Orthohantaviridae in Barbados: the Effect of Tropical Climates on Viral Prevalence in the Caribbean

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ABSTRACT

Orthohantaviridae, or hantaviruses, are a family of enveloped, single-stranded, tri-segmented, negative-sense (-)RNA viruses of the order *Bunyavirales* and can be found in human and rodent populations globally. Hantavirus' relationship to climate and ecosystems is well-studied in North America and Europe but is understudied in Latin America and the Caribbean–which are notably distinguished from other regions by their tropical climate. One such Caribbean country is Barbados, a small island in the east Caribbean that has experienced nearly 900 cases of hantavirus in the last 15 years–the same number of cases reported in all of the U.S. since 1992. This study aims to explore the relationship between climate and hantavirus prevalence through epidemiological methods. Correlation and regression, t-tests, and analyses of anomaly were performed to better understand how climate impacts transmission, reservoir populations, and human behavior. Significant results were limited to a weak, positive correlation between precipitation and hantavirus cases as well as greater amounts of precipitation in outbreak years both in the wet and dry seasons. These results suggest that the main climate measure influencing hantavirus prevalence in Barbados is precipitation. Higher precipitation increases viral prevalence by creating more favorable conditions for rodent breeding and altering rodent behavior to favor the home–increasing the potential for human-rodent contact. Challenges to diagnosing hantavirus cases in the region may potentially explain the lack of statistical significance of these results. Efforts to increase the accessibility of testing and longitudinal studies of hantavirus in rodent populations are needed to further explore this relationship.

KEYWORDS

Hantavirus, climate, viral zoonosis, disease ecology, epidemiology.

INTRODUCTION

Orthohantaviridae (referred from this point forward generally as hantavirus) are a family of enveloped, single-stranded, tri-segmented, negative-sense (-)RNA viruses of the order *Bunyavirales* (Meier et al 2021, Vaheri et al 2013). Many *Bunyaviridae* share these characteristics, however, hantaviruses are notably distinguished by their lack of any arthropod vector. Instead, hantavirus is amplified in and transmitted by rodent populations commonly of the family *Cricetidae*. Hantavirus replicates in these populations by chronically infecting the rodents with asymptomatic viremia (Meier et al 2021). Hantavirus spills over into humans through the inhalation of aerosolized rodent feces–most often through occupational or home exposures–and there is very little evidence of spread via human-to-human contact (Douglas et al 2021, Meier et al 2021). The incubation period of hantavirus in humans has yet to be clearly defined but currently is estimated to be between 1-8 weeks (CDC).

Hantavirus can be found in human and rodent populations globally, causing an estimated 150,000-200,000 human cases annually (Douglas et al 2021). Hantaviruses are notably distinguished geographically by the disease they cause. Old World (Europe and Asia) hantaviruses (Hantaan virus (HNTV), Puumula virus (PUUV), etc.) cause hemorrhagic fever with renal syndrome (HFRS) whereas New World (North and South America and the Caribbean) hantaviruses (Sin Nombre virus (SNV), Andes virus (ANDV), etc.) cause hantavirus pulmonary syndrome (HPS) (Douglas et al 2022). The specific strain found in Barbados has yet to be isolated. In HPS infections, hantaviruses replicate in the endothelial cells of capillaries and lungs, causing chest tightness and the lungs to fill with fluid. HPS has a mortality rate of 38% and can affect otherwise healthy, young, hosts (CDC). Currently, there are no vaccines or therapeutics to protect humans from hantavirus-caused disease, however, work is being done to better understand the body's immune response to hantavirus, and thus, potential immunization strategies (Engdahl et al 2020).

Understanding the potential impact of environmental conditions on viral prevalence is vital to managing diseases caused by viruses. Hantavirus' relationship to climate and ecosystems is well-studied in North America and Europe but is understudied in South America and the Caribbean–which are notably distinguished from other regions by their tropical climate (Douglas et al 2022). The tropical climates of these southern areas vary from those of North America and

Europe, particularly in temperature and humidity–both of which have been shown to have an effect on hantavirus transmission in other regions (Linard et al 2007, Prist et al 2017). These climatic differences add to the significance of this research seeing that models predicting disease interactions in northern regions may not be applicable to the southern regions where hantaviruses are found. In their review of the current literature on hantavirus in Latin America and the Caribbean (LAC), Douglas et al 2021 concluded that more research needs to be done both on how these climatic factors are influencing hantavirus transmission and on how hantavirus has interacted with these populations over time. This region lacks a model for predicting hantavirus risk, and collecting more evidence of these interactions could aid in future disease prevention efforts.

In this study, I will ask how the tropical climate of Barbados has affected the prevalence of human cases of hantavirus. My current hypotheses for how climate has impacted hantavirus spread are by directly impacting transmission, by having an indirect impact on the reservoir population, and by having an indirect impact on human behavior. I will explore these hypotheses by analyzing how temperature and humidity are correlated with hantavirus cases in the area and what the strength of this relationship is. I will then additionally analyze seasonal climatic differences between outbreak and non-outbreak years. Lastly, I will explore how anomalies in climate are correlated with hantavirus outbreaks. I plan on doing a secondary analysis of preexisting data that will contain monthly readings of temperature, humidity, and hantavirus cases. My current hypotheses predict that there will be positive trends of hantavirus cases with more precipitation and negative trends of hantavirus cases with higher temperatures. By analyzing these relationships in multiple ways, I hope to conclude whether temperature or precipitation is having a larger impact on viral prevalence.

