{1.128}$$
$$CL = \bar{x}$$
$$UCL = \bar{x} + z_{\alpha/2} \frac{\overline{MR}}{1.128}$$

Where \bar{x} is the mean value of events, $z_{\alpha/2}$ is the standardized value of the normal distribution to control the rate of false positive alarms and $\frac{\overline{MR}}{128}$ is the standard deviation (sd) of the data calculated using a method based on the scaled mean of moving ranges. This procedure is frequently used for data that may have severe deviations able to inflate the sample standard deviation, which will

increase the control limits and possibly hide individual deviations within the limits (Benneyan, 2003). We adopted sd = 3, which under the normal distribution corresponds to a false alarm rate of 0.27%.

The Cumulative Sum Control Chart (CUSUM) was developed to detect small changes in the process mean. It is more sensible than the Shewhart chart because it incorporates all the information from a historical series of data. Although, to plot this graph, it is necessary to set a predetermined target value, typically the mean of the process under control. The following step is obtained for each deviation from the target value, the weighting also for having the same weight. To prepare this graph, the variables were scaled by the formula Z-score.

The CUSUM chart is sensitive to changes in the average of the epidemiological event of interest. When the mean increases, the cumulative sum of C increases and when it decreases, the amount of C decreases. It must take assumptions: normal distribution of data and independence of events, the latter rarely observed in epidemiological events (O'Brien, 1997). The upper (Ci +) and lower (Ci-) CUSUM limits are calculated respectively as:

Ci + = max [0, x_i- (\bar{x}_0 + k) + Ci-1 +] Ci - = max [0, (\bar{x}_0 - k)- xi + Ci-1 -] with the starting value Ci + = Ci - = 0.

In the equation, k is a reference value (also called tolerance value), being approximately half of the standardized target value, being specified in "sigma" units. We adopted k=0.5 which is equivalent to detecting a deviation of 1 sigma.

The lower and upper limits of the CUSUM control table are determined using a parameter h, which corresponds to the number of standard deviations that Ci + and CI- can be exceeded to classify the process as out of control. For the analysis, h = 5 was adopted.

Similar to CUSUM, the EWMA chart is able to detect small changes in the process average. However, by means of the EWMA chart, we can model autocorrelated data and there is no need to assume independence between the observations of the sample. The EWMA method is more robust to the assumption of non-normality than Shewhart and CUSUM (Montgomery, 2018). The graph is controlled by two parameters: an arbitrary value λ , which represents the weight given to the most recent average and must satisfy $0 < \lambda \leq 1$, and, L, a multiple of the standard deviation that establishes the control limits. We adopted $\lambda = 0.3$, and L = 3 to allow comparisons with the Shewhart graph. The lower control limit (LCL) and the upper (UCL) were calculated as:

$$LCL = \mu_0 - 3 \frac{\sigma}{\sqrt{n}} \sqrt{\frac{\lambda}{2 - \lambda} [1 - (1 - \lambda)^{2t}]}$$
$$UCL = \mu_0 + 3 \frac{\sigma}{\sqrt{n}} \sqrt{\frac{\lambda}{2 - \lambda} [1 - (1 - \lambda)^{2t}]}$$

The graphics have been compared for the occurrence of abnormal events by sensitizing rules (Montgomery, 2018)

- a. one or more points outside the control limit;
- b. two or three consecutive points outside the two σ alert limits;
- c. four or five consecutive points beyond the limits of a σ ;
- d. a sequence of eight consecutive points on the same side of the center line;
- e. six points in an ever increasing or decreasing sequence;
- f. fifteen points in a row in zone C (one σ), both above and below the central line;
- g. fourteen points in a sequence alternating up and down;
- h. eight points in a sequence on both sides of the center line with none in zone C (one σ);
- i. an unusual or non-random pattern of data.

3. Results

We evaluated 120 monthly records of diarrhea in children aged less than 4 years between 2009 and 2019. The average monthly rate of cases per 100,000 children was similar to the average in the three regions, indicating that the variable distribution is relatively symmetric. However, only the rates recorded in the mesoregion of Presidente Prudente presented parametric distribution (Table 1).

Table 1

Statistical parameters of the mesoregions included in the study (2009-2019).

