



The influence of temperature and rainfall in the human viral infections

A influência da temperatura e índice pluviométrico nas infecções virais humanas

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Abstract

It is well described by many authors the occurrence of viruses outbreaks that occurs annually at the same time. Epidemiological studies could generate important information about seasonality and its relation to outbreaks, population fluctuations, geographical variations, seasonal environmental. The purpose of this study was to show the influence of temperature and rainfall on the main viral diseases responsible for high rates of morbidity and mortality. Data were collected from samples performed at the Virology Laboratory of the Hospital de Clínicas da Universidade Federal do Paraná (HC-UFPR), which is a university tertiary hospital, in the period of 2003 to 2013. The temperature (°C) and mean monthly rainfall (mm) data was provided by the Sistema Meteorológico do Paraná (SIMEPAR-PR). The study of viral respiratory infection has revealed an incidence and pattern of seasonal prevalence of the respiratory viruses in Curitiba city, Southern Brazil. It was observed that in the months when the temperatures were lower, especially during June and July, there were an increasing number of samples collected as well as positive scores. For Rotavirus infections it was observed an increase in positive cases was observed in certain years, particularly during the colder months. Enteroviruses circulated in higher frequency during summer months with a median temperature of 21.5°C. Herpesviruses were distributed along the year but its circulation was not observed during the winter months. In conclusion it was observed the seasonality pattern of the viruses' circulation in Curitiba city, on the other hand rainfall did not demonstrated the same pattern.

Key words: seasonality, rainfall, respiratory viruses, viral gastroenteritis, nervous system viral diseases.

Resumo

É bem descrito por muitos autores a ocorrência de surtos de vírus que ocorrem anualmente ao mesmo tempo. Estudos epidemiológicos podem gerar informações importantes sobre a sazonalidade e sua relação com surtos, flutuações populacionais, variações geográficas, sazonais ambientais. O objetivo deste estudo foi mostrar a influência da temperatura e da precipitação nas principais doenças virais responsáveis por altas taxas de morbimortalidade. Os dados foram coletados de amostras realizadas no Laboratório de Virologia do Hospital de Clínicas da Universidade Federal do Paraná (HC-UFPR), que é um hospital universitário terciário, no período de 2003 a 2013. A temperatura (° C) e a média dos

dados pluviométricos mensais (mm) foram fornecidas pelo Sistema Meteorológico do Paraná (SIMEPAR-PR). O estudo da infecção respiratória viral revelou uma incidência e padrão de prevalência sazonal dos vírus respiratórios na cidade de Curitiba, sul do Brasil. Observou-se que nos meses em que as temperaturas foram mais baixas, especialmente nos meses de junho e julho, houve um número crescente de amostras coletadas, bem como escores positivos. Para as infecções por rotavírus, observou-se um aumento nos casos positivos em certos anos, particularmente durante os meses mais frios. Os enterovírus circulavam em maior frequência durante os meses de verão com uma temperatura mediana de 21,5 °C. Herpesvírus foram distribuídos ao longo do ano, mas sua circulação não foi observada durante os meses de inverno. Em conclusão, observou-se o padrão de sazonalidade da circulação dos vírus na cidade de Curitiba, por outro lado, a precipitação não demonstrou o mesmo padrão.

Palavras chave: sazonalidade, índice pluviométrico, vírus respiratórios, diarreias virais, meningites virais, encefalites virais.

INTRODUCTION

It is well described the occurrence of viruses' outbreaks that occurs annually at the same time by many authors, due to host and etiologic agents of infectious diseases. In this context, Altizer et al., 2006 reinforce that epidemiological studies could generate important information about seasonality and its relation to outbreaks, population fluctuations, geographical variations, seasonal environmental. Additionally, the author remarks that seasonality could be related to the onset and severity of infectious diseases as well as with the persistence of the viral agents and this information could help in the adoption of strategies to control the these diseases (ALTIZER et al., 2006). According to World Health Organization respiratory infections, diarrheas, Central Nervous System (CNS) diseases, are the main problems of public health especially in young children. The high rate of mortality in young children by acute respiratory infections (ARI) has important distinctions between developed and in developing countries as well as it is closely related to the seasonal environmental (MONTTO, 1994). The impact of respiratory tract infections in high-risk populations such as individuals with asthma and chronic bronchitis has been confirmed in several studies (FERNANDEZ et al., 1998) Patients with compromised immune function seem to be