RELEVANT BACKGROUND

Barbados Health System Overview

In 2019, Barbados scored a Universal Health Coverage (UHC) effective coverage index of 61 out of 100 (compared to USA 82) (Lozano et al 2019) and a Human Development Index (HDI) of 0.79–slightly above the LAC average of 0.754 (PAHO). A majority of total health expenditures come from out-of-pocket spending on health with only 2.8% of gross domestic product (GDP) being invested in health (PAHO). The proportion of adults 65 years old and older has been increasing over the past years, making Barbados on average one of the oldest populations in the Caribbean (PAHO). In regards to population health, disease burden is dominated by non-communicable diseases namely diabetes, cancers, kidney disease, and heart disease (IHME). Said non-communicable diseases account for a majority of deaths in Barbados, however, the increasing prevalence of non-communicable disease also grows concerns about disease from communicable pathogens as these conditions often increase the risk of developing severe disease from viral and other infections. Efforts to reduce communicable disease in the last few years have been centered on HIV/AIDS and have generally been successful–adding to the motivation to address non-communicable disease (PAHO).

Challenges to Hantavirus Research

Beyond the recent focus on non-communicable disease, there have been other challenges to hantavirus research important to understanding the limited availability of hantavirus data and literacy. Barbados is endemic to a handful of infectious diseases that have similar clinical manifestations as hantavirus, namely Dengue (DENV), leptospirosis, Zikavirus (ZIKV), and Chikungunya (CHIKV) (Kumar et al 2015). These diseases pose a challenge to hantavirus identification and research because clinicians in Barbados typically identify and treat disease through symptomology versus diagnostics–resulting in many hantavirus infections being misdiagnosed as one of these other endemic diseases or going undiagnosed altogether. The favoring of symptomology has grown out of the lacking accessibility of testing materials and other expensive diagnostic tools. Researchers such as Dr. Kirk Douglas and his team at UWI Cave Hill are working to combat this lack of access by studying potentially more accessible forms of diagnosis, although, hantavirus has continued to be arduously elusive. Unsurprisingly, the prioritization of this subject has also been disrupted by the increasing relevance of coronaviruses due to the COVID-19 pandemic.

METHODS

Study Site

The study site for the entirety of the project is the island of Barbados, located in the Caribbean Sea. Barbados is 430 km^2 with a population of 290,000 people. A majority of the population is congregated in Bridgetown, the capital, on the Southwest side of the island, with others scattered through more rural areas (Barbados Population Live, 2023). The climate of the area is defined by a wet and a dry season–the year beginning with the dry season and ending with the wet season. The wet season has minorly higher temperatures and higher precipitation whereas the dry season has cooler temperatures and less precipitation–although it is warm and rains year-round.

Data Collection

The data for temperature and precipitation were collected from the World Bank's Climate Change Knowledge Portal which processes and analyzes the data collected by the Climatic Research Unit at the University of East Anglia in Norwich, England. The Climatic Research Unit was developed to collect climate data globally for the purpose of studying climate change. Temperature was measured in degrees Celsius and precipitation was measured in millimeters. Both yearly and monthly average temperature and precipitation were collected between the years of 2008-2018–the study period defined by available hantavirus data.

Hantavirus data was provided by Dr. Kirk Douglas, the director of the Centre for Biosecurity Studies at the University of the West Indies at Cave Hill. Douglas has pioneered hantavirus research in Barbados which provided much of the ideological foundation for this study. Douglas et al performed a serological reconstruction of hantavirus cases in Barbados as well as prospective detection of hantavirus in patients presenting symptoms. They did so by performing enzyme-linked immunosorbent assays (ELISA) and confirming cases with immunofluorescent assays (IFA), immunochromatographic (ICG) tests, and pseudotype focus reduction neutralization tests (pFRNT) (Douglas et al 2021). Case data were collected to the same level of precision as the climate data–yearly and monthly case numbers.

Table 1. Hantavirus, precipitation, and temperature data summary.

Year	Total Hantavirus Cases	Total Precipitation (mm)	Average Temperature (°C)
2008	12	1628.19	26.3558
2009	46	1264.61	26.6783
2010	262	1926.61	27.0367
2011	91	1952.39	26.6317
2012	94	1586.78	26.5025
2013	50	1407.18	26.5808
2014	77	1429.99	26.62
2015	10	1095.53	26.9383
2016	107	1575.15	26.9133
2017	40	1677.1	26.7492
2018	33	1452.05	26.43

Data Analysis

The collected data were imported to R Studio Version 4.1.1. I then performed multiple tests of normality including observation of the quantile-quantile **comparison** plot and running the Shapiro-Wilk test of normality. From there, Pearson's coefficient was calculated using cor.test to determine the strength and direction of correlation between the yearly readings of temperature, precipitation, and hantavirus cases. I also used linear regression to scale these correlations and calculate the R^2 value.

For the seasonal analysis, I first identified outbreak years as years at or above the 3rd quartile of cases across the study period. After outbreak years were identified, I calculated climate measures for the wet season and dry season for each year (average temperature/precipitation). Using this grouped data, I developed box plots using R Commander to visualize the difference in groups and performed the Wilcoxon Rank Sum nonparametric t-test to scale the difference between groups.

Finally, for my analysis of anomalies, I used the devtools Anomaly Detection package in R to perform an anomaly detection analysis on the hantavirus, temperature, and precipitation data. The anomaly detection vector used a period of 12 to account for the yearly seasonal patterns in climate and detected anomalies in both directions (anomalously low or high). The anomaly vector provided a list of anomalous data points as well as a plot of the anomalies across the time period.