Mesorregion	Ν	Mean	Median	Sd	Min.	Max.	KS test	DW
Araçatuba	120	22.2	15.9	15.8	0.09	131.7	0.001	0.058
Marília	120	17.7	15.2	11.2	0	121.8	0.004	<0.001
Presidente Prudente	120	21.2	18.5	12.1	0.02	71.0	0.395	0.004

Sd= standard deviation; **Min**= minimum value; **Max**= maximum value; **KS test**= Kolmogorov-Smirnov test; **DW**= Durbin-Watson test.

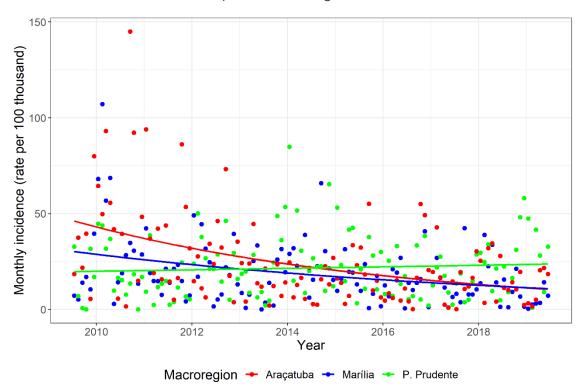
Source: own elaboration, 2020.

The Durbin-Watson test indicated significant serial autocorrelation in monthly rates for the mesoregions of Marília and Presidente Prudente. Thus, the incidence rates in these regions violated the assumptions Graphics Shewhart and CUSUM.

Figure 1 shows the Incidence per 100,000 cases/month in 2009-2019 for the regions of Araçatuba, Marília and Presidente Prudente. The lines represent the values predicted by the linear model using the quasi-Poisson regression.

Figure 1

Incidence per 100,000 cases/month in 2009-2019 for the regions of Araçatuba, Marília and Presidente Prudente. The lines represent the values predicted by the linear model using the quasi-Poisson regression.



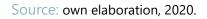
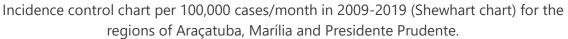
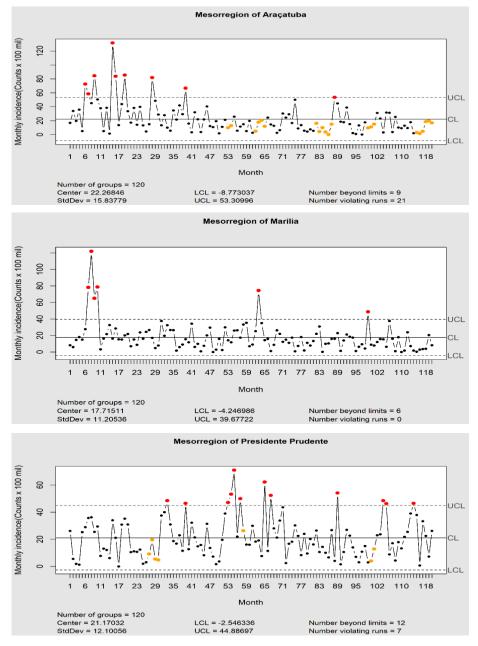


Figure 2 shows the Shewhart chart for the three mesoregions, where 9, 6,12 events that exceeded the control limits were detected for mesoregions Aracatuba, Marília and Presidente Prudente, respectively. In the region of Araçatuba, adverse events were concentrated at the beginning of the period studied. This was also observed for the region of Marilia, yet the number of events was lower than the number of events observed in Aracatuba. In Presidente Prudente, adverse events were observed mainly in the second half of the decade evaluated.

Figure 2





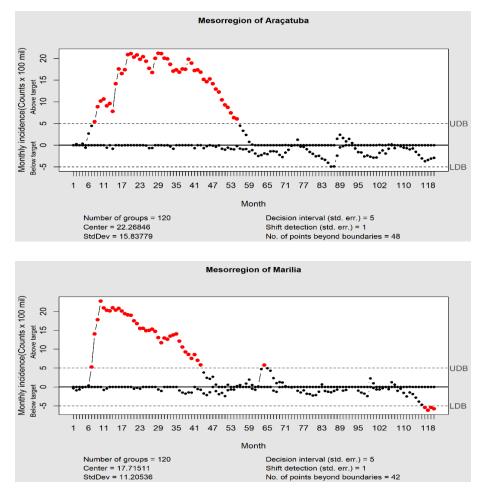
UCL = upper control limit; CL = control limit; LCL = lower control limit

Source: own elaboration, 2020.

