JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Dengue on the rise in Encarnación, Paraguay (2023–2024): an emerging threat to regional transmission dynamics

Diana P Dressler[1,3], Mónica M González[1,2], Andrea Gómez de la Fuente[3], Cesar A Cantero[3], Tania M Alfonzo[3], Victor H Aquino[4]

[1] Facultad de Medicina, Universidad Nacional de Itapua, Paraguay
[2] Laboratorio de Biología Molecular, Hospital Regional de Encarnación, Paraguay
[3] Laboratorio Central de Salud Pública, Asunción, Paraguay
[4] Departamento de Inmunología, Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Asunción, San Lorenzo Paraguay

Abstract

Introduction: Dengue remains a public health concern in Paraguay. Paraguay's 2023–2024 epidemic was examined, emphasizing on the Itapua department in the southern region bordering Argentina.

Methodology: This retrospective, cross-sectional observational study analyzed confirmed dengue cases from 17 September 2023, to 4 May 2024. Demographic and clinical data of the participants were gathered from Paraguay's national surveillance system.

Results: Among the 307,058 suspected dengue cases reported, 77,675 were confirmed through laboratory testing. The Itapua department contributed 8,310 (2.7%) and 1,910 (2.5%) of the suspected and confirmed cases; pediatric cases comprised 33% nationwide and 35% in Itapua. Intensive care needs were higher in Itapua (n = 18, 11.2%) than in other Paraguayan regions (n = 152, 2.0%). Mortality rates were also elevated in Itapua (n = 11, 0.6%) compared to the national average (n = 95, 0.13%). DENV-1 and DENV-2 were responsible for this epidemic. Encarnacion, the capital of Itapua State and a neighboring city to Posadas, Argentina, was the most severely affected (1,262 reported cases).

Conclusions: The elevated rates of pediatric cases, intensive care admissions, and mortality in Itapua highlight the need for multicomponent health strategies, including enhanced vector control through community-led *Aedes aegypti* elimination programs and insecticide residual spraying in high-incidence zones, vaccination campaigns targeting high-risk pediatric populations with World Health Organization (WHO)-approved dengue vaccines (e.g., TAK-003), and cross-border collaboration with Argentina (e.g., Posadas-Encarnacion) to synchronize outbreak surveillance, share real-time epidemiological data, and coordinate vaccine deployment in binational hotspots.

Key words: dengue; epidemic; Itapua.

J Infect Dev Ctries 2025; 19(11):1694-1704. doi:10.3855/jidc.21624

(Received 19 March 2025 – Accepted 06 August 2025)

Introduction

Dengue is a viral illness primarily spread by the *Aedes aegypti* mosquito, posing a significant threat to public health in tropical and subtropical regions around the world. Dengue virus (DENV) circulation in Paraguay has been characterized by cyclical outbreaks involving multiple serotypes, reflecting its endemic status. The country has experienced repeated waves of dengue in recent decades that are influenced by both local conditions and regional viral dynamics. The complexity of dengue control in Paraguay is heightened by the country's geographical, environmental, and socio-economic factors, exacerbating the transmission risks [1].

Dengue is caused by one of four serotypes (DENV-1, DENV-2, DENV-3, DENV-4) and manifests in a range of clinical symptoms, from mild, flu-like discomfort to severe complications like dengue hemorrhagic fever and dengue shock syndrome. According to the Pan American Health Organization (PAHO), the Americas witnessed a historic dengue outbreak in 2023, with over 4.5 million cases, particularly severe in Southern Cone countries such as Brazil, Paraguay, and Argentina, including 7,665 severe cases and 2,363 deaths. This alarming trend continued into 2024, with cases surpassing 8.9 million by epidemiological week 22, more than triple the figures from the previous year [2]. The growing number of severe cases and fatalities underscores the region's vulnerability to dengue epidemics.

Paraguay's battle with dengue dates back to the late 1980s, when the country's first major outbreak, caused by DENV-1, resulted in over 40,000 cases [3,4]. Over the subsequent decades, dengue became endemic with multiple serotypes introduced, particularly through neighboring Brazil [5–10]. The cross-border movement

of people and the geographical closeness facilitated the reintroduction of different viral strains, compounding the difficulty of outbreak management.

One of the most severe dengue outbreaks in Paraguay occurred in 2013, overwhelming the healthcare system as hospitals struggled to manage over 150,000 suspected cases and 250 deaths, primarily due to the prevalence of DENV-2 [11]. Similarly, the 2019-2020 epidemic, driven largely by DENV-4, resulted in over 160,000 suspected cases and 75 deaths, with nearly 94% of confirmed cases attributed to this serotype [12]. This outbreak spread extensively across urban and rural areas, severely damaging medical infrastructure and underscoring the urgent need for enhanced public health preparedness.

Despite ongoing control efforts, dengue remains a significant challenge in Paraguay. The adaptability of the *Aedes aegypti* mosquito, persistent viral circulation, and the rise in severe dengue cases, demand a comprehensive, multi-pronged approach to management.

The rising number of dengue cases in Itapua, a southern department bordering Argentina, underscores the critical importance of enhanced surveillance and disease monitoring. The area's environmental conditions, such as high rainfall and urban water storage practices, create an ideal habitat for *Aedes aegypti*, the mosquito vector responsible for transmitting dengue.