RESULTS

Seasonal Climatic Trends

Initial processing of the data and calculations of average monthly temperature and precipitation, total yearly precipitation, and average yearly temperature revealed the assumed climatic patterns between the wet and dry seasons. Precipitation was on average higher in the later months of the year (June-November) and this pattern was reflected across the study period (2008-2018) (Figure 1,2). Similarly, temperature was on average higher during these months, however, the discrepancy between dry and wet season temperatures was less than for precipitation–temperature staying between 25-28 °C during the study period (Figure 3,4).

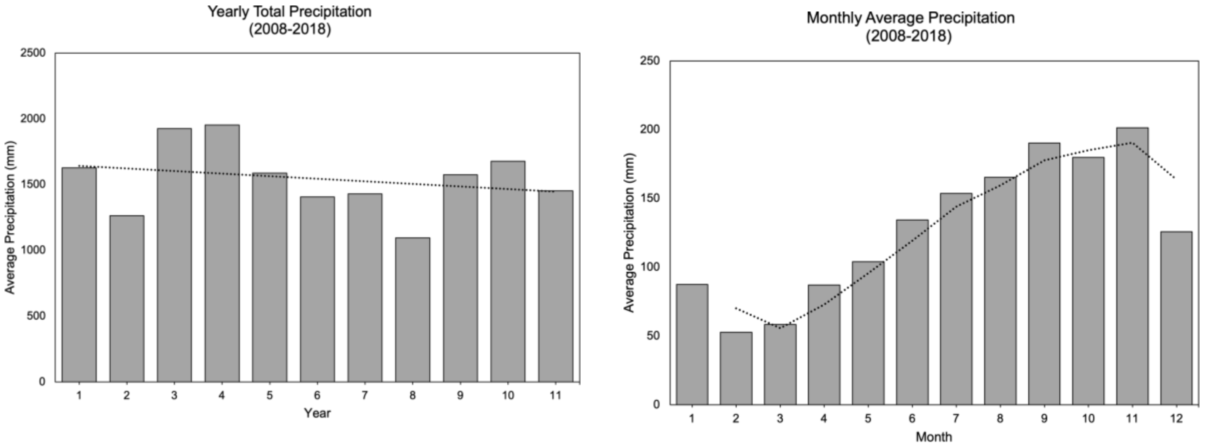

Figure 1. Monthly and yearly precipitation summaries. Histogram summaries of the collected precipitation data: a) Yearly total precipitation between the years 2008-2018, measured in millimeters; b) Average precipitation by month between 2008-2018, measured in (mm).

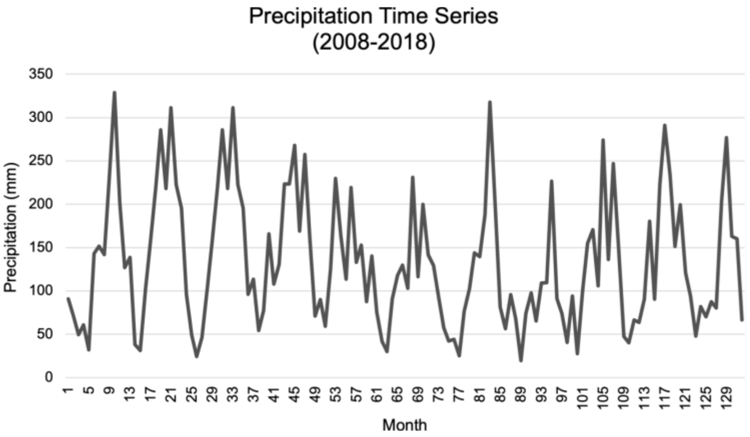

Figure 2. Precipitation time series. Total precipitation by month over the study period (2008-2018), measured in mm.

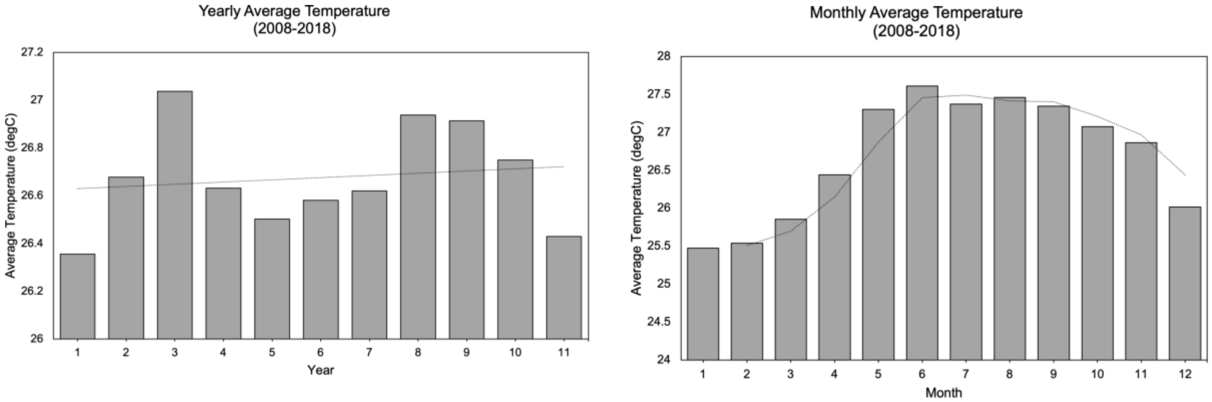

Figure 3. Monthly and yearly temperature summaries. Histogram summaries of the collected temperature data: a) Daily average temperature by year, measured in degrees Celsius; b) Daily average temperature by month, measured in degrees Celsius.