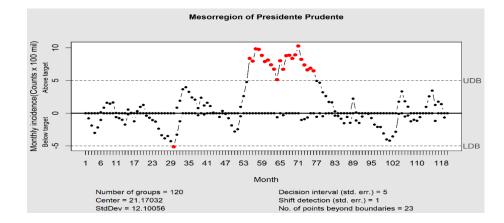
The Cumulative Sum Control Charts for the three mesoregions are shown in Figure 3. The graphs suggest that the incidence rate remained under control for the three mesoregions until the 8th, 7th and 55th months, for Araçatuba and Marília, and Presidente Prudente, respectively. The incidence exceeds the limits for persistent periods exceeding 20 months. There was a significant decrease in the last four months in the mesoregion of Marília.

Figure 3

Graph of incidence control per 100,000 case/month in 2009-2019 (CUSUM chart) of the mesoregions of Araçatuba, Marília and Presidente Prudente.



Continúa...

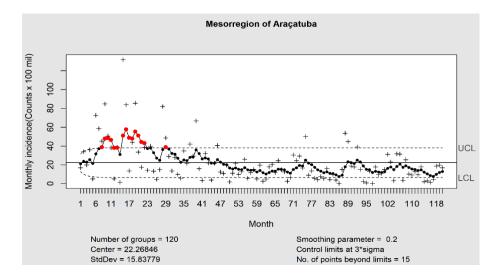


Source: own elaboration, 2020.

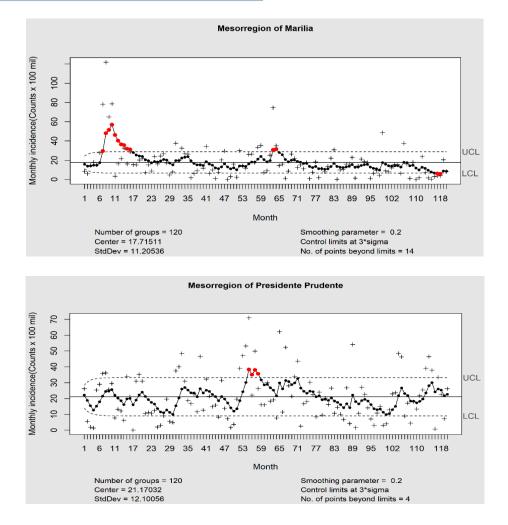
In Figure 4, the EWMA chart for the three mesoregions present events that exceeded the control limits at the beginning of the decade in the mesoregions of Araçatuba and Marília. The chart also showed sufficient sensitivity to detect four epidemic events in half of the decade in Presidente Prudente.

Figure 4

Incidence control chart per 100,000 cases/month in 2009-2019 (EWMA chart) for the Araçatuba, Marília and Presidente Prudente mesoregions.



Continue...



Source: own elaboration, 2020.

The prediction of abnormal events by the sensitivity rules for the three mesoregions is described in table 2. It was not possible to verify the compliance of all the described rules, since some require limits corresponding to one, two and three standard deviations around the mean. We believe that this process is more suitable for parametric Shewhart-type graphs, which consider a parametric distribution of data.

Table 2

Occurrence of abnormal events by sensitizing rules (Montgomery, 2018), in the three mesoregions assessed, according to the type of control chart adopted.

