Risk of Dengue Transmission in the Metropolitan Area of Mexico City

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ABSTRACT (250-300 words)183

Dengue is endemic to tropical and subtropical regions worldwide, where climate change, human mobility, and urbanization contribute to the expansion of mosquito vector distribution and increase the risk of active transmission in previously unaffected areas.

In Mexico, *Aedes aegypti* mosquitoes are the primary vectors of dengue viruses (DENV-1 to DENV-4) playing a crucial role in local transmission and spread of the disease. Over the past decade, these mosquitoes have established populations within the Metropolitan Area of Mexico City (MAMC) (2240 meters above sea level, with 21,436,911 inhabitants), where national surveillance systems have reported an increase in imported dengue cases. Notably, one case of local transmission was reported in 2023.

Dengue poses the greatest risk in densely populated regions with seasonal rainfall, where *Aedes aegypti* populations frequently interact with infected humans. This study aimed to develop predictive models to identify high-risk scenarios and areas susceptible to active dengue transmission within the MAMC based on bioclimatic variables and epidemiological surveillance data. Our results identified seven municipalities as high-risk areas for active transmission, providing a foundation for enhancing entomological and epidemiological surveillance in this metropolitan area.

AUTHOR SUMMARY

INTRODUCTION

Dengue fever has become an increasingly critical public health concern due to its rapid geographic expansion and growing global burden. Dengue virus infection in humans is often asymptomatic but can present a wide range of clinical spectrum from mild fever to severe and potentially life-threatening illness. Between 2000 and 2019, reported dengue cases surged from 0.5 million to 5.2 million, predominantly in tropical and subtropical regions, where the disease is endemic in over 100 countries (WHO, 2023). In 2024, over 14 million dengue cases and more than 10,000 dengue-related deaths were reported globally. The Americas region alone accounted for over 12 million cases, including 20,056 severe cases and 7,420 deaths (PLISA-PAHO). Brazil has reported the most cases in 2024 (over 10 million) followed by Argentina, Mexico, Colombia and Paraguay.

Dengue viruses comprise four serotypes (DENV1 to DENV4), that are primarily transmitted by the mosquito vectors *Aedes aegypti* and *Aedes albopictus (REF)*. Female mosquitoes acquire the virus during a blood meal by biting a person infected with one of virus serotypes. Transmission occurs if the mosquito feeds during the viremic period when the infected individual has high levels of the virus in their bloodstream. Once ingested, the virus spreads within the mosquito's body over an incubation period of 8–12 days (Extrinsic incubation period). After this, the mosquito

becomes infectious and can transmit the virus to another person during subsequent blood meals. Infected mosquitoes remain capable of transmitting the virus for the remainder of their lifespan, which typically lasts three to four weeks (REF).

The geographic range of dengue has expanded significantly in recent decades and is expected to continue spreading driven by interconnected factors such as climate change, urbanization, population growth and the adaptation of its primary mosquito vectors to new environments (Nakase et al., 2024; Messina et al., 2015; Kramer, 2019). The disease, traditionally confined to tropical and subtropical regions, is now reported in higher-altitude and cooler regions, underscoring its dynamic and evolving nature (Kraemer, 2019; Mexico-Brazil study, 2024). This upward trend in altitude and latitude poses significant challenges for healthcare systems, especially in regions previously unexposed to the disease. For instance, recent outbreaks in high-altitude areas of Nepal, India, Bolivia, and Colombia highlight the urgent need for robust surveillance, prevention, and control strategies (Pallavi Kache, 2024; REF).

Dengue is endemic throughout Mexico, with significant outbreaks occurring every 3 to 5 years. DENV transmission has been reported in 29 of the country´s 32 states, with approximately 80% of cases concentrated in the southeastern region (Dzul, 2021). All four dengue virus serotypes circulate in Mexico, though serotypes 1 and 2 have been the most prevalent over the past decade (Vásquez-Pichardo et al., 2011; Gómez-Dantes et al., 2014). In 2023, the reintroduction of serotype 3 triggered a major outbreak across endemic states (SSA, 2023). While transmission is most intense in areas below 600 meters, outbreaks have also been reported at altitudes above 1,700–2,000 meters in Mexico and ~~other parts of the Americas~~ (Herrera-Basto et al., 1992(Taxco); García-Gutiérrez et al., 2013; Espinosa-Gómez et al., 2021)..