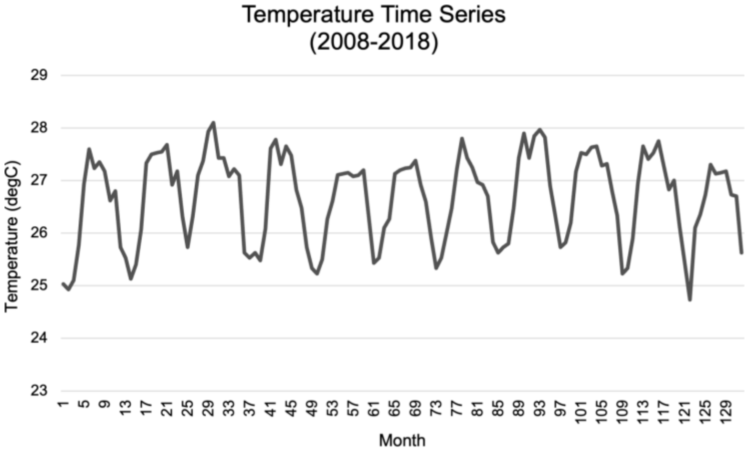

Figure 4. Temperature time series. Temperature over the study period (2008-2018), measured in °C.

Hantavirus Cases

Initial processing of the hantavirus cases data reflected patterns previously noted by Douglas et al 2021. The first recorded case of hantavirus was in 2008. Calculating the average cases per month revealed that the majority of cases were congregated in the wet season (Figure 5). Of the total (822) cases recorded during the study period, 555 or 67.5% (~⅔) of cases occurred between the months of June and November. Using the standard of case numbers at or above the 3rd quartile of cases (92.5 cases), four significant outbreak years were identified–the largest outbreak occurring in 2010 with subsequent outbreaks in 2011, 2012, and 2016 (Figure 6).

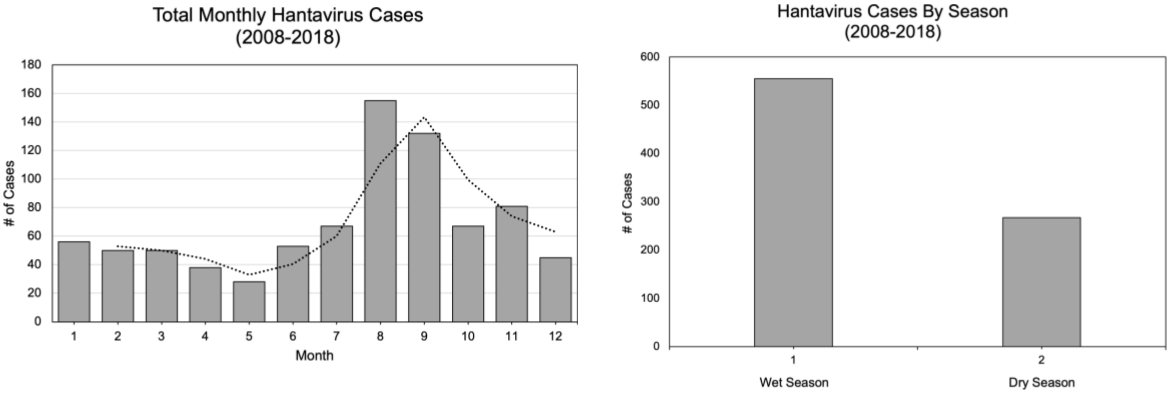

Figure 5. Monthly and seasonal breakdown of hantavirus cases.

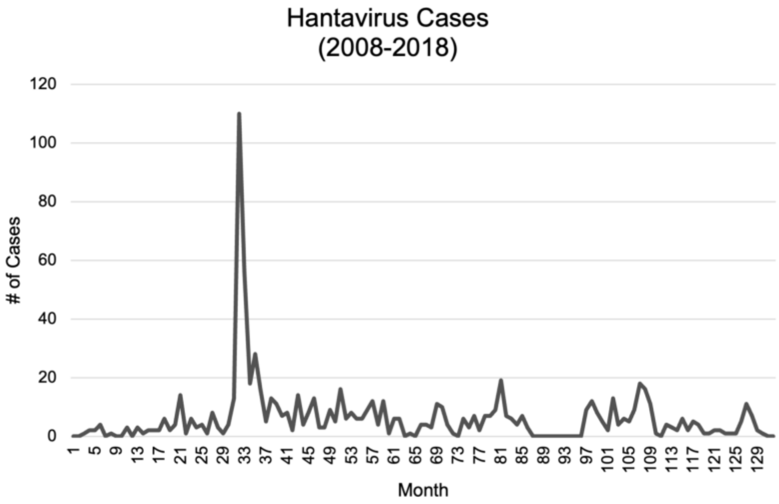

Figure 6. Hantavirus time series. Recorded cases of hantavirus over the study period (2008-2018).

Regression and Correlation

Initial regression and correlation models using yearly averages of the study variables revealed a weak, positive correlation between both precipitation and hantavirus ($R^2 = 0.07816$) and temperature and hantavirus ($R^2 = 0.2231$) (Figure 5). However, neither of these relationships were statistically significant ($p_1 = 0.4051$, $p_2 = 0.1424$; $\alpha = 0.05$). To increase precision, the process was repeated using monthly measures of the study variables, which revealed similar trends (Figure 6). The weak, positive correlation between temperature and hantavirus cases was still not statistically significant ($p_4 = 0.2094$), however, precipitation did have a statistically significant, weak, positive correlation with hantavirus cases ($R^2 = 0.0573$, $p_3 = 0.0075$).