susceptible to the same respiratory viruses that circulate in the general population. However, immunosuppression could generate conditions of serious complications (RABONI et al., 2003). The Group A rotaviruses (RVA) are the mainly responsible by of acute watery diarrhea in children aged less than 5 years worldwide. On a global scale, they are responsible for approximately 611,000 deaths per year, mostly in low-income countries (PARASHAR et al., 2006). RVA infections remain an important cause of pediatric hospitalization, particularly in developing countries, where demographic and socio-economic factors are associated with increased mortality rates (HARRINGTON et al., 2003). Viral meningitis is a common infectious disease of CNS that occurs worldwide, especially during the summer. Almost 90% of cases are caused by enterovirus such as, coxsackievirus and echovirus (SAWYER, 2002). They are easily transmitted by direct contact with respiratory secretions that can cause outbreaks with high financial impact and morbidity rates. These viruses are geographically confined and some serotypes may arise in endemic regions, with gradual changes in the predominant serotypes present year to year (SAWYER, 2002). The purpose of this study was to show the influence of temperature and rainfall on the principal viral diseases responsible for high rates of morbidity and mortality.

METHODOLOGY

An observational and retrospective was carried out. Viral circulation information were evaluated from analysis of Virology Laboratory database of the Hospital de Clínicas da Universidade Federal do Paraná (HC-UFPR), which is a University tertiary Hospital, from 2003 to 2013. This study was based on the researches approved by the HC-UFPR Institution Research Board (IRB). The temperature (°C) and mean monthly rainfall (mm) data from 2003 to 2013 were provided by the Sistema Meteorológico do Paraná (SIMEPAR), Curitiba, Paraná, Brazil (SIMEPAR-PR).

Casuistic

In the period of 2000 to 2003 a total of 1621 nasopharyngeal aspirate (NPA) or brochoalveolar lavage (BAL) samples were analyzed. From this total, 273 samples were obtained from primary healthcare units and 1348 samples from the Hospital of the Federal University in Paraná (HC-UFPR), comprising 666 samples from the Human Stem Cell Transplant (HSCT) Unit and 682 from pediatric patients attended at the combined facilities of the intensive care unit (ICU), along with the emergency and infectious disease units. HSCT patients have a heterogeneous age distribution that ranged from less than one to 70 years old, the majority of the samples were from patients with 20 to 39 years old. In the period from 2006 to 2008 1,572 NPAs samples were analyzed for hMPV diagnosis, of these 723 samples (723/1572, 46%) from pediatric inpatients, 356 (356/1572, 22.6%) from patients submitted to Human Stem Cell Transplant (HSCT) and 493 (493/1572, 31.4%) from outpatients were analyzed. Additionally, 163 samples collected from 153 patients through the winter months were tested for hMPV. The age range of the patients was 15 days to 4 years (mean 7.7 months) and 62.8% were male. One thousand and two cases were identified in both databases. A cross-sectional study was performed with 1,140 stool samples were

collected from April of 2001 to December of 2008 referred to HC-UFPR of outpatients and inpatients with acute gastroenteritis. The patients were admitted in the pediatric wards or to the hematopoietic stem cells transplantation (HSCT) unit. During July 2005 to December 2006 period a total 671 CSF samples were evaluated, with 460 samples (460 patients) fulfilling the inclusion criteria for the study. All the studies included in this evaluation were approved by the Ethics of Research on Human Beings Committee of the HC-UFPR.

RESULTS

The study of viral respiratory infection in Curitiba, Southern Brazil, has revealed an incidence and pattern of seasonal of the viruses (Figure 1 A, B, C and D). The trimester distribution of respiratory viruses is shown in figure 1. These figures illustrate the number of positive samples and monthly median outdoor temperature at time of samples collection during the 3 years of monitoring. In all figures it can be observed that in the months when the temperatures were lower, especially during June and July, there were an increasing number of samples collected as well as positive results. A similar distribution was observed for outpatient and hospitalized patients Figure 1 (A and B). Figure 1 (C) shows the incidence of the Human Metapneumovirus (hMPV) in the winter months, the virus was detected in 10 (6.4%) samples. Figure 1 (D) shows that hMPV circulated throughout the year with two annual peaks, one in the autumn and another in the late winter. A higher incidence of hMPV (18/37, 48.6%) was observed in May and June 2007. In this period was reported the alternance of the hMPV B2 subtype circulated in May and the hMPV B1 subtype circulated in June. Figure 1 (E) shows the same pattern of respiratory viruses, it shows the number of positive samples for FLUA and FLUB and the monthly median outdoor temperature during the three-year period. It was observed an increase in the number of

samples that tested positive for FLUA as well as FLUB during the winter season, which is associated with a lower outdoor temperature. Cases of HRV infection occurred throughout the study period (Figure 1 F). The months of May to August demonstrated the highest

number of HRV infections during 2012, peaking in August (17 cases; 10%). In 2013, the seasonality of HRV infection was from March to May, peaking in May (19 cases; 12%). Comparing the monthly distribution of HRV cases with average temperature (°C) and