	Mesorregion									
Role		Araçatuba			Marilia			P. Prudente		
	Sh	CS	Ew	Sh	CS	Ew	Sh	CS	Ew	
One or more points outside the control limit		Ρ	Ρ	Ρ	Ρ	Ρ	Ρ	Ρ	Ρ	
Two or three consecutive points outside the two σ alert limits		Ρ	Ρ	Ρ	Ρ	Ρ	Ρ	Ρ	Ρ	
Four or five consecutive points beyond the limits of a $\boldsymbol{\sigma}$		Ρ	Ρ	Ρ	Ρ	Ρ	A	Ρ	Ρ	
A sequence of eight consecutive points on the same side of the center line		Ρ	Ρ	A	Ρ	Ρ	A	Ρ	A	
Six points in an ever increasing or decreasing sequence		Ρ	A	A	Ρ	A	A	Ρ	A	
Fifteen points in a row in zone C (one σ), both above and below the central line		NA	NA	NA	NA	NA	NA	NA	NA	
ourteen points in a sequence alternating up nd down		A	A	A	A	A	A	A	A	
Eight points in a sequence on both sides of the center line with none in zone C (one σ)		NA	NA	NA	NA	NA	NA	NA	NA	
An unusual or non-random pattern of data		Ρ	Ρ	Ρ	Ρ	Ρ	А	Ρ	А	
Sh = Shewhart chart; CS = CUSUM chart; Ew = EWMA chart; P = present; A = absent; NA = not										

applicable.

Source: own elaboration, 2020.

4. Discussion

Effective epidemiological surveillance systems are crucial for early detection of disease outbreaks, since some diseases have high transmission rate. For example, the rotaviroses in children and adults (Kotloff, 2017). However, a simple analysis of incidence rates does not provide enough evidence to state whether or not they are within the normal range expected. An alternative for that limitation is the use of control charts, which are able to generate alerts to detect epidemics and trigger early action of enteric viruses control with high transmissibility (Ilmi, Darti, & Suryanto, 2020; Mohammed, 2004).

Our data show that the three epidemics control detection methods were able to provide at least one epidemic alert, denoted by red dots (active points) in the graphs. The distribution of alerts during the study period varied depending on the technique employed.

For instance, in the Shewhart chart, the mesoregion Araçatuba had concentrated epidemic events early in the first half of the decade studied. These standards do not necessarily indicate the occurrence of diarrhea outbreaks in these regions at this time. However, it may be a reflection of the reduction in the incidence of the disease in the second half of the decade, after the implementation of control measures, including the implementation of vaccination programs against rotavirus disease (Ilmi et al., 2020). In Presidente Prudente, this pattern was not observed, in this area cyclical epidemics occurred over several years, possibly reflecting seasonal disease occurrences in this region.

In contrast, the CUSUM chart featured epidemic events for longer periods or ongoing in the three mesoregions. We observed the increase in the number of monthly cases, the stabilization leading to a plateau or a peak, and its decrease, especially for the mesoregions Araçatuba and Marília. In Presidente Prudente, the curve appears to behave with two peaks that show an epidemic period. These results reinforce the usefulness of CUSUM charts, when the purpose of health care is to monitor small deviations in control of hospitalizations for diarrhea (O'Brien, 1997).

For the CUSUM chart, the process stabilized and possibly remained under control when there were few consecutive months with low incidence rates in the mesoregions. This phenomenon is the result of accumulated information to early detect a change in the average, and return to the control (O'Brien, 1997). Each mesoregion differed on the time of the decrease of the incidence, Marilia being the earliest and Presidente Prudente the latest.

The CUSUM chart has a useful explanatory effect for the control of diarrhea because it allows early detection when the period of process deviations began. This early detection provides an opportunity to prevent progression of outbreaks because once a period of increasing trend starts, actions can be taken to prevent the curve to exceeding the upper control limit (O'Brien, 1997).

The Shewhart charts are most commonly used by health systems than the CUSUM because they require relatively simple calculations with well-known statistics such as mean and standard deviation. However, as only analyze specific events and isolated, have no memory like the CUSUM graphs, being ineffective for the detection of more moderate changes. One way to minimize this problem is the use of sensitizing rules in Shewhart charts. These rules improve the sensitivity for detection of epidemic events but also increase the complexity in the interpretation of standards and might lead to false alarms (Woodall & Faltin, 2019). This phenomenon was observed in the mesoregion Aracatuba (21 anomalous events), followed by Presidente Prudente (seven) and Marilia (zero). These results indicate that the region of Araçatuba features many anomalous events, requiring further investigation for the cause of these anomalies.