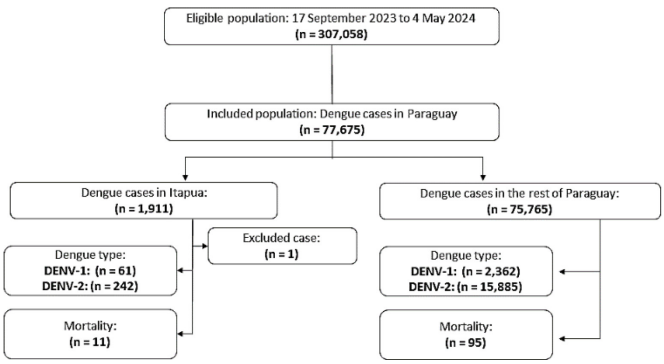
In this study, the 2023–2024 dengue epidemic in Paraguay was examined, with a particular focus on the Itapua region, to assess the potential impact of cross-border dengue transmission between Paraguay and neighboring Argentina.

Methodology

Study design

This retrospective, observational study with cross-sectional analysis was conducted from 17 September 2023 to 4 May 2024, at the Regional Hospital of Encarnacion in the Itapua Department, Paraguay (coordinates: 27°20'28"S 55°51'35"W.). This tertiary care hospital serves 500,000 patients monthly from various districts within the Itapua Department. The sampling method was consecutive sampling, which allowed the inclusion of all suspected dengue cases during the study period. The demographic and clinical characteristics of these patients were subsequently compared with those of patients from other regions across the country.

Figure 1. Patients' selection.



Study population

Patients of all ages with suspected dengue who sought medical care were eligible for inclusion. A suspected case is defined as any person who presents with a fever lasting 2 to 7 days, without apparent focal signs, accompanied by two or more of the following clinical manifestations: nausea, vomiting, rash, itching, myalgia, arthralgia, headache, retro-ocular pain, petechiae, leukopenia, any warning sign and/or any criterion of severe dengue. Inclusion criteria required laboratory confirmation of dengue through positive NS1 protein, real-time reverse transcriptase polymerase chain reaction (RT-PCR) for RNA, and/or IgM-IgG serology tests, along with an epidemiological correlation, classifying them as dengue cases. Patients with insufficient data on these criteria were excluded from the study.

The data for the participants managed at the Regional Hospital of Encarnacion during the study period were obtained from the General Directorate of Health Surveillance database, Ministry of Public Health and Social Welfare. Patient information from other regions of the country was extracted from the weekly reports published by the same Directorate, which did not include symptom data. Symptom data for dengue cases at the national level were unavailable in the database used for this study.

Description of the dengue epidemic in Paraguay: geographical, climatic, socioeconomic, and demographic context.

Characteristics of the dengue epidemic in Paraguay were obtained from national surveillance data and epidemiological reports provided by the Ministry of Health [13], General Directorate of Health Surveillance (IT-DGVS), General Directorate of Statistics, Surveys, and Censuses of Itapua [14], and the Climatological Yearbook [15,16].

Data analysis and interpretation

Tables and graphs were employed for the description of variables. Categorical variables were presented as both absolute and relative frequencies. Quantitative variables were summarized using measures of central tendency (mean and median) and dispersion (standard deviation and interquartile range). The data were entered into a form created specifically for this study using the statistical program Epi Info v7.2.4.0 for analysis. Bivariate analysis was performed using Chi-square tests, with a significance level set at $p < 0.05$.

The standardized morbidity ratios (SMRs) were calculated for four age groups, children (0–14 years), young individuals (15–29 years), adults (30–59 years), and the elderly (60 years or older), in Itapua and nationwide. The SMRs were calculated using the indirect standardization method. This method is based on the age-specific population distribution and compares the observed number of dengue cases in each age group with the expected number of cases. The expected cases were calculated for a population of 100,000. The expected number of cases was calculated by multiplying the age-specific population distribution by the overall incidence rate of dengue.