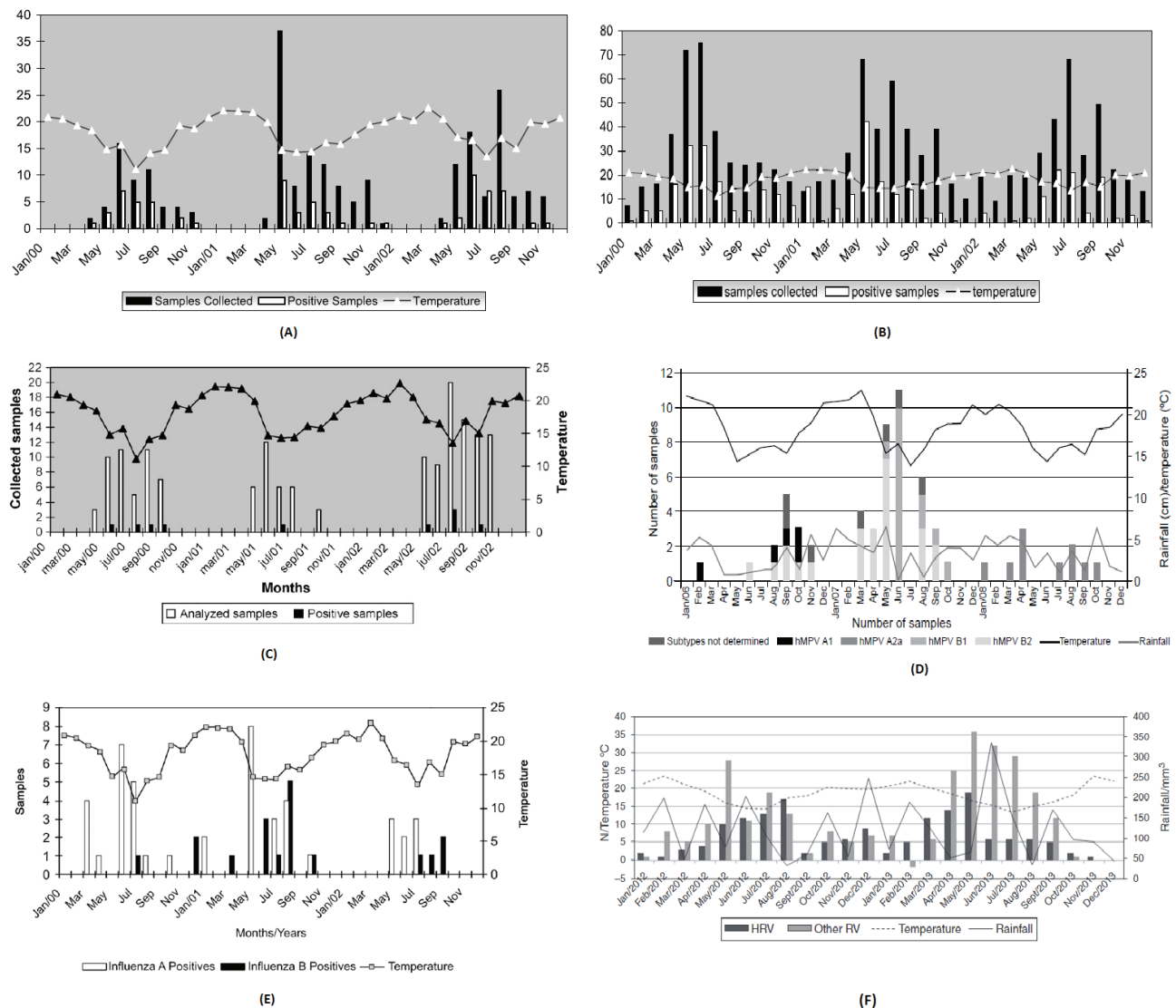


Figure 1. Incidence of viral respiratory infection in nasopharyngeal aspirates and the relationship to average day time temperature. (A) Incidence of viral infection, RSV, FLU A and B, PIV and ADV, from NPA samples in outpatients, positive samples and its relation to average daytime temperature from April 2000 to November 2003. (B) Incidence of viral infection RSV, FLU A and B, PIV and ADV, from samples of hospitalized patients and its relation to average daytime temperature from January 2000 to December 2003. (C) Distribution of hMPV in NPA and relationship to average daytime temperature in the winter months. (D) Distribution of hMPV positive samples and its relationship with the average daytime temperature and rainfall from January 2006 to December 2008 in Curitiba. (E) Seasonal distribution of FLU cases in Curitiba and monthly medium outdoor temperature during 2000 to 2003. (F) HRV infections: data on seasonality mean monthly temperature and precipitation, 2012 to 2013, Curitiba. Abbreviation: RSV- Respiratory Sincytial Viral; FLU - Influenza virus; PIV – Parainfluenza virus; ADV – Adenovirus; NPA – Nasopharyngeal Aspirate; hMPV – Human Metapneumovirus; HRV – Human Rhinovirus.