The mesoregions Marília and Presidente Prudente showed significant serial autocorrelation in the Durbin-Watson test. Thus, for these two areas, the EWMA chart would be the most suitable, or alternatively, a Shewhart inclusion graph of moving averages (Senouci, Bendaoud, Medles, Tilmatine, & Dascalescu, 2008). The EWMA type graphs left more evident than in the regions of Araçatuba and Marília, there were significant cases of diarrhea between the first and second half of the decade.

The EWMA graphs seem to be more suitable because of their robustness regarding violations of the assumptions of normality of the data and serial autocorrelation. It was found that in the three regions studied, at least one of these assumptions was violated (Table 1).

The EWMA charts showed good results in situations where there are small changes but do not react to large changes as quickly as the Shewhart graphs. However, the EWMA graph is generally better than the CUSUM for detecting major changes, particularly if the parameter λ > 0.1 is used (Saleh, Mahmoud, Jones-Farmer, Zwetsloot, & Woodall, 2015). Thus, we consider reasonable performance with λ = 0.3.

The control limits by the CUSUM and EWMA method were calculated considering all available observations, including those observations whose values were outside the control region defined in the Shewhart charts. Thus, these graphs can be influenced by atypical years one of the options to

minimize this problem is to redo the graphs excluding these limits, which may be more reasonable to monitor the incidence rates of diarrhea in children under four years old.

As shown in Table 2, the CUSUM graphics are the most sensitive to abnormal events and Shewhart charts less sensitive. Graphics type EWMA showed intermediate performance. It should be considered that very sensitive graphics tend to detect false-positive events, as well as less sensitive may result in false-negative events. Thus, it may be interesting to use cross-validation procedures to estimate the sensitivity and specificity of each graph in the face of real epidemic events. We consider also that the sensitivity rules are designed to industrials standards, but have been adapted for epidemic events, and thus may not be suitable for epidemic with complex temporal distribution. Some illnesses show curves with more than one epidemic wave, sometimes distinct or confluent, underreported cases and chronic illnesses detected late by the notification systems.

Some pathogens are seasonal, peaking at different times of the year. The seasonality of diarrheal disease is conditioned to the rainy season, which promotes the survival and multiplication of pathogens, transmission between human hosts by water accumulated in flooding, contamination of drinking water and the multiplication of transmitting vectors that use the water for breeding. The climate is statistically correlated with the incidence of infectious diarrhea, such as rotavirus (Chao et al., 2019).

The elaborate graphs for different mesoregions suggest that hospitalizations for diarrhea in children showed similar patterns in Araçatuba and Marilia. In mesoregion of Presidente Prudente, anomalies emerged in a period later in the timeline, which suggests that in this area, the occurrence of diarrhea has different pattern from the others or it is a consequence of the spread of an arising outbreak of the two mentioned regions. Indeed, geographical proximity between the two regions can influence the spread of infectious agents associated with diarrhea in children. This hypothesis is supported by studies that found significant spatial correlation in cases of hospitalizations for diarrhea in children in the state of São Paulo, where it was observed extensively by the clustering of cases in the Northwest region (Vaz & Nascimento, 2017). These charts can not only be useful for monitoring epidemics, but can also be used to compare patterns in different epidemic diseases and locations.

Visible fluctuations in the sequential periods of epidemic are noticed in the CUSUM graphs. These fluctuations are also observed outside the periods of anomaly and are less evident in the Shewhart and EWMA charts. Probably this is due to the seasonality of agents associated with diarrhea in children, such as rotavirus. In the months of lower temperatures or drought, the incidence of these viruses increases between May and September, in the states of the Midwest, South and Southeast. In

the North and Northeast, its occurrence is distributed almost throughout the year (Meneguessi, Mossri, Segatto, & Reis, 2015).

Another possibility is that the fluctuations are due to norovirus, which has been identified as the etiologic agent of gastroenteritis in children predominate, although the age of hospitalized patients differs between studies, ranging from under one year to less than three years. These viruses, however, have occurrences of peaks in the warmer months, pattern consistent with seasonality studies in the Southern Hemisphere, in regions characterized by humid subtropical climate with dry winter and rainy summer enough (Kamioka et al., 2019).