Ethics statement

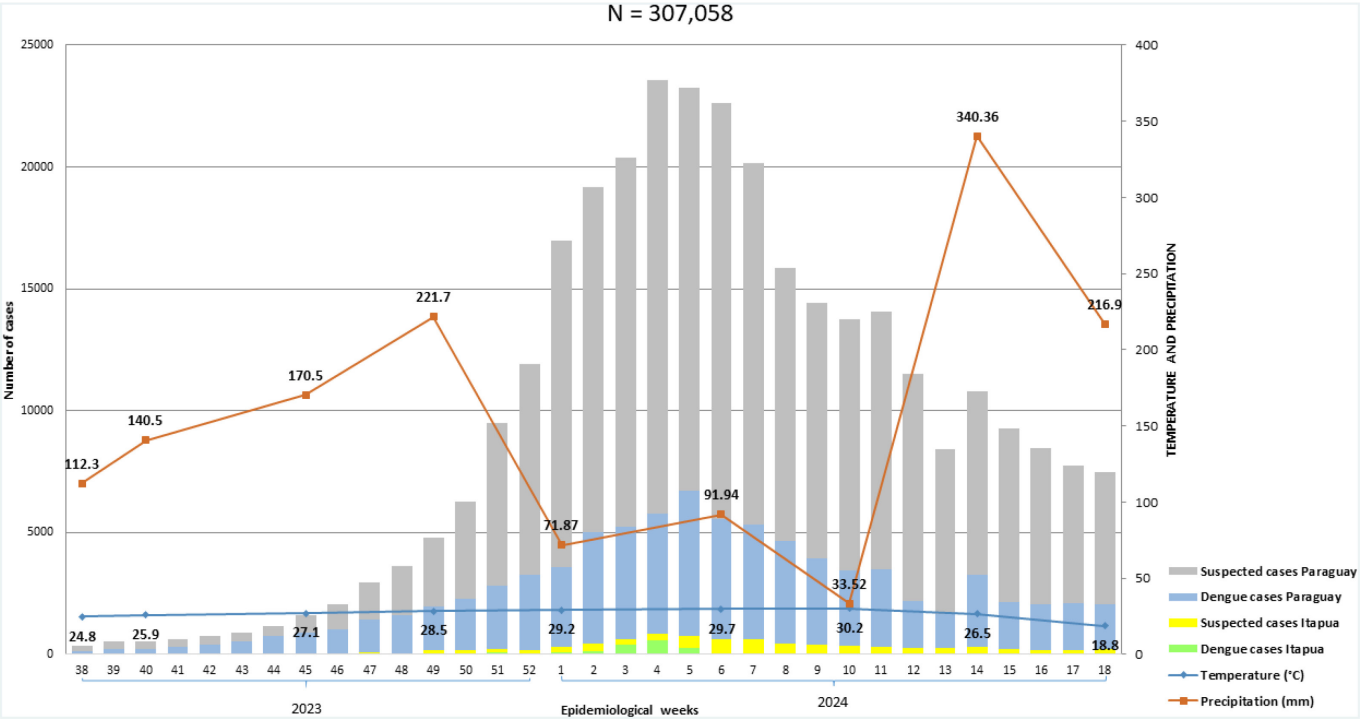
This study adhered to the principles outlined in the Declaration of Helsinki, ensuring ethical conduct throughout the research process. Participants' data records were thoroughly de-identified to ensure complete anonymity, protecting their privacy and confidentiality. The requirement for informed consent was waived because this was a descriptive and retrospective study, and the privacy and confidentiality of clinical data and the subjects involved were assured. The Ethical Committee of the Central Laboratory of Public Health reviewed and approved this study on 26 August 2024 (CEI-LCSP 249-2024).

Results

Characteristics of the study population

A total of 307,058 suspected dengue cases were reported in Paraguay between 17 September 2023, and 4 May 2024 and they formed the eligible population for the study. Of these, 77,675 cases met the inclusion criteria and were confirmed as dengue. The Regional Hospital of Encarnacion managed 8,310 suspected dengue cases during the same period, with 1,911 confirmed diagnoses. One individual was excluded due to incomplete data (Figure 1).

Figure 2. Seasonal distribution of dengue cases in Paraguay and the Itapua Department, from epidemiological week 38 of 2023 to epidemiological week 18 of 2024.



Correlation with total monthly precipitation and average temperature [14,15].

The participants had a median age of 28.7 years (Q1:17, Q3: 56), and 54.9% were female. Table 1 provides a comprehensive overview of the characteristics of the study population.

Distribution of dengue cases during the study period

The incidence of dengue in Paraguay followed a typical epidemic curve, with cases beginning to rise toward the end of spring, coinciding with the onset of warmer temperatures (average 28.5°C) and increased rainfall (from 112.3 mm at the beginning of spring up to 221.7 mm at the beginning of summer). The number of cases peaked in summer (epidemiological weeks 3–6, 2024), when the lowest precipitation levels were observed, and began to decline in early autumn as temperatures cooled (average of 26.5 °C). The Itapua department accounted for 2.7% of the nation's reported dengue cases, displaying a similar seasonal distribution pattern (Figure 2).

Description of dengue cases in Itapua and nationally

In this study, 59% (n = 1,118) of the participants from Itapua were female, while 41% (n = 792) were male. The gender distribution was similar nationally, with 54.7% (n = 41,498) of the participants being female and 45.7% (n = 34,627) male.

The participants from Itapua had a median age of 27.7 years (Q1: 11, Q3: 42), while the national median age was 28.7 years (Q1: 17, Q3: 56).

Table 2 summarizes the observed and expected dengue cases, populations at risk, and SMRs across four age groups in Itapua and nationally: children (0–14 years), young (15–29 years), adults (30–59 years), and elderly (60+ years). Dengue cases among children doubled expectations in Itapua (SMR = 2.0), while the cases exceeded expectations nationally (SMR = 19.17), indicating a disproportionately high burden. Among young individuals, Itapua showed a moderately elevated burden (SMR = 1.3), with a significant but lower national burden (SMR = 12.27). Adults in Itapua experienced nearly triple the expected cases (SMR = 2.8), with the highest and most disproportionate impact nationally (SMR: 33.5). The elderly were the least affected, with the lowest SMRs in both regions.

The most common clinical manifestations among the Itapua participants were fever (82.8%), headache (59.6%), and nausea (52.1%). Data on clinical manifestations at the country level were unavailable (Table 3).

The frequency of cases with comorbidities was similar in Itapua (6.7%) and nationwide (7.1%). Likewise, the rate of pregnant women during the period

Table 1. Characteristics of the study population (n = 77,675).

Characteristics	n (%)
Age (years) Median (Q1–Q3)	28.7 (17–56)
Gender	
Female	42616 (54.9)
Male	35419 (45.6)
Presenting comorbidities	5254 (6.8)
Pregnant	354 (0.5)
Outpatients	70029 (90.2)
Inpatients	7635 (9.8)
Intensive care unit (ICU) patients	170 (0.2)

Table 2. Comparison of dengue cases, population, expected cases, and standardized morbidity ratios (SMR) between Itapua and national levels across age groups.