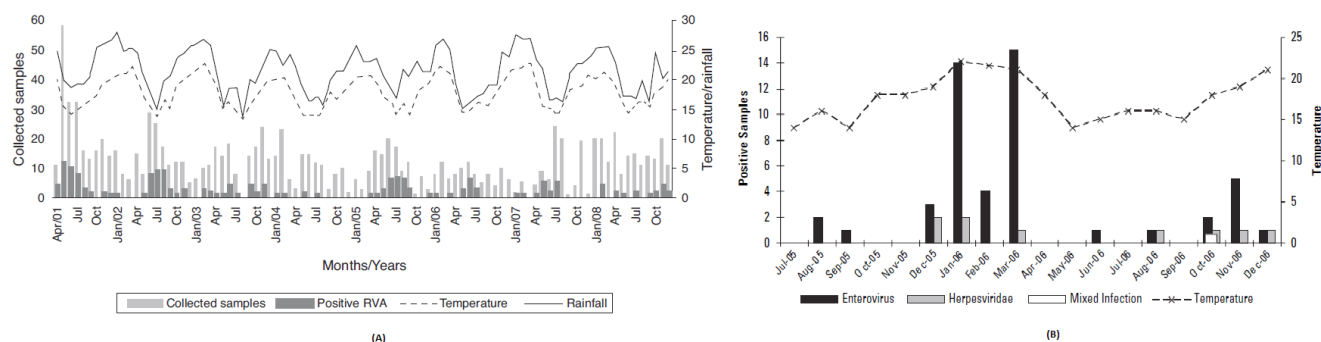


Figure 2. Incidence of RVA, Enterovirus and Hepesviruses in nervous system infection and the relationship to average day time temperature.

rainfall (mm), a negative correlation between the number of HRV cases and the average temperature ($rs=-0.636$, $p<0.001$) was demonstrated, but there was no significant correlation with rainfall ($rs=-0.036$, $p=0.866$). Figure 2 (A) shows the distribution of RVA during the eight-year study and its relation to monthly average temperature ($^{\circ}\text{C}$) and rainfall (mm). RVA infections presented an increase in positive cases was observed particularly during the colder months. However, it has been found that the frequency of the disease varied throughout the year. RVA infections presented an increase in positive cases was observed particularly during the colder months. However, it has been found that the frequency of the disease varied throughout the year. In 2008, it was observed that RVA circulate with a peak in the spring, which represented a delay of almost five months when compared to pre-immunization period. This was probably a result of a less susceptible population and, consequently, the virus required more time to spread. The incidence of nosocomial infections in this study was 12.5%. All patients had serious underlying diseases and this infection may have contributed to the increase in severity. CSF samples from patients who presented lymphomonocytary meningitis were investigated for enterovirus and herpesviridae family. During the July 2005 to December 2006 period a total 671 CSF samples were evaluated, with 460 samples (460 patients) filled the inclusion criteria for the study. A total of 59/460 (12.8%) samples showed

positive results for enterovirus ($n=48$), herpes simplex virus ($n=6$), Epstein Barr virus ($n=1$), human herpes virus type 6 ($n=2$) and a mixed infection with both enterovirus and Epstein Barr virus ($n=1$). There were higher numbers of positive samples during summer months with a median temperature of 21.5°C (Figure 2 B), mainly for enteroviruses. Herpesviruses were distributed along the year but its circulation was not observed during the winter months.

DISCUSSION

Located in the southern region of Brazil, Curitiba city is the coldest capital of Brazil, presenting a temperate climate, with four seasons well defined. The average temperature of the hottest month is less than 22°C , and the coldest temperature below 18°C . Precipitations in Curitiba are abundant throughout the year. The pluviometric index is approximately 1 480 mm annually, with January being the month of greatest precipitation (172 mm). Seasonality is an important attribute in human viral infections, but the mechanisms are poorly understood. Fisman 2012 reaffirmed in a review that better understanding of drivers of seasonality could provide insights into the relationship between the physical environment and infection risk, which is particularly important in the context of global ecological change in general, and climate change in particular. In broad terms, seasonality represents oscillation in pathogens'