The studied techniques detected different fluctuation patterns in each of the mesoregions studied. In CUSUM technique, the cases seem to have been concentrated between the years 2012 and 2014 to then present significant decrease. One possible explanation for this decrease is the vaccine strategy for rotavirus, considered the main infectious agent prevalent in childhood. According to official data from Brazil, in 2012 the region of Marilia had vaccination coverage of 91%, 100% and 94%, respectively in Araçatuba, Marília and Presidente Prudente. In 2013, this parameter has changed to 95%, 100% and 98%, respectively for the same areas (Ministério da Saúde - Brasil). The vaccine was introduced in the infant immunization schedule in 2006 and expanded to other age groups in 2013, with a significant reduction of cases in childhood periods, pregnancy, adolescence, adulthood and elderly life with 60 years or more (Oliveira, Leite, & Valente, 2015).

Although rotavirus is recently more common, noravirus has been increasing in prevalence, changing the epidemiological pattern of viral gastroenteritis in childhood. Data about this pathogen are not available in official notification systems, but it is highlighted that it is extremely important to differentiate it from other pathogens (Kamioka et al., 2019).

We acknowledge the limitations of our dataset from recorded and publicly available data, which are subject to biased underreporting and inconsistent data acquisition. Additionally, control charts should be interpreted carefully, since false-positive alarms can generate the mobilization of resources for investigations innocuous.

5. Conclusion

The process control charts CUSUM, EWMA and Shewhart can be used for surveillance of diarrhea epidemics in children, with the possibility of early intervention by health managers. These graphs show variable performance, suggesting the EWMA based method which presents results parsimonious as compared to other methods. Epidemic events observed in control charts of spatially contiguous areas may suggest directions in the spread of infectious diarrhea in children. In the coming years, studies with larger datasets can create artificial intelligence systems to handle control charts should be able to detect more accurately the epidemic events.

Funding Sources

This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel - (Brazil) CAPES - Financing Code 001.

6. References

- Abujiya, M. R., Riaz, M., & Lee, M. H. (2013). Enhancing the Performance of Combined Shewhart-EWMA Charts. *Quality and Reliability Engineering International, 29*(8), 1093–1106. doi: https://doi.org/10.1002/qre.1461
- Assis, F. E. A., Wolf, S., Surek, M., De Toni, F., Souza, E. M., Pedrosa, F. O., ... Fadel-Picheth, C. M. T. (2014). Impact of Aeromonas and diarrheagenic Escherichia coli screening in patients with diarrhea in Paraná, southern Brazil. *The Journal of Infection in Developing Countries, 8*(12), 1609–1614. DOI: https://doi.org/10.3855/jidc.4434
- Baker, J. M., & Alonso, W. J. (2018). Rotavirus vaccination takes seasonal signature of childhood diarrhea back to pre-sanitation era in Brazil. *Journal of Infection,* 76(1), 68–77. DOI: https://doi.org/10.1016/j.jinf.2017.10.001
- Benneyan, J. C. (2003). Statistical process control as a tool for research and healthcare improvement. *Quality and Safety in Health* Care, *12*(6), 458–464. DOI: https://doi.org/10.1136/qhc.12.6.458