Age Group	Age (years)	Itapua (n = 1910) (%)						National (n = 75765) (%)					
		Female	Male	Total	Total population	Expected cases	SMR	Female	Male	Total	Total population	Expected cases	SMR
Children	0–4	82 (4.3)	80 (4.2)	162 (8.5)	196492	339.2	2	2813 (3.7)	3088 (4.0)	5901 (7.7)	1916798	1327.1	19.1
	5–10	130 (6.9)	125 (6.6)	255 (13.5)				4959 (6.6)	5379 (7.1)	10338 (13.7)			
	11–14	103 (5.2)	147 (7.7)	250 (12.9)				4185 (5.5)	5014 (6.6)	9199 (12.1)			
				667 (34.9)						25438 (33.6)			
Young	15–19	90 (4.8)	61 (3.2)	151 (8.0)	128908	237.4	1.3	3361 (4.4)	3158 (4.1)	6519 (8.5)	1226896	992.5	12.2
	20–24	111 (5.9)	44 (2.4)	155 (8.3)				3316 (4.4)	2342 (3.1)	5658 (7.5)			
				306 (16.0)						12177 (16.1)			
Adults	25–29	98 (5.1)	58 (3.1)	156 (8.2)	279323	287.1	2.8	3634 (4.8)	2365 (3.1)	5999 (7.9)	3345292	979	33.5
	30–34	96 (5.0)	41 (2.2)	135 (7.7)				3527 (4.7)	2291 (3.0)	5818 (7.7)			
	35–39	87 (4.5)	38 (1.9)	125 (6.4)				3016 (4.0)	2055 (2.7)	5071 (6.7)			
	40–44	64 (3.3)	35 (1.9)	99 (5.2)				2649 (3.5)	1867 (2.5)	4516 (5.5)			
	45–49	46 (2.4)	24 (1.3)	70 (3.7)				2003 (2.6)	1291 (1.7)	3294 (4.3)			
	50–54	52 (2.7)	30 (1.6)	82 (4.3)				1829 (2.5)	1109 (1.4)	2938 (3.9)			
	55–59	44 (2.3)	31 (1.6)	75 (3.9)				1619 (2.2)	1066 (1.4)	2685 (3.6)			
	60–64	38 (1.9)	22 (1.1)	60 (3.0)				1459 (1.9)	972 (1.3)	2431 (3.2)			
				802 (42.0)						32752 (43.2)			
Elderly	65–69	26 (1.3)	27 (1.4)	53 (2.7)	38030	355	0.4	1130 (1.4)	805 (1.1)	1935 (2.5)	533362	1012.1	5.3
	70–74	23 (1.2)	15 (0.8)	38 (2.0)				859 (1.2)	627 (0.8)	1486 (2.0)			
	75–79	8 (0.4)	10 (0.5)	18 (0.9)				527 (0.7)	406 (0.5)	933 (1.2)			
	≥ 80	20 (1.0)	6 (0.2)	26 (1.2)				626 (0.8)	418 (0.5)	1044 (1.3)			
				135 (7.1)						5398 (7.1)			
Total					642753						7022348		

Table 3. Symptoms presented by the participants of the Itapua department.

Symptoms	Itapua (n = 1910) (%)
Fever	1583 (82.8)
Headache	1140 (59.6)
Nausea	997 (52.1)
Myalgia	943 (49.3)
Vomiting	767 (40.1)
Retro-orbital pain	622 (32.5)
Arthralgia	553 (28.9)
Rash	231 (12.1)
Severe abdominal pain	51 (2.6)
Petechiae	37 (1.9)
Mucosal bleeding	33 (1.7)

was below 1% (Table 4).

Most dengue cases were managed on an outpatient basis receiving care without hospitalization. The need for intensive care was significantly (p = 0.033) higher in Itapua, where 11.2% of patients required intensive care unit (ICU) admission, compared to 2.0% in other regions of Paraguay. The prevalence of comorbidities among patients who died from dengue was 96.8% nationwide and 72.7% in Itapua, which was statistically significant (p < 0.096). Cardiovascular disease was the most frequently reported comorbidity, followed by obesity (Table 4). DENV-1 and DENV-2 were the viruses responsible in the country for the 2023–2024 dengue epidemic, with DENV-2 (87%) being the predominant strain. A similar distribution was observed in Itapua, where DENV-2 represented 79.8% of the cases (Table 5).

Dengue cases in the Itapua were reported mainly in Encarnacion (n = 1262), Cambyreta (n = 490), and San Juan del Parana (n = 41). Figure 3 shows the geographic distribution of dengue cases in the Itapua Department.

Most dengue cases in Encarnacion were reported in the central area (Figure 4 and Table 6).