effective reproductive number, which, in turn, must reflect oscillatory changes in infectiousness, contact patterns, pathogen survival, or host susceptibility. In Brazil, since the influenza A pandemic of 2009, referral hospitals have been conducting active surveillance to detect respiratory viruses. Such surveillance includes notification and laboratory investigation of cases meeting the diagnostic criteria of severe acute respiratory infection (SARI). This viral respiratory infection monitoring has resulted in important information about the circulation of other community-acquired respiratory viruses (CRV) (LITWIN et al., 2014). In the present evaluation it can be observed that in the months when the temperatures were lower, especially during June and July, there were an increasing number of respiratory samples collected as well as positive results. A similar distribution was observed for outpatient and hospitalized patients. The viruses investigated were RSV, FLU types A and B, ADV and PIV groups, by the indirect immunofluorescence (IFI) and cellular culture methods (TSUCHIYA et al., 2005.). It is of prime importance to establish some criteria to differentiate the viruses due to their high mortality and morbidity rates and in consideration of the fact that at present, influenza infection is potentially preventable by vaccination and infected patients can be managed with specific antivirals (SELWYN, 1990). We observed FLU virus to be involved in a significant proportion of respiratory diseases in the studied population; and the results are in accordance with the rates reported in other studies where both influenza and RSV are major contributors to the increase of respiratory disease associated morbidity seen during the winter (MONTANO, 2002; SELWYN, 1990; ZAMBON, 2001). It is estimated that between 5.000 and 29.000 additional annual deaths were caused by influenza in the U.K. between 1975 and 1990—five times the number directly attributed to influenza on death certificates (ZAMBON, 2001). The occurrence of these viruses in Curitiba in the period of late March to July were

showed, and many authors have reported the same seasonal of the virus in Brazil (STRALIOTTO et al., 2002; RABONI et al., 2003; TSUCHIYA et al., 2005; DEBUR et al., 2007; GARDINASSI et al., 2012). The studies developed in the virology laboratory revealed the involvement of viruses as etiologic agents in respiratory diseases in HSCT patients and viruses have been described as causing serious diseases in the immunosuppressed patients, elderly or persons with chronic lung disease, which tend to peak in the autumn or spring (RABONI et al, 2003; TSUCHIYA et al., 2005; DEBUR et al, 2007 and 2010). Another study by our group was on acute respiratory infection by hMPV in children hospitalized children in Paraná State, Brazil (DEBUR et al 2007). It was observed that hMPV circulates during winter and spring, consistent with the findings of another studies (JARTTI et al., 2002.; MULLINS et al., 2004; VAN DEN HOOGEN et al., 2004; CHANO et al., 2005; BOUSCAMPBERT-DUCHAMP et al., 2005; GRAY et al., 2006). Cuevas et al. (2003) reported a correlation between respiratory virus circulation and rainy periods, but we did not observe any such relationship in southern Brazil, where hMPV circulation could only be correlated with lower temperatures (CUEVAS et al., 2003). In other Brazilian regions, the presence of the hMPV correlates with rainy seasons, as reported by Cuevas et al. (2003), and with temperature decreases. Human rhinovirus (HRV) is the most common cause of upper respiratory tract infections, being responsible for at least 50% of cases of the common cold. HRVs have also been linked to lower airway effects that result in significant morbidity and mortality. In general, HRV infections occur during spring and autumn and manifest differently depending on whether the lower or upper respiratory tract is infected (LITWIN et al., 2014). It was observed in Curitiba a negative correlation between the number of HRV cases and the average temperature and an incidence of positives cases in the months may to august (LEOTTE et al., 2016). Rotavirus type A infections remain an important cause of pediatric

hospitalization, particularly in developing countries, where demographic and socio-economic factors are associated with increased mortality rates. Vaccination has a significant impact on the frequency of disease; nevertheless, severe infections persist, and the possible emergence of new genotypes must be considered. The diversity of rotavirus strains underscores the need for intensive surveillance; thus, the implementation of laboratory surveillance is critical to prevent outbreaks (RAMANI et al., 2009). RVA infections are most common in the wintertime in temperate regions, and year-round in tropical areas (KANE et al., 2004). In Brazil, an increase in positive cases was observed in certain years, particularly during the colder months (SANTOS et al., 2008). The same pattern was observed in the studies developed in the virology laboratory (PEREIRA et al., 2013). However, it has been found that the frequency of the disease varied throughout the year, suggesting that factors other than weather can influence the seasonality of this pathogen (NUNES et al., 2010; PEREIRA et al., 2013). Furthermore, in 2008, it was observed that RVA activity was spread throughout the entire year, peaking in the spring, which represented a delay of almost five months when compared to pre-immunization period. This was probably a result of a less susceptible population and, consequently, the virus took more time to spread (SÁFADI et al., 2010). It is worth mentioning the importance of RVA associated to hospital-acquired infections among children. Several factors, such as age, immune status, underlying disease, diagnostic and therapeutic interventions, season of the year, and duration of hospitalization may influence the acquisition of these infections. The genotypes of RVA found in these patients reflected the same genotype circulating in the community, highlighting the importance of measures for hospital infection control to prevent the spread of the pathogen in this environment (GLEIZES et al., 2006). Viral meningitis is a common infectious disease of the CNS that occurs