Mexico City (CDMx), the capital of Mexico, along with 56 municipalities from the State of Mexico and one from the State of Hidalgo, forms the Metropolitan Area of Mexico City (ZMCMx). It is home to approximately 21 million people, with a population density of 87.5 inhabitants per hectare. The ZMCM is recognized for its high levels of mobility (Flores-Garrido et al., 2024) and accessibility (CONAPO, 2024). This region is the largest urban center in Mexico and one of the most densely populated in the world, is situated at an average altitude of 2,240 masl. The area has a temperate climate, with seasonal summer rains, an average annual precipitation of 720 mm, and temperatures ranging from -2 to 28°C (INEGI, 2024; SEMARNAT, 2024). Historically, this altitude was considered unsuitable for Aedes aegypti survival. However, recent studies confirm the mosquito's presence in the region (Kuri-Morales et al., 2017; Dávalos-Becerril et al., 2019; Mejia-Guevara et al., 2020). Ae. aegypti populations in the northeastern part of the city remained stable from 2015 to 2018 (Mejia-Guevara et al., 2020).

The establishment of DENV transmission in the ZMCMx can be influenced by the volume of infected returning travelers (with or without symptomatology), the number of detected imported dengue cases, the presence of mosquito vectors, and favorable climatic conditions. Notably, a rise in imported dengue cases has been recorded in the MAMC over the past decade (SINAVE, 2024) and the first autochthonous

dengue case in the area was reported in 2023, although active local transmission has not yet been notified (Arellano-Rivera et al., 2024).

Identifying high-risk areas for dengue transmission is crucial to guide targeted prevention and control efforts. This involves implementing integrated *Aedes* management strategies to prevent dengue establishment and mitigate the likelihood of outbreaks. In this study, predictive models were developed by combining Aedes *aegypti* presence records, imported dengue case data, and climatological information to assess transmission risk and identify vulnerable areas within the metropolitan area of Mexico City.

METHODS

STUDY AREA

The Metropolitan Zone of the Valley of Mexico (ZMCM) encompasses 63 municipalities across Mexico City, the State of Mexico, and Hidalgo, covering an area of 608,852 hectares. It is home to approximately 21 million people, with a population density of 87.5 inhabitants per hectare. The ZMCM is recognized for its high levels of mobility (Flores-Garrido et al., 2024) and accessibility (CONAPO, 2024).

For this study, the urban area of the ZMCM (referred to as Zone M) was delineated as the study area, comprising 33% of the total ZMCM surface (Figure 1, Table 1). This delimitation was based on Meta's Data for Good high-resolution global urban areas database (https://dataforgood.facebook.com/dfg/tools/globalurbanareas). According to Meta's algorithms, global urban areas are defined as land covered by buildings, including residential and industrial zones, roads, and other artificial structures such as railways.

DATA COLLECTION

Epidemiological data.

The database of dengue cases in the Metropolitan Area of the Valley of Mexico (ZMCM) was provided by the Vector-Borne Diseases module (ETVs) to the National Epidemiological Surveillance (SINAVE, for its initials in Spanish) (https://vectores.sinave.gob.mx). Dengue is an illness of mandatory notification in Mexico, it includes variables related to clinical diagnosis (probable, confirmed, clinical presentation), case status (imported or autochthonous), laboratory tests used (serology, PCR, serotype), and patient information (age, sex, place of residence, etc.). Because ZMCMx is an non endemic dengue region in the country, all probable cases are confirmed by laboratory. The residential address of positive cases was used for geocoding through Google's Geocoding API Key (https://developers.google.com/maps/documentation/geocoding/get-api-key).