Table 4. Characteristics of dengue cases in Itapua department and nationally

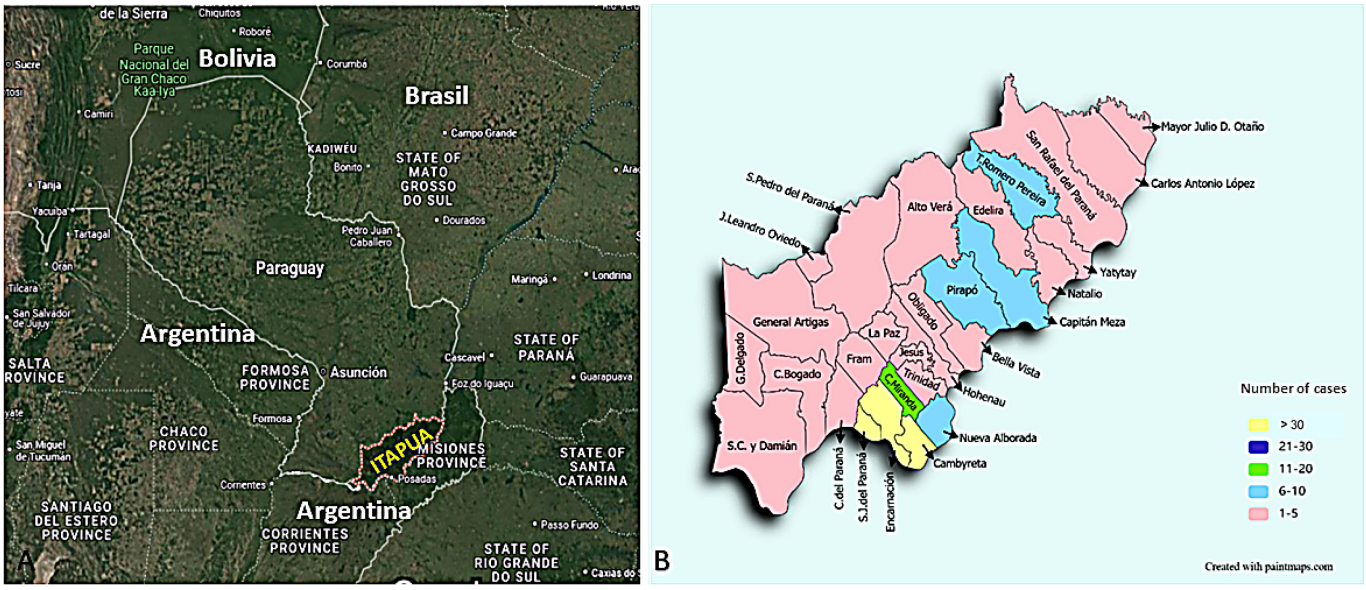
Characteristics	Itapúa (n = 1910) (%)	National (n = 75765) (%)
Outpatients	1750 (91.6)	68279 (90.1)
Inpatients	160 (8.4)	7475 (9.8)
ICU patients	18 (11.2)	152 (2.0)
Presenting comorbidities	134 (7.1)	5120 (6.7)
Pregnant women	10 (0.6)	344 (0.45)
Mortality	11 (0.6)	95 (0.13)
Presenting comorbidities	8 (72.7)	92 (96.8)
Cardiovascular disease	4 (50)	25 (27.1)
Obesity	2 (25)	20 (21.7)
Diabetes	1 (12.5)	17 (18.4)
Immunosuppression	0	6 (6.52)
Chronic kidney disease	1 (12.5)	5 (5.43)
Neurological disease	0	5 (5.43)
Chronic pulmonary disease	0	3 (3.26)
Malnutrition	0	3 (3.26)
Alcoholism	0	3 (3.26)
Smoking	0	2 (2.17)
Chronic liver disease	0	2 (2.17)

ICU: intensive care unit.

Table 5. Comparison of DENV serotypes distribution in Itapua department and other regions of Paraguay.

DENV type	Itapúa (303) (%)	National (18247) (%)
DENV-1	61 (20.1)	2362 (13)
DENV-2	242 (79.8)	15885 (87)

Figure 3. Geographic distribution of dengue cases in Itapua, Paraguay. (A) map of Paraguay and neighboring countries, highlighting the location of the Itapua department. (B) political division of Itapua, with districts colored according to the number of reported dengue cases.



Maps were created using Google Earth [17] and Paintmaps [18].

Table 6. Dengue cases in Encarnacion's neighborhoods.

Encarnacion's neighborhoods	Dengue cases	Case start date	Case end date
San Pedro	235	9/18/23	4/28/24
San Isidro	176	10/2/23	4/20/24
Pacu Cua	98	11/1/23	4/14/24
Chaipe	71	11/9/23	4/21/24
San Roque Gonzalez	51	11/16/23	2/27/24
Ita Paso	48	10/30/23	3/15/24
Ka'aguy Rory	36	12/18/23	4/27/24
Sagrada Familia	35	12/21/23	4/29/24
Santo Domingo	34	12/25/23	3/16/24
Hospital	33	11/7/23	3/29/24
Catedral	24	12/2/23	3/26/24