worldwide, especially during the summer. In Curitiba it's responsible for approximately 50% of inpatients (Brasil, Ministério da Saúde, 2007). Almost 90% of cases are caused by enterovirus (EV) such as, coxsackievirus and echovirus which contain several serotypes (SAWYER, 2002; MONTO, 2002). EV meningitis is the most common agent identified in most cases, followed by herpesviridae family viruses (VIDAL et al., 2011). In addition to morbidity, these infections cause a major economic impact on developed and developing countries (BROWN et al., 2003). There is little information on viral infections of the CNS in Southern Brazil. The circulation of the EV in Curitiba occurred mainly in the summer and autumn, similarly to that described for the northern hemisphere (VIDAL et al., 2011). However, a high year-round incidence occurs in tropical and subtropical areas. It is believed that fecal-oral spread of these agents is facilitated, particularly among children, during periods of warm weather. In addition to direct person-to-person transmission, EVs may be recovered from houseflies, wastewater and sewage (KLOWDEN et al., 1974). This evaluation reports the incidence of respiratory viruses, gastroenteritis and meningitis related to the seasonality and rainfall. Certainly, the information of seasonality will contribute to improved understanding of the epidemiology of this infections and etiology thus the management of antiviral drugs and establishment of strategies to minimize the impact of these viruses in many patients including immunocompromised patients.

CONCLUSION

In conclusion it was observed the seasonality pattern of the viruses' circulation in Curitiba city, on the other hand rainfall did not demonstrated the same pattern. The perspective of the established the influence and determine the mechanisms of the seasonality, rainfall and the development of infectious diseases could improve the comprehension of its dynamics

and complications, in different regions of Brazil. Principally it could provide insights to developing epidemiological strategies to control the spread of viral agents as well to prevention the viral diseases.

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REFERENCES

- ALTIZER S.S.; DOBSON A.; HOSSEINI P.; HUDSON P.; PASCUAL M.; ALTIZER P.R. Seasonality and the dynamics of infectious diseases. *Ecol. Lett.*, 9:467–484, 2006. doi/ 10.1111/j.1461-0248.2005.00879
- BOUSCAMPBET-DUCHAMP M.; LINA B.; TROMPETTE A.; MORET H.; MOTTE J.; ANDRÉOLETTI L. Detection of human metapneumovirus RNA sequences in nasopharyngeal aspirates of young French children with acute bronchiolitis by real-time reverse transcriptase PCR and phylogenetic analysis. *J. Clin. Microbiol.*, 43:1411–1414, 2005. doi: 10.1128/JCM.43.3.1411-1414.2005
- BRASIL. Ministério da Saúde. Sistema de Informações de Saúde [updated 2007 Feb 01]. Available from: <http://tabnet.datasus.gov.br>.
- BROWN B.; OBERSTE MS.; MAHER K.; PALLANSCH MA. Complete genomic sequencing shows that polioviruses and members of human enterovirus species c are closely related in the noncapsid coding region. *J Virol*, 77:8973–8984, 2003. doi: 10.1128/JVI.77.16.8973-8984.2003