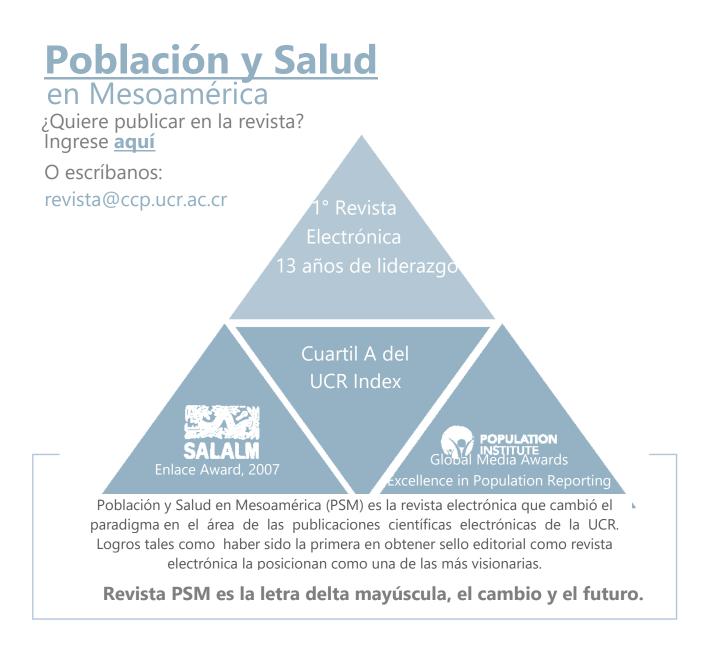
- Chao, D. L., Roose, A., Roh, M., Kotloff, K. L., & Proctor, J. L. (2019). The seasonality of diarrheal pathogens: A retrospective study of seven sites over three years. *PLOS Neglected Tropical Diseases, 13*(8), e0007211. DOI: https://doi.org/10.1371/journal.pntd.0007211
- Fonseca, P. A. M., Hacon, S. de S., Reis, V. L., Costa, D., & Brown, I. F. (2016). Using satellite data to study the relationship between rainfall and diarrheal diseases in a Southwestern Amazon basin. *Ciência & Saúde Coletiva*, 21(3), 731–742. DOI: https://doi.org/10.1590/1413-81232015213.20162015
- Fontoura, V. M., Graepp-Fontoura, I., Santos, F. S., Santos Neto, M., Tavares, H. S. de A., Bezerra, M. O. L., ... Nascimento, L. F. C. (2018). Socio-environmental factors and diarrheal diseases in under five-year old children in the state of Tocantins, Brazil. *PLOS ONE*, *13*(5), e0196702. DOI: https://doi.org/10.1371/journal.pone.0196702
- Gandy, A., & Lau, F. D.-H. (2013). Non-restarting cumulative sum charts and control of the false discovery rate. *Biometrika*, *100*(1), 261–268. DOI: https://doi.org/10.1093/biomet/ass066
- Gomes, I. C., Mingoti, S. A., & Oliveira, C. D. L. (2011). A novel experience in the use of control charts for the detection of nosocomial infection outbreaks. *Clinics*, *66*(10), 1681–1689. DOI: https://doi.org/10.1590/S1807-59322011001000004
- Ilmi, N. B., Darti, I., & Suryanto, A. (2020). Dynamical Analysis of a Rotavirus Infection Model with Vaccination and Saturation Incidence Rate. Journal of Physics: *Conference Series, 1562*, 012018. DOI: https://doi.org/10.1088/1742-6596/1562/1/012018
- Kamioka, G. A., Madalosso, G., Pavanello, E. I., Sousa, S. C. Z. de, Bassit, N. P., & Sato, A. P. S. (2019). Norovírus no município de São Paulo, 2010-2016: estudo transversal sobre a principal causa de gastroenterite infantil. *Epidemiologia e Serviços de Saúde, 28*(2), e2018290. DOI: https://doi.org/10.5123/S1679-49742019000200016
- Kotloff, K. L. (2017). The Burden and Etiology of Diarrheal Illness in Developing Countries. *Pediatric Clinics of North America*, 64(4), 799–814. DOI: https://doi.org/10.1016/j.pcl.2017.03.006
- Lima, A. A. M., Oliveira, D. B., Quetz, J. S., Havt, A., Prata, M. M. G., Lima, I. F. N., ... Guerrant, R. L. (2019). Etiology and severity of diarrheal diseases in infants at the semiarid region of Brazil: A

case-control study. *PLOS Neglected Tropical Diseases, 13*(2), e0007154. DOI: https://doi.org/10.1371/journal.pntd.0007154