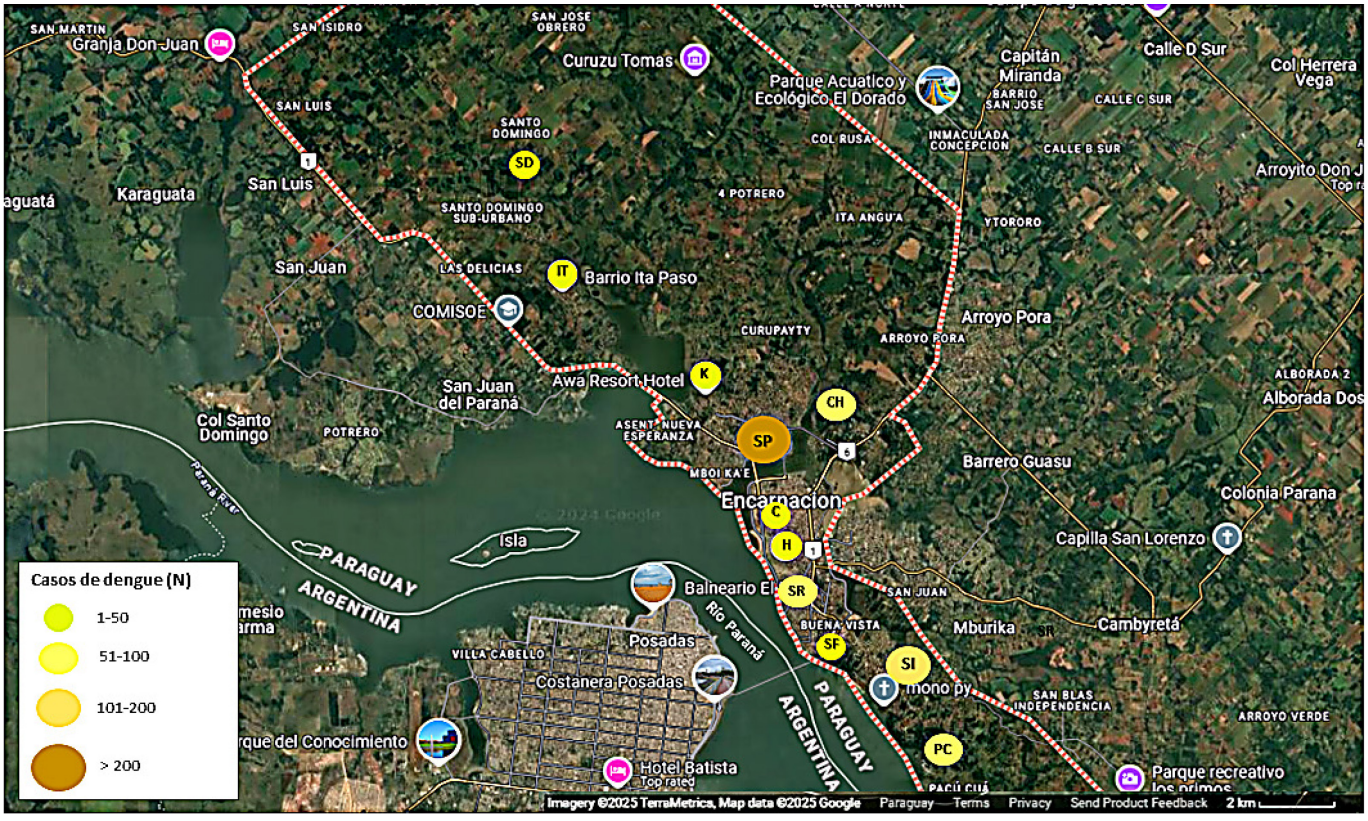
Discussion

The 2023–2024 dengue epidemic in Paraguay reached unprecedented levels, particularly in the Itapua Department, and marked the largest outbreak in the country since the virus was first documented. With 307,058 suspected cases, the epidemic nearly doubled the scale of the previous major outbreak in 2019–2020, which had recorded over 160,000 suspected cases [12,13]. This surge reflects broader trends across Latin America. In 2023, the Pan American Health Organization (PAHO) reported a record-breaking dengue outbreak across the Americas, with over 4.5 million cases, including 7,665 severe cases and 2,363 deaths. By mid-2024, dengue cases had exceeded 8.9 million, which is more than three times the previous year's figures [2]. These alarming statistics underscore the growing threat of dengue throughout the region.

Table 2 shows that children and adults experienced the highest dengue burden in both Itapua and nationwide, with SMRs far exceeding expectations, particularly among adults (SMR = 2.8 in Itapua; 33.5 nationally). The elderly had the lowest incidence. These findings underscore the importance of age-targeted interventions, particularly for school-aged children and working adults, in reducing transmission and severe outcomes.

This study underscores significant regional disparities in dengue severity and clinical outcomes

Figure 4. Geographic distribution of reported dengue cases (n = 1262) in Encarnacion.



The map was based on a satellite image available on Google Maps [19].

across Paraguay, with Itapua emerging as a hotspot for severe disease. While the majority of dengue cases nationwide were managed in outpatient settings, the rate of ICU admission in Itapia (11.2%) was higher than in other regions (2.0%); a statistically significant difference ($p = 0.033$). This finding suggests possible delays in diagnosis, differences in viral virulence, higher transmission pressure, or limited access to early supportive care in this border region. The increased demand for intensive care highlights the need for enhanced local preparedness and targeted resource allocation.

Comorbidities were overwhelmingly present among fatal cases, affecting 96.8% of patients nationwide. In contrast, 72.7% fatal cases in Itapua had documented comorbid conditions, a difference approaching statistical significance ($p < 0.096$). Cardiovascular disease and obesity were the most common underlying conditions, consistent with global evidence linking these risk factors to severe dengue through mechanisms such as heightened vascular permeability and immune dysregulation. The relatively lower prevalence of comorbidities among fatal cases in Itapua may reflect underreporting, different demographic profiles (e.g., younger patients), or possible circulation of more virulent viral strains in the region, hypotheses that merit further investigation.