- CHANO F.; ROUSSEAU C.; LAFERRIÈRE C.; COUILLARD M.; CHAREST H. Epidemiological survey of human metapneumovirus infection in a large pediatric tertiary care center. *J. Clin. Microbiol.*, 43:5520–5525, 2005. doi: 10.1128/JCM.43.11.5520-5525
- CUEVAS L.E.; NASSER A.M.; DOVE W.; GURGEL R.Q.; GREENSILL J.; HART C.A.. Human metapneumovirus and respiratory syncytial virus, Brazil. *Emerg. Infect. Dis.*, 9:1626–1628, 2003. doi: 10.3201/eid0912.030522
- Dados meteorológicos. Sistema Meteorológico do Paraná (Simepar). Novembro de 2018. Disponível em: http://www.simepar.br/site_pw/faleconosco#collapse3
- DEBUR M.C.; BORDIGNON J.; SANTOS C.N.D.; VIDAL L.R.; NOGUEIRA M.B.; ALMEIDA S.M.; RABONI S.M. Acute respiratory infection by human metapneumovirus in children in southern Brazil. *J. Clin. Virol.*, 39:59–62, 2007. doi: 10.1016/j.jcv.2007.01.012
- DEBUR M.C.; VIDAL L.R.R.; STROPARO E.; NOGUEIRA M.B.; ALMEIDA S.M.; TAKAHASHI G.A.; ROTTA I.; PEREIRA L.A.; SILVEIRA C.S.; DELFRARO A.; NAKATANI S.M.; SKRABA I.; RABONI S.M. Impact of human metapneumovirus infection on in and outpatients for the years 2006–2008 in southern Brazil. *Mem. Inst. Oswaldo Cruz*, 105(8):1010–8, 2010. doi: [org/10.1590/S0074-02762010000800010](https://doi.org/10.1590/S0074-02762010000800010)
- FERNÁNDEZ S.O.; PERALTA D.R.; HERNÁNDEZ A.G. Detección y caracterización rápida de los virus de influenza A y B em secreciones nasofaríngeas mediante el método de la inmunoperoxidasa. *Rev. Cubana Med. Trop.* 50:36–41; 1998.
- FISMAN D. Seasonality of viral infections: mechanisms and unknowns. *Clin. Microbiol. Infect.*, 18: 946–954, 2012.
- GARDINASSI L.G.; SIMAS P.V.M.; SALOMÃO J.B.; DURIGON E.L.; TREVISAN D.M.Z.; CORDEIRO J.A.; LACERDA M.N.; RAHAL P.; SOUZA F.P. Seasonality of viral respiratory infections in southeast of Brazil: the influence of temperature and air humidity. *Braz. J. Microbiol.*, (1): 98–108, 2012. doi: 10.1590/S1517-838220120001000011.
- GLEIZES O.; DESSELBERGER U.; TATOCHENKO V.; RODRIGO C.; SALMAN N.; MEZNER Z., et al. Nosocomial rotavirus infection in European countries: a review of the epidemiology, severity and economic burden of hospital-acquired rotavirus disease. *Pediatr. Infect. Dis. J.*, 25:S12–21, 2006. doi: 10.1097/01.inf.0000197563.03895.91
- GRAY G.C.; CAPUANO A.W.; SETTERQUIST S.F.; SANCHEZ J.L.; NEVILLE J.S.; OLSON J., et al. Human metapneumovirus, Peru. *Emerg. Infect. Dis.*, 12:347–50, 2006. doi: 10.3201/eid1202.051133
- HARRINGTON M.; BUTLER K.; CAFFERKEY M. Rotavirus infection in hospitalised children: incidence and impact on healthcare resources. *Ir. J. Med. Sci.*, 172:33–6, 2003. doi: [org/10.1007/BF02914784](https://doi.org/10.1007/BF02914784)
- JARTTI T.; VAN DEN HOOGEN B.; GAROFALO R.P.; OSTERHAUS A.D.M.E.; RUUSKANEN O. Metapneumovirus and acute wheezing in children. *Lancet*, 360:1393–1394, 2002. doi: 10.1016/S0140-6736(02)11391-2
- KANE E.M.; TURCIOS R.M.; ARVAY M.L.; GARCIA S.; BRESEE J.S.; GLASS R.I. The epidemiology of rotavirus diarrhea in Latin America. Anticipating rotavirus vaccines. *Rev. Panam. Salud Publica*, 16:371–377, 2004. doi: 10.1590/S1020-49892004001200002
- KLOWDEN M.; GREENBERG B. House fly and *Drosophila* cell cultures as hosts for human enteroviruses. *J. Med. Entomol.* 4:428–432, 1974. doi: 10.1093/jmedent/11.4.428