The geocoded database includes geographic variables (longitude and latitude), year, age, and serotype. For the analysis of the temporal heterogeneity of imported cases, data from 2008 to 2023 were used. For the analysis of non-autochthonous transmission risk, data from the recent dengue serotype 3 epidemic outbreak (2023 and 2024) were employed to align them with entomological data.

Entomological Data.
The entomological database of *Aedes aegypti* in the Metropolitan Area of the Valley of Mexico (ZMCM) was compiled through database consultations and literature reviews. Data sources included the Arthropod Collection of Medical Importance (CAIM) of the Institute of Epidemiological Diagnosis and Reference (InDRE), the Surveillance Module for Species of Medical Importance from the Vector Monitoring System of CENAPRECE (http://geosis.mx/aplicaciones/EspeciesMedicas/), the National Commission for the Knowledge and Use of Biodiversity (CONABIO) (http://www.conabio.gob.mx/web/transparencia.html), and the mosquito dashboard (Uelmen et al., 2023). These were integrated into a unified database containing the geographic coordinates (longitude and latitude) of each record.

FALTA MODELOS, lo debo trabajar con Felipe.

RESULTS

Ae. aegypty presence in the Metropolitan Area of Mexico City (ZMCMx)

The first record of *Ae. aegypti* in the Metropolitan Area of Mexico City (ZMCMx) was documented in 2015 by Kuri-Morales et al. (Ref 2017). Subsequently, other studies reported the presence of *Ae. aegypti* larvae and adult mosquitoes, as well as the emergence of adults from eggs collected through Mexico City's entomological ovitrap surveillance system (Davalos-Becerril et al., 2019; Mejía-Guevara et al., 2020; Sanches-Reyes et al., 2023). Since 2019, the Surveillance System for Species of Medical Importance (VEIM) and the Institute of Epidemiological Diagnosis and Reference (InDRE) have also documented the presence of *Ae. aegypti* in the ZMCMX, supported by entomological evidence of larvae and adult mosquitoes (see Table 1).

Comentado [vp1]: Reporta huevos y adultos...ello no esta en la tabla

The reports of *Ae. aegypti aligns* with data from ovitrap surveillance in Mexico City (Figure 2). Unfortunately, this data is not continuous in the time, during the COVID-19 pandemic stop the register. Ovitrap records began in 2013, revealing the collection of eggs from *Ae. aegypti* and *Ae. epactius*. From 2013 to 2018, the prevalence of positive ovitraps for remained at 4% or less. In 2019, the maximum reported prevalence increased to 6%, reaching 8% by 2024. It has been noted that the percentage of *Ae. aegypti* in ovitraps is approximately %? (REF).

Our findings suggest that, although entomological surveillance for the primary dengue virus vector, *Aedes aegypti*, in the ZMCM are not constant, the available data indicate that its low-level presence remains steady in certain areas of the metropolitan region. However, it is essential to monitor its presence regularly across different seasons of the year, to clarify if Ae. Aegypty population is stablish in the ZMCMx or entry every year from regions near to the metropolis with active dengue transmission (presence of vectors and reported dengue cases).

Imported dengue cases notified in the ZMCMx

Travelers infected with the dengue virus during their trips can pose a risk to the local population upon returning home in ZMCMx, especially in areas where the primary urban vector, *Aedes aegypti* is present. In regions without autochthonous dengue virus transmission, reporting of dengue cases to health services is mandatory and 100% of probably dengue cases must be laboratory-confirmed (REF). ~~To analyze the dynamics of imported dengue cases in ZMCMX, data were obtained from the epidemiological surveillance system (SINAVE) as described in methodology.~~