Cross-border transmission remains a significant concern, particularly as underreporting likely obscures the true number of cases. Although Paraguay is a landlocked country with a relatively low volume of international air travel, its porous borders and high levels of land-based mobility with neighboring countries facilitate frequent viral exchange. Historically, Paraguay has functioned as a recipient and a source of dengue virus introductions in the Southern Cone. In the early 2000s, major dengue epidemics in Paraguay were fueled by viral strains introduced from neighboring Brazil. Conversely, Paraguay later served as the origin of dengue outbreaks in Buenos Aires, Argentina, highlighting its role in regional dissemination [19,20]. Additionally, phylogenetic evidence shows shared DENV strains between Paraguay, Argentina, and Bolivia during past outbreaks, confirming bidirectional viral flow [8]. This underscores the importance of coordinated surveillance and response strategies across national borders.

While Asunción and its metropolitan area have traditionally been the epicenter of dengue outbreaks in Paraguay, the recent epidemic spread to nearly all regions. The Itapua department saw 8,310 reported cases, more than double the 3,529 cases recorded during the 2020 outbreak [21]. Encarnacion, the department's capital, with its metropolitan area, accounted for over 20% of these cases. Its proximity to Argentina raises concerns about cross-border transmission, particularly given the extensive daily interactions between Encarnacion and the neighboring city of Posadas in Misiones Province. These cities are connected by a bridge over the Paraná River, facilitating trade, work, and tourism. During the peak summer season, Encarnacion welcomed an estimated 25,000 to 30,000 tourists every weekend, creating a high-risk environment for disease transmission. Argentina reported 120,007 dengue cases in 2023–2024, including 23,537 cases in Misiones Province, between week 31 of 2023 and week 18 of 2024 [22,23]. Some of these cases were likely introduced by Encarnacion, highlighting the urgent need for enhanced cross-border surveillance and cooperation.

The dengue outbreak in Encarnacion exhibited a heterogeneous spatial distribution, with certain neighborhoods being disproportionately affected. San Pedro emerged as the primary epicenter, accounting for the highest number (n = 235) and longest duration of dengue cases. San Pedro's large population (approximately 11,500 inhabitants) may have contributed to the prolonged outbreak activity.

The San Isidro neighborhood followed closely behind San Pedro in terms of case count and outbreak duration, despite its relatively small population of 3,445 inhabitants. This disparity underscores the significance of factors beyond population size in shaping dengue transmission dynamics.

In contrast, other neighborhoods exhibited different patterns. While the number of cases generally correlated with population size in some areas, more urban neighborhoods like Catedral and Hospital showed sporadic patterns with significantly fewer cases. This variation may be attributed to differences in environmental factors, such as vector breeding sites and waste management practices.

The timely intervention of health authorities, particularly the National Service for the Eradication of Malaria (SENEPA), the institution responsible for vector control in Paraguay, may have contributed to the reduced cases in certain areas. As noted by Guzman and Harris (2015), "Vector control is the mainstay of dengue prevention and control"[24]. In this context, the intensified vector control measures implemented in several locations throughout the city during the outbreak may have helped mitigate the spread of dengue [25–27]. Additionally, the rural setting and low-density population of some neighborhoods may have

contributed to the reduced level of cases compared to national reports.

In this study, DENV-1 and DENV-2 were the predominant serotypes in Itapua, with DENV-2 accounting for 79.87% of cases. This aligns with national data, where DENV-2 was dominant [28]. In contrast, Brazil reported the circulation of all four dengue serotypes with a predominance of DENV-1, while Argentina reported the presence of three serotypes (DENV-1, DENV-2, and DENV-4), with DENV-1 as the most prevalent [29,30]. The epidemiology of serotypes varies widely worldwide, influenced by differences in diagnostic tools and regional ecological and socioeconomic characteristics. A molecular epidemiological study is required to trace the spread of DENV types across South America and understand the regional dynamics of the virus.

The distribution of dengue cases in Itapua followed a typical epidemic pattern, rising at the end of spring and peaking in summer [31,32], coinciding with the national pattern during epidemiological weeks 3 to 6. This pattern aligns with favorable climatic conditions, including rising temperatures and increased rainfall, which support mosquito reproduction and create an ideal environment for dengue transmission. As noted by previous studies [33], the combination of high temperatures, humidity, and rainfall creates an ideal environment for mosquito breeding and dengue transmission. Consistent with these findings, recent studies have highlighted the importance of climatic and environmental factors in dengue transmission [9,12,34–35]. Furthermore, demographic and societal changes, decreasing resources for vector-borne infectious disease prevention and control, and changes in public health policy have all contributed to increased epidemic dengue activity [36]. Encarnacion and its metropolitan area are particularly vulnerable to dengue epidemics due to several factors contributing to the region's susceptibility. The city's rapid and unplanned urban expansion has led to inadequate waste management, stagnant water accumulation, and an environment conducive to mosquito breeding. The region's high human mobility during vacation periods, slow outbreak responses, and limited access to healthcare services in some areas further exacerbate the epidemic.

The distribution of dengue cases across age groups revealed notable differences between national and Itapua levels. Specifically, children, young adults, and adults exhibited higher case rates nationally than in Itapua, as reflected in the significantly elevated national SMRs. These disparities likely highlight systemic gaps in national dengue control efforts, particularly in urbanized and underserved areas where vector control measures may be less effective. As mentioned above, SENEPA implemented containment efforts in Itapua during the 2023–2024 epidemic [25–27]. These measures included the elimination of mosquito breeding sites and the proper management and disposal of waste. While similar activities were conducted nationwide, Itapua's predominantly rural setting, along with the lower population density of its metropolitan hub, Encarnacion (184.62 inhabitants per square kilometer, compared to Asunción's 3,950.78 inhabitants per square kilometer), likely contributed to reduced exposure to dense mosquito populations compared to more urbanized national hotspots.