- LEOTTE J, TROMBETTA H, FAGGION HZ, ALMEIDA BM, NOGUEIRA MB, VIDAL LRR, RABONI SM. Impact and seasonality of human rhinovirus infection in hospitalized patients for two consecutive years. *J. Pediatr.* 93(3):294-300, 2017. doi: 10.1016/j.jpmed.2016.07.004.
- LITWIN C.M.; BOSLEY J.G. Seasonality and prevalence of respiratory pathogens detected by multiplex PCR at a tertiary care medical center. *Arch. Virol.*, 159:65-72, 2014.
- MONTO A.S. Studies of the community and family: acute respiratory illness and infection. *Epidemiol. Rev.* 16:351-73, 1994. doi: 10.1093/oxfordjournals.epirev.a036158
- MONTO A.S. Epidemiology of viral respiratory infections. *Am. J. Med.* 112:6A, 2002. doi.org/10.1016/S0002-9343(01)01058-0
- MULLINS J.A.; ERDMAN D.D.; WEINBERG G.A. EDWARDS K., HALL C.B.; WALKER F.J., et al. Human metapneumovirus infection among children hospitalized with acute respiratory illness. *Emerg. Infect. Dis.*, 10:700-705, 2004. doi: 10.3201/eid1004.030555
- NUNES A.A.; DE MELLO L.M.; PARRODE R.N.; BITTAR J.P.; DOMINGUES A.L. Prevalence of rotavirus in acute diarrhea and its association with clinical signs and symptoms. *J. Trop. Pediatr.*, 56:212-213, 2010. doi: 10.1093/tropej/fmp091
- PARASHAR U.D.; GIBSON C.J.; BRESEE J.S.; GLASS R.I. Rotavirus and severe childhood diarrhea. *Emerg. Infect. Dis.* 12:304-6, 2006. doi:10.3201/eid1202.050006
- PEREIRA L.A., FERREIRA C.E.O.; TURCHETTO G.D.; NOGUEIRA M.B.; VIDAL L.R.; CRUZ C.R.; DEBUR M.C.; ALMEIDA S.M.; RABONI S.M. Molecular characterization of rotavirus genotypes in immunosuppressed and non-immunosuppressed pediatric patients. *J. Pediatr.* 89(3):278-285, 2013. doi: 10.1016/j.jpmed.2012.11.002
- RABONI S.M.; NOGUEIRA M.B.; TSUCHIYA L.R.R. V.; TAKAHASHI G.R.A.; PEREIRA L.A.; PASQUINI R.; SIQUEIRA M.M. Respiratory tract viral infections in bone marrow transplant patients. *Transplantation*, 76:142-146, 2003. doi: 10.1097/01.TP.0000072012.26176.58
- RAMANI S.; ITURRIZA-GOMARA M.; JANA A.K.; KURUVILLA K.A.; GRAY J.J.; BROWN D.W.; et al. Whole genome characterization of reassortant G10P[11] strain (N155) from a neonate with symptomatic rotavirus infection: identification of genes of human and animal rotavirus origin. *J. Clin. Virol.* 45:237-244, 2009. doi: 10.1016/j.jcv.2009.05.003
- SÁFADI M.A.; BEREZIN E.N.; MUNFORD V.; ALMEIDA F.J.; DE MORAES J.C.; PINHEIRO C.F.; et al. Hospital-based surveillance to evaluate the impact of rotavirus vaccination in São Paulo, Brazil. *Pediatr. Infect. Dis. J.*, 29:1019-1022, 2010. doi: 10.1097/INF.0b013e3181e7886a
- SANTOS J.S.; ALFIERI A.F.; LEITE J.P.; SKRABA I.; ALFIERI A.A. Molecular epidemiology of the human group A rotavirus in the Paraná State, Brazil. *Braz. Arch. Biol. Technol.*, 51:287-294, 2008. doi.org/10.1590/S1516-89132008000200008
- SAWYER M.H. Enterovirus Infections: diagnosis and treatment. *Seminars in pediatrics infections diseases*, 53:40-47, 2002. doi.org/10.1053/spid.2002.29756
- SELWYN B.J. The epidemiology of acute respiratory tract infection in young children: comparison of findings from several developing countries. *Rev. Infect. Dis.*, 2 (Suppl 8), 1990. doi.org/10.1093/clinids/12.Supplement_S870
- STRALIOTTO S.M.; SIQUEIRA M.M.; MULLER R.L.; FISCHER G.B.; CUNHA M.L.T.; NESTOR S.M. Viral etiology of acute respiratory infections among children in Porto Alegre, RS, Brazil. *Rev. Soc. Bras. Med. Trop.*, 35:1-9, 2002. doi.org/10.1590/S0037-86822002000400002
- TSUCHIYA L.R.R.V.; COSTA L.M.D.; RABONI S.M.; NOGUEIRA M.B.; PEREIRA L.A.; ROTTA I.; TAKAHASHI G.R.A.; COELHO M, SIQUEIRA MM. Viral respiratory infection in Curitiba, Southern Brazil. *J. Infect.*, 51:401-407, 2005. doi:10.1016/j.jinf.2004.12.002
- VAN DEN HOOGEN B.G.; OSTERHAUS A.D.M.E. Clinical impact and diagnosis of human metapneumovirus infection. *J. Ped. Infect. Dis.*, 23:S25-32, 2004a. doi: 10.1097/01.inf.0000108190.09824.e8
- VIDAL L.R.R.; ALMEIDA S.M.; MESSIAS-REASON I.J.; NOGUEIRA M.B.; DEBUR M.C.; PESSA L.F.C.; PEREIRA L.A.; ROTTA I.; TAKAHASHI G.R.A.; SILVEIRA C.S.; ARAÚJO J.M.R.; RABONI S.M. Enterovirus and herpesviridae Family as etiologic agents of lymphomonocytary meningitis, Southern Brazil. *Arq. Neuropsiquiatr.*, 69(3):475-481, 2011. doi.org/10.1590/S0004-282X2011000400013
- VIDAL L.R.R.; SIQUEIRA M.M.; NOGUEIRA M.B.; RABONI S.M.; PEREIRA L.A.; TAKAHASHI G.R.A.; ROTTA I.; DEBUR M.C.; DALLA-COSTA L.B. The epidemiology and antigenic characterization of influenza viruses isolated in Curitiba, South Brazil. *Mem. Inst. Oswaldo Cruz*, 103(2): 180-185, 2008.
- ZAMBON M.C.; STOCKTON J.D.; CLEWLEY J.P.; FLEMING D.M. Contribution of influenza and respiratory syncytial virus to community cases of influenza-like illness: an observational study. *Lancet*, 358:1410-1416, 2001. doi.org/10.1016/S0140-6736(01)06528-X