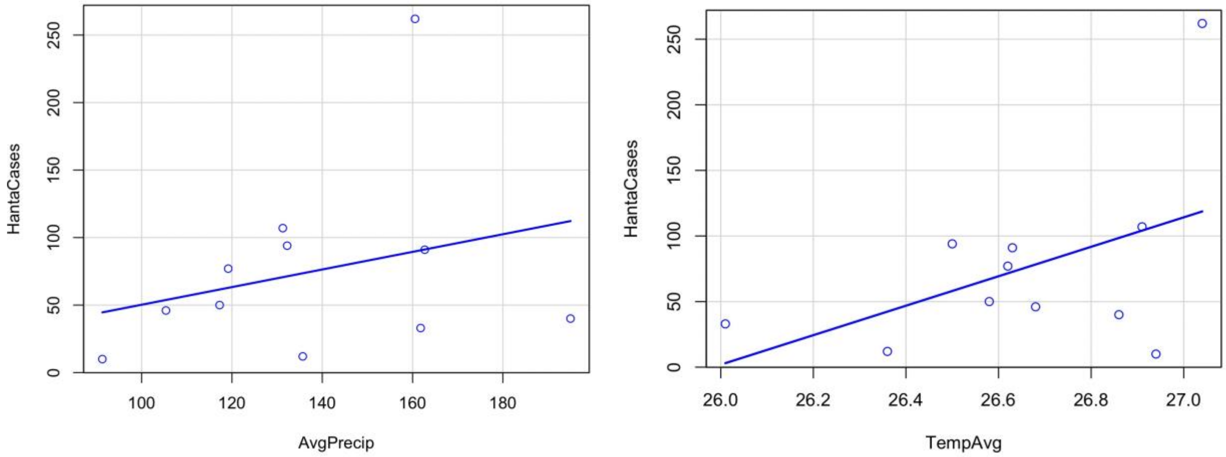

Figure 7. Visualization of linear regression for yearly measures of temperature, precipitation, and hantavirus cases.

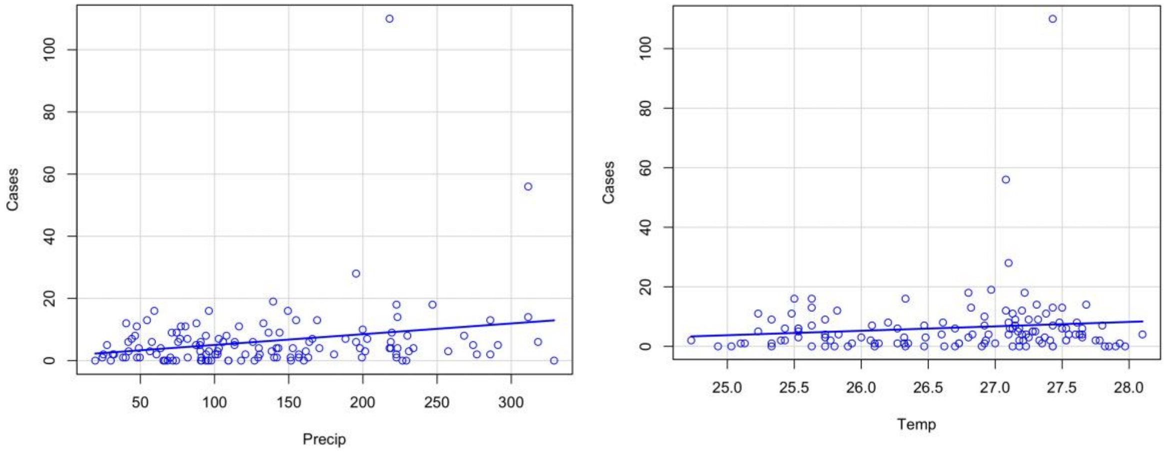

Figure 8. Visualization of linear regression for monthly readings of temperature, precipitation, and hantavirus cases.

Seasonal Analysis (T-tests)

For the Wilcoxon Rank Sum test, the difference between the two groups is significant if the test W value is less than or equal to the critical value. The critical value for a Wilxcoxin Rank Sum test with a precision level α = 0.05 and n = 11 is W = 11. Precipitation was on average significantly higher in outbreak years, in both the dry (W = 6) and wet seasons (W = 7) (Figure 7). Similarly, but with less statistical significance, temperature was on average higher in both the dry season (W = 9) and wet season (W = 11) (Figure 8).

Table 2. Summary of outbreak and non-outbreak year climate measures. Outbreak years: 2010, 2011, 2012, 2016.

Variable	Disease Status	Wet Season Avg	Dry Season Avg	Total (If applicable)
Precipitation	Outbreak	195.1225	98.2495833	146.686042
	Non-Outbreak	159.071667	77.9438095	118.507738
Temperature	Outbreak	27.2845833	26.2575	N/A
	Non-Outbreak	27.2535714	25.99	N/A