Approximately 1,000 imported cases were reported during the study period, with 600 providing complete travel information. The figure 3A illustrates the distribution of dengue cases by year, period, and locality within Mexico City and the municipalities of the State of Mexico and Hidalgo that constitute the ZMCMx. The data reveal a heterogeneous spatial and temporal pattern of dengue importation. Between 2008 and 2024 the boroughs of Iztapalapa, Gustavo A. Madero, and Coyoacán in Mexico City, along with the municipalities of Ecatepec, Naucalpan, Nezahualcóyotl, and Tlalnepantla in the State of Mexic, reported the highest number of imported cases. In 2023, 55% of ZMCMx municipalities and 93.7% of Mexico City boroughs reported at least one imported case, rising to 61% and 87.5%, respectively, in 2024. Six boroughs recorded 15 or more cases in 2023: Benito Juárez, Iztapalapa, Tlalpan, Cuauhtémoc, Gustavo A. Madero, and Álvaro Obregón. By mid-October 2024, the number of affected boroughs had doubled, with new cases reported in Ecatepec, Coyoacán, Azcapotzalco, Iztacalco, Tláhuac, Naucalpan, and Nezahualcóyotl. Figure 3B highlights fluctuations in confirmed imported dengue cases, increasing from 8 in 2008 to 522 in 2024. All serotypes were detected in 2023 and 2024, with DENV-3 being the most prevalent, reflecting its epidemiological dominance in Mexico over the past two years. During the transmission periods of serotypes 1 and 2 (2008–2019) and the COVID-19 pandemic (2020–2022), case importation remained relatively stable, apart from peaks in 2012–2013, 2016, and 2019, linked to dengue outbreaks. An increase in imported cases was noted during the transmission period of DENV-3 (2023–2024). DENV-4 cases were reported in 2014, 2021, and 2023. Figure 3 C demonstrated that most dengue imported cases occurred during the rainy season in the second half of the year epidemiological week (?-?), with peak years recorded in 2019, 2023, and 2024, in concordance with dengue epidemiology in the country. These findings indicate a steady increase in imported dengue cases over the study period, with a significant rise in the last two years.

Destination and Origen of imported dengue cases

To evaluate the flow of travelers from the ZMCMx and their places of infection, a Sankey diagram was created to visualize the origin and destination of imported dengue cases concerning the distance from the place of residence. Figure 4 shows that imported dengue cases are reported across all municipalities, originating from

various cities in states with active dengue transmission, both near and far from the ZMCMx.

The municipalities with the highest number of imported cases are Iztapalapa (12%), Gustavo A. Madero (11%), Benito Juárez (10%), Coyoacán (10%), and Cuauhtémoc (9%), while La Magdalena Contreras and Milpa Alta report the fewest cases. Regarding the distance of places of infection, three travel patterns are observed: short-distance, medium-distance, and long-distance travel. Short-distance travel, accounting for 26% of imported cases, involves trips of less than 250 km to eight states (Guanajuato, Guerrero, Hidalgo, Michoacán, Morelos, State of Mexico, Puebla, and Querétaro), with the majority linked to tourist destinations in Morelos (70%), Puebla (12%), and Guerrero (11%). Medium-distance travel (250–500 km) represents 47% of cases, spanning 11 states (Aguascalientes, Guanajuato, Guerrero, Jalisco, Michoacán, Oaxaca, Puebla, San Luis Potosí, Tamaulipas, and Veracruz). At this range, the highest contributions come from Guerrero (43%), Veracruz (21%), and Oaxaca (20%). Long-distance travel accounts for 28% of imported cases, originating from 16 states, primarily Oaxaca (31%), Guerrero (10%), Yucatán (10%), Quintana Roo (9%), Chiapas (8%), and Jalisco (8%).

Overall, regardless of travel distance, this visualization identifies four states with the highest number of trips, which also contribute the most to imported dengue cases reported in the ZMCMx: Guerrero (25%), Morelos (18%), Oaxaca (18%), Veracruz (11%).

Epidemiological Scenarios of transmission. Revisar el la redacción.