- Mbuya, M. N. N., & Humphrey, J. H. (2016). Preventing environmental enteric dysfunction through improved water, sanitation and hygiene: an opportunity for stunting reduction in developing countries. *Maternal & Child Nutrition*, *12*, 106–120. DOI: https://doi.org/10.1111/mcn.12220
- Mello, C. S., Rodrigues, M. S. do C., Filho, H. B. de A., Melli, L. C. F. L., Tahan, S., Pignatari, A. C. C., & de Morais, M. B. (2018). Fecal microbiota analysis of children with small intestinal bacterial overgrowth among residents of an urban slum in Brazil. *Jornal de Pediatria*, 94(5), 483–490. DOI: https://doi.org/10.1016/j.jped.2017.09.003
- Meneguessi, G. M., Mossri, R. M., Segatto, T. C. V., & Reis, P. O. (2015). Morbimortalidade por doenças diarreicas agudas em crianças menores de 10 anos no Distrito Federal, Brasil, 2003 a 2012. *Epidemiologia e Serviços de Saúde*, *24*(4), 721–730. DOI: https://doi.org/10.5123/S1679-49742015000400014
- Mohammed, M. A. (2004). Using statistical process control to improve the quality of health care. *Quality and Safety in Health Care*, 13(4), 243–245. DOI: https://doi.org/10.1136/qshc.2004.011650
- Montgomery, D. . . (2018). Introdução ao Controle Estatístico de Qualidade. In *Introdução ao Controle Estatístico de Qualidade.*
- O'Brien, S. (1997). Do CuSums have a role in routine communicable disease surveillance? *Public Health*, *111*(4), 255–258. DOI: https://doi.org/10.1016/S0033-3506(97)00044-9
- Oliveira, A. F. de, Leite, I. da C., & Valente, J. G. (2015). Global burden of diarrheal disease attributable to the water supply and sanitation system in the State of Minas Gerais, Brazil: 2005. *Ciência & Saúde Coletiva, 20*(4), 1027–1036. DOI: https://doi.org/10.1590/1413-81232015204.00372014
- Reis, R. O. dos, Souza, M. N., Cecconi, M. C. P., Timm, L., Ikuta, N., Simon, D., ... Lunge, V. R. (2018).
 Increasing prevalence and dissemination of invasive nontyphoidal Salmonella serotype
 Typhimurium with multidrug resistance in hospitalized patients from southern Brazil. The
 Brazilian Journal of Infectious Diseases, 22(5), 424–432. DOI:

https://doi.org/10.1016/j.bjid.2018.08.002

- Saleh, N. A., Mahmoud, M. A., Jones-Farmer, L. A., Zwetsloot, I., & Woodall, W. H. (2015). Another Look at the EWMA Control Chart with Estimated Parameters. *Journal of Quality Technology*, 47(4), 363–382. DOI: https://doi.org/10.1080/00224065.2015.11918140
- Senouci, K., Bendaoud, A., Medles, K., Tilmatine, A., & Dascalescu, L. (2008). Comparative Study between the Shewhart and CUSUM Charts for the Statistic Control of Electrostatic Separation Processes. In 2008 IEEE Industry Applications Society Annual Meeting (pp. 1–5). IEEE. DOI: https://doi.org/10.1109/08IAS.2008.103
- Troeger, C., Colombara, D. V, Rao, P. C., Khalil, I. A., Brown, A., Brewer, T. G., ... Mokdad, A. H. (2018). Global disability-adjusted life-year estimates of long-term health burden and undernutrition attributable to diarrhoeal diseases in children younger than 5 years. *The Lancet Global Health*, 6(3), e255–e269. DOI: https://doi.org/10.1016/S2214-109X(18)30045-7
- Troeger, C., Forouzanfar, M., Rao, P. C., Khalil, I., Brown, A., Reiner, R. C., ... Mokdad, A. H. (2017). Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet Infectious Diseases*, 17(9), 909–948. DOI: https://doi.org/10.1016/S1473-3099(17)30276-1
- Vaz, F. P. C., & Nascimento, L. F. C. (2017). Spatial distribution for diarrhea hospitalization in São Paulo State. *Revista Brasileira de Saúde Materno Infantil, 17*(3), 475–482. DOI: https://doi.org/10.1590/1806-93042017000300004
- Woodall, W. H. (2006). The Use of Control Charts in Health-Care and Public-Health Surveillance. *Journal of Quality Technology, 38*(2), 89–104. DOI: https://doi.org/10.1080/00224065.2006.11918593
- Woodall, W. H., & Faltin, F. W. (2019). Rethinking control chart design and evaluation. *Quality Engineering*, *31*(4), 596–605. DOI: https://doi.org/10.1080/08982112.2019.1582779



Indexada en los catálogos más prestigiosos. Para conocer la lista completa de índices, ingrese aquí.



Revista Población y Salud en Mesoamérica -

Centro Centroamericano de Población Universidad de Costa Rica