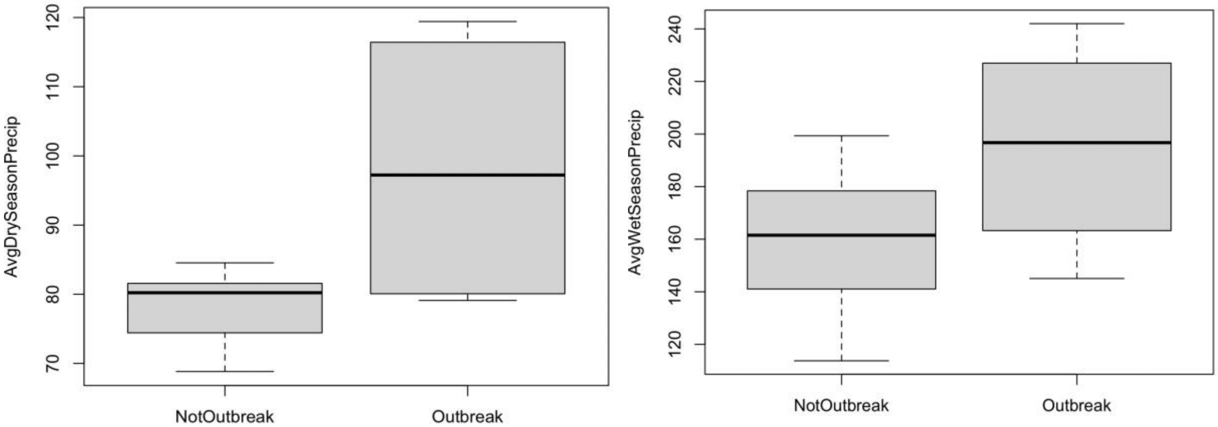

Figure 9. Difference in precipitation between outbreak and non-outbreak years in the study period (2008-2018).

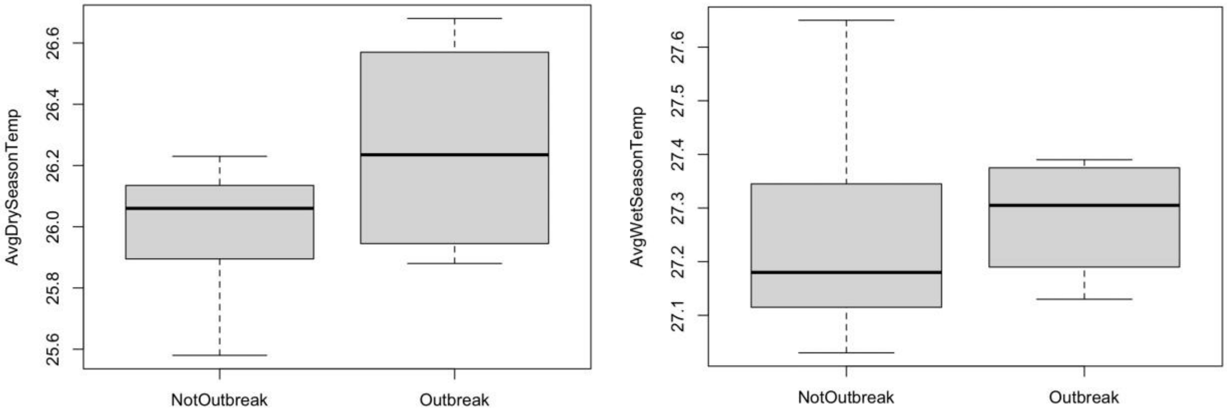

Figure 10. Difference in temperature between outbreak and non-outbreak years in the study period (2008-2018).

Analysis of Anomaly

Nine significant anomalies were recorded in hantavirus cases during the study period (Figure 9). The first five of these anomalies occurred during the 2010 outbreak–August, September, October, November, and December 2010. The subsequent outbreaks were in March 2012, September 2014, November 2016, and December 2016. Notably, these anomalies occur every other year–an unexpected pattern if repeated on a larger scale potentially signifying a cyclic pattern of outbreaks. There was only one recorded anomaly in temperature over the study period in March 2010, preceding the 2010 outbreak. No significant anomalies in precipitation were found.

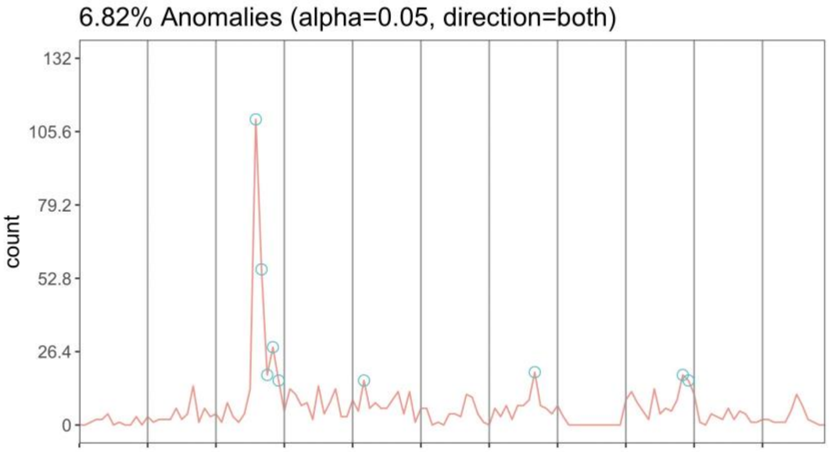

Figure 11. Anomaly vector for hantavirus cases. Beginning in 2008, segmented in 12-month periods, anomalies circled in blue.