The epidemiological scenarios obtained through PCA and cluster analysis (Figure 3F) identify the boroughs of Cuauhtémoc, Benito Juárez, Coyoacán, Miguel Hidalgo, Azcapotzalco, Venustiano Carranza, Iztacalco, and Iztapalapa as areas of very high risk for the invasion or establishment of autochthonous dengue transmission in the ZMCM. These boroughs constitute 7% of the total area, where 24% of the census population (20,674,746) resides in 43,036 city blocks (26% of the total blocks). In the high-risk areas, the disease burden was 41% in 2023 and 40% in 2024.
Moreover, the maximum temperature in the very high-risk area exceeded 20°C for most of the year, except from mid-April to mid-June and mid-November to December (Figure 4). The maximum temperature in the high-risk area was consistently higher than in the very low-risk area throughout 2023 (with positive coefficients) (Figure 4). These temperatures facilitate the adaptation, establishment, and dispersion of the vector in the ZMCM (as indicated by the prevalence of positive ovitraps, which has increased from 4% to 6% over the years) and support its presence for most of the year (Figure 5)."

Comentado [vp2]: Esto en Amarillo es lo que traduje de la versión de Nov 23...pero según yo, esto ha cambiado, podrías enviarme una descripción actualizada

Los escenarios de epidemiológicos obtenidos con el PCA y el clúster análisis (Figura 3F), identifican a las alcaldías de Cuauhtémoc, Benito Juárez, Coyoacán, Miguel Hidalgo, Azcapotzalco, Venustiano Carranza, Iztacalco e Iztapalapa como áreas de

muy alto riesgo para la invasión o el establecimiento de transmisión autóctona del dengue en ZMCM. Este grupo de alcaldías constituyen el 7% del total de área donde vive el 24% de la población total censada (20,674,746) en 43036 manzanas (26% del total de manzanas). En el área de alto riesgo la carga de la enfermedad fue del 41% y del 40% para el 2023 y 2024, respectivamente. Así mismo, la temperatura máxima en el área de muy alto riesgo fue superior a 20°C durante la mayor parte del año, excepto entre mediados de abril a mediado de junio y mediados de noviembre a diciembre (Figura 4). La temperatura máxima del área de alto riesgo fue mayor que el área de muy bajo riesgo durante todo el año del 2023 (coeficientes mayores a 0) (Figura 4). Estas temperaturas permiten que el vector se adapte, establezca y disperse en el ZMCM (la prevalencia de ovitrampas positivas se ha incrementado con el paso de los años de 4% al 6%) y se presente durante la mayor parte del año (Figura 5).

Temperature and Epidemiological risk of dengue transmission

Recognizing that temperature is a critical factor in the development of the Aedes aegypti vector, the fluctuation of weekly maximum temperatures was analyzed in relation to the epidemiological risk scenarios for the establishment of active dengue transmission in the ZMCMx.

Figure 6A presents the daily maximum temperature profiles for 2023 and 2024. The data indicate that maximum temperatures exceeded 25°C for most of the year, except from mid-April to mid-June and mid-November to December. The highest temperature peaks were recorded in March and July, surpassing 30°C.

The results of the Generalized Linear Model (GLM) suggest that maximum temperatures in high-risk areas were consistently higher than in very low-risk areas throughout 2023 (this is supported by positive coefficients, as credible intervals did not include zero). These findings support the scenarios of risk transmission in the ZMCMx, however, it is necessary generate more data about the presence of vector in the city as well measure of vectorial competence of the mosquitoes adapted to grown at high altitude (2,240 masl).

DISCUSSION

The One Health approach has emerged as a critical paradigm, recognizing the intrinsic connections between human, animal, and environmental health. Rising global temperatures have expanded the dissemination of *Aedes aegypti* mosquitoes, increasing the risk of transmitting pathogens as dengue, chikungunya, and Zika virus in previously unaffected areas. This study aimed to identify high-risk scenarios and areas susceptible to active dengue transmission within the Metropolitan Area of Mexico City (MAMC), using bioclimatic variables and epidemiological surveillance data. Spatial analysis revealed seven municipalities as high-risk areas, with more clusters higher relative risks identified.