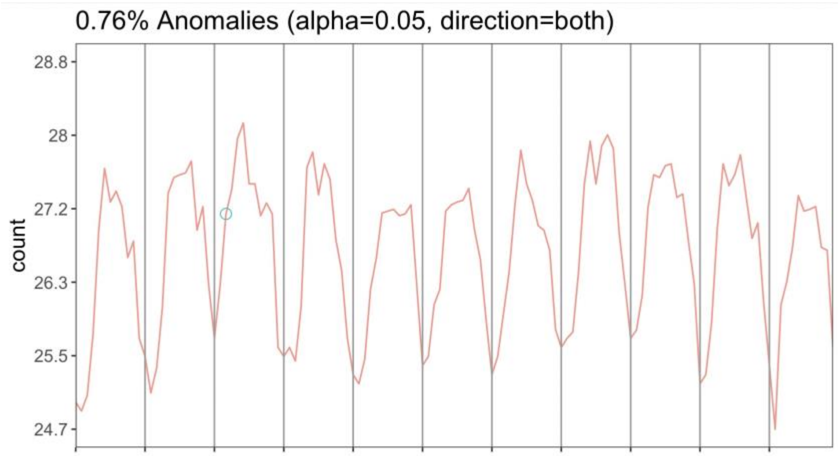

Figure 12. Anomaly vector for temperature readings. Beginning in 2008, segmented in 12-month periods, anomalies circled in blue.

DISCUSSION

General Conclusions

Results from the tests of correlation and regression and t-tests suggest that, in Barbados, precipitation has a larger impact on human cases of hantavirus than temperature. Impacts of temperature on hantavirus observed in other regions are likely dulled in the tropical climate of the Caribbean due to persistently warm temperatures. The interpretation of these results will parallel the three hypotheses for how climate impacts hantavirus prevalence outlined in the introduction and by the three subquestions: direct impact on transmission, impact on the reservoir population, and impact on human behavior. Likely causes for unique variations in climate that may impact hantavirus prevalence are the El Niño Southern Oscillation (ENSO) and anthropogenic climate change.

Impact on Transmission

Climate can have a direct impact on the transmission of viruses between hosts or on spillover events from the reservoir into host populations by creating more or less favorable conditions for the virus to survive outside its host (e.g. in the air, in excreta, etc.). This phenomenon is particularly relevant to hantaviruses because they are most often transmitted "*ex* *vivo*” or outside the host, since they are transmitted via rodent excreta as opposed to being directly transmitted from rodent to human (Hardestam et al 2007). *In vitro* studies of Puumula hantavirus have shown that PUUV particles can survive in culture at room temperature (23°C) for 5-11 days (Kallio et al 2005). However, when dried, the virus was no longer infectious at room temperature after 24hrs–showing that the moist environment of the culture helped to cushion inactivation (Kallio et al 2005). Both Kallio et al and Hardestam et al showed that in wet environments, there was a negative correlation between temperature and hantavirus’ ability to infect cells. Hardestam et al compared Haantan virus's ability to withstand dried environments to that of two other *bunyaviridae*–Sandfly fever Sicilian virus (SFSV) and Crimean-Congo hemorrhagic fever virus (CCHFV). The results of their study revealed that the hantavirus had not evolved to better withstand dry environments despite its *ex vivo* nature, again suggesting wet conditions are vital to hantavirus’ ability to survive and replicate outside its host (Hardestam et al 2007). The results of these studies are consistent with the weak, positive correlation between precipitation and hantavirus cases found in this study, suggesting hantaviruses favor wet environments for transmission. That being said, how these interactions manifest *in vivo* need to be more closely and directly investigated.

Impact on Reservoir Population Density

One of the most compelling arguments for how climate impacts hantavirus, and zoonotic viruses in general, is how climate impacts reservoir population dynamics. Climate can impact reservoir populations by creating more or less favorable conditions for breeding. Previous studies suggest that dramatic increases in precipitation result in more successful breeding seasons and therefore increased population densities of rodents by increasing food resources for rodents (Gubler et al 2001, Klempa 2009, Luis et al 2009, Tian et al 2017). My results suggest precipitation is higher in the dry season of outbreak years than in non-outbreak years which is consistent with these findings and the hypothesis that increased precipitation increases rodent population densities and therefore the risk of infection. Increased dry season precipitation increases the breeding of rodents and therefore increases the incidence of hantavirus cases in the wet season–as shown by a majority of the cases occurring in the wet season. This phenomenon of cases increasing towards the end of the rainy season was also replicated by Tian et al, who studied the climate and seasonal dynamics of HNTV in central China. Increased population densities of rodents can increase the likelihood of spillover events in a few ways, namely, by increasing the likelihood of contact between rodents and humans and increasing levels of disease in rodent populations in the case the disease is density-dependent (Gubler et al 2001, Klempa 2009, Luis et al 2009, Tian et al 2017). Initial studies of Sin Nombre Virus suggest that SNV is potentially density-dependent (abundance of rodent populations–which can be affected by predation or environmental conditions–was correlated with SNV antibody prevalence), however, how these dynamics apply generally to hantaviruses as a whole and how island geography uniquely influences them is still being explored (Carver et al 2011, Orrock et al 2011).

Impact on Reservoir and Human Behavior

It is hypothesized that when conditions–either climatic or ecosystem quality–are less favorable, rodents are more likely to move into peridomestic spaces (Carver et al 2015, Gubler et al 2001). This behavioral change in rodents can once again increase the likelihood of spillover events by increasing the interface between humans and rodents. Similarly, extreme weather can impact human behavior by increasing the time spent at home or in sheltered areas, increasing the risk of inhalation of rodent excreta (Dearing et al 2010). That being said, it is likely that these effects are dampened in environments that have persistent levels of precipitation, like Barbados (Carver et al 2015). This hypothesis is consistent with the lack of anomalies in precipitation and, therefore, the lack of correlation between anomalies in precipitation and hantavirus in my findings. That being said, Tian et al also experienced interannual oscillations of HFRS, suggesting my findings of cyclic anomalies of hantavirus in Barbados may be worth exploring further and/or attributed to rodent population dynamics.

Causes of Climate Abnormalities

The El Niño Southern Oscillation is a 2-7 year cycle of weather events dictated by ocean surface temperature and pressure differences in the tropical Pacific. Although originating in the tropical Pacific, ENSO can have profound effects on climate, and thus disease, globally (Anyamba et al 2019, Cai et al 2015, Dearing et al 2010). Warmer and wetter years resulting from ESNO are referred to as "El Niño" years whereas "La Niña" years bring cooler temperatures and drought (Dearing et al 2010). The Caribbean is known to experience ENSO effects, most notably increasing dry season precipitation in El Niño years (NOAA). Studies of hantavirus in the Southwestern U.S. have shown that ENSO is often the cause of the extreme precipitation events that increase food resources for reservoir population breeding (Dearling et al 2010). These results are once again consistent with my finding that outbreak years on average had higher dry season precipitation, suggesting a potential influence by ENSO (although detailed, accurate data to confirm this was not available). Additionally, Tian et al found that their observed interannual fluctuations of HFRS were strongly correlated with ENSO patterns. Another source of climate anomalies of ever-present concern is anthropogenic climate change. Climate change is predicted to impact the Caribbean, like many places, in a number of ways– notably increasing temperatures and a potential increase in the intensity and frequency of tropical storms with a varied impact on total precipitation (Reyer et al 2015). Warming attributed to greenhouse gas emissions has been projected to increase the frequency of extreme El Niño and La Niña events if emissions go unchecked (Cai et al 2015). The frequency and intensity of these ENSO events, how they are being impacted by climate change, and how they are impacting hantavirus in Barbados appear to be compelling areas of additional exploration.

Limitations

I believe the main limitation of this study is the amount and accuracy of hantavirus data in Barbados. Barbados is a relatively small study site to produce statistically significant results from. However, I do think distinguishing between the islands of the Caribbean was important taking into account each may have unique ecological interactions occurring because of their geographic separation. Additionally, because of the underdiagnosis of hantavirus due to the practice of symptomology, lack of accessible and affordable testing, and similarity of clinical manifestations of multiple endemic diseases, we must assume that these case numbers are not completely accurate–although they are the most accurate we currently have. Additionally, the exact strain of hantavirus present in Barbados has yet to be isolated, also posing challenges to applying prior knowledge to these results. Additional limitations to the methods of this study include the robustness of the regression and correlation models. Once the main variables impacting human cases of hantavirus in Barbados have been identified, more robust tests that account for these confounding variables may be developed.

Future Directions

These results clearly indicate that interactions between the environment and hantaviruses observed in studies of more northern latitudes are not widely applicable to areas with tropical climates such as Barbados. Although certain findings were consistent with studies from other regions, having consistently warm temperatures and high levels of precipitation greatly dampens how we can assume these trends carry over. Additional analysis revealed the added uniqueness of island geography in particular when discussing reservoir population dynamics. Thus, more studies need to be conducted to address this gap in knowledge. Specifically, I believe the most effective approach would be longitudinal studies in rodents similar to those of Luis et al 2010– studying how different climate measures directly impact the population dynamics of rodents. Additionally, isolating and tracking hantavirus in the rodent populations of Barbados to better understand how these population dynamics impact the levels of virus in said populations. That being said, hantavirus is persistently evasive and continues to be very challenging to isolate and diagnose. Thus, continued research is needed to increase the success and accessibility of testing not only to better understand the dynamics of viral spread but also to reduce disease in these populations. Researchers in Barbados like Dr. Kirk Douglas are currently working towards developing rapid antigen tests and improving RNA sequencing of the hantavirus genome, both of which are very promising in this regard.

Broader Implications

Beyond just a knowledge gap to explore further, understanding how climate impacts disease is an issue of human health and well-being. I believe there is significant evidence to show that the studies done on hantavirus in North America and Europe cannot be holistically applied to LAC populations–leaving these populations in especially vulnerable positions in regard to an extremely morbid disease. Additionally, as we continue to cope with the effects of anthropogenic climate change, understanding these dynamics will become increasingly important to prevent major disease outbreaks. The regions in which hantavirus is well-studied–and therefore are better protected from hantavirus-caused diseases–are the regions responsible for the majority of greenhouse gas emissions. As we discussed, warming scenarios caused by said emissions will contribute to climate changes that could influence the prevalence of disease in the LAC region. More research in these regions where hantaviruses are present and currently affecting human health is important to ensure all populations are equitably protected from the potential of increased disease due to anthropogenic climate change. As discussed, there are many different projections for how climate change looks for different regions, thus, it is important we are well-equipped to cope with these changes.

ACKNOWLEDGEMENTS

Thank you to Dr. Kirk Douglas from the University of West Indies, Cave Hill for not only providing me with his most current data but also for spearheading the work on hantavirus in Barbados–your work is crucial to the public health of not only Barbadians but also global populations. Thank you to the ESPM 175 teaching team for being both an academic and emotional support system through this process and beyond. Thank you to all of the professors I've had over the years that have passed along the knowledge that made me capable of completing a project of this size (too many to name!). Thank you to my "big sister" Joy He for inspiring me to pursue environmental health and being an incredible role model. Lastly, thank you to my family–Mom, Dad, and Grace–for being my stability as I navigated the highs and lows of completing a senior thesis and for encouraging me to see this project through to the end even when I didn't see the light at the end of the tunnel. We made it!

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