The findings show a nonlinear relationship between precipitation and dengue incidence (Figure 1). There was a marked increase in both suspected and confirmed dengue cases after the first major rainfall peak of 221.7 mm during epidemiological week 50 of 2023, consistent with the expected lag due to mosquito development and viral incubation. In contrast, the second and more intense rainfall event of 340.36 mm during week 11 of 2024 did not lead to a subsequent rise in cases. One possible explanation is the concurrent drop in average temperature, from 30.2 °C to 26.5 °C in week 13 and further to 18.8 °C by week 18. *Aedes aegypti* mosquitoes are temperature-sensitive; lower ambient temperatures can slow down mosquito development, reduce biting activity, and impair dengue virus replication within the vector. Therefore, the combination of heavy rainfall and declining temperatures likely disrupted the conditions necessary for sustained dengue transmission.

The elderly represented the smallest age group affected by dengue in Paraguay. Given that dengue is endemic in the country, the elderly's previous exposure to various virus serotypes may have granted them some level of immunity, contributing to the relatively low incidence of 6.8% of cases at the departmental level and 3.9% nationally. However, it is essential to note that these figures might be underestimated due to underreporting or a lack of healthcare seeking among this age group.

The high association between dengue cases, ICU admission, and mortality observed in this study reflects the elevated risk of fatal outcomes among severe cases. Although only a small proportion of patients typically require intensive care, those who do, face a significantly higher risk of death. While the overall mortality rate for dengue cases in ICU settings has decreased over the past 15 years due to earlier admission and continuous monitoring, the highest mortality rates are still seen in

patients with severe dengue complications, such as shock and organ failure [37]. This finding emphasizes the importance of rigorous monitoring and specialized care for severe cases to prevent fatal complications.

This study has some limitations. Hospitalized and outpatient cases may not capture the full epidemiology of dengue in the broader community. This disparity likely stems from underreporting, under-diagnosis, or limited access to healthcare services, particularly in rural areas. Furthermore, resource constraints may hinder the availability of diagnostic tests, potentially leading to misidentification or under-diagnosis of cases. Additionally, the limited serotyping conducted across the country constrains the ability to monitor serotype-specific epidemiological patterns accurately. The absence of molecular epidemiology analysis also restricted the ability to investigate the genetic diversity and transmission patterns of DENV within the population. Addressing this gap will be important for a more comprehensive understanding of dengue epidemiology in the region.

Conclusions

The 2023–2024 dengue epidemic in Encarnacion, Paraguay, underscores the pressing need for coordinated bi-national efforts to address the growing threat of cross-border transmission. The city's proximity to Argentina, combined with high population mobility and favorable climate conditions, creates an ideal environment for sustained dengue circulation. Enhancing surveillance and integrated interventions are crucial to combat this emerging public health challenge. Strategic deployment of TAK-003 vaccination, alongside strengthened vector control measures, offers a promising approach to curbing transmission and mitigating the impact of future outbreaks. Equally important are educational campaigns to inform the population about preventive measures, such as eliminating mosquito breeding sites and recognizing early symptoms of dengue. Empowering communities with knowledge is key to long-term prevention and control. Protecting vulnerable pediatric populations is of utmost importance. Therefore, sustained cooperation between Paraguay and Argentina is essential to reduce the dengue burden and prevent further outbreaks.

Acknowledgements

We extend our most sincere gratitude to each member of the Virology Department of the Central Public Health Laboratory and the Molecular Laboratory of the Regional Hospital of Encarnacion for the processing of the samples.

Institutional Review Board statement

The Ethical Committee of the Central Laboratory of Public Health reviewed and approved this study (approval number 294, approved on 26 August 2024).

Data availability statement

The data sets used and/or analyzed during this study are available on the website of the General Directorate of Health Surveillance

Author contributions

Conceptualization, MMG, VHA, DPD; methodology, MMG, VHA, CC, AGF, TA, DPD; investigation, MM, DD; data curation, DD, MMG; formal analysis, DD, MMG; resources, DPD, ACF, TA, CA; validation, CA, AGF; writing—original draft preparation, MMG, VHA, DPD; writing—review and editing, VHA, DD, AGF; supervision, VHA. All authors have read and agreed to the published version of the manuscript.

Corresponding authors

Diana Paola Dressler, Mg. Bioq
Facultad de Medicina, Universidad Nacional de Itapua, Paraguay
Tel: +595975608135
Email: dpdressler@uni.edu.py

Victor Hugo Aquino, PhD
Departamento de Inmunología, Instituto de Investigaciones en Ciencias de la Salud
Universidad Nacional de Asunción, San Lorenzo Paraguay
Tel: +595971279047
Email: vhaquino@iics.una.py

Conflict of interest

No conflict of interest is declared.

References

1. Gómez Gómez R, Kim J, Hong K, Jang JY, Kisiju T, Kim S, Chun BC (2022) Association between climate factors and dengue fever in Asuncion, Paraguay: a generalized additive model. Int J Environ Res Public Health 19: 1–10. doi: 10.3390/ijerph191912192.
2. Pan American Health Organization, World Health Organization (2024) Dengue. Available: https://www.paho.org/es/temas/dengue. Accessed; 7 Jul 2024.
3. Pereira Y, Samudio M, Ojeda A, Cabello A (2015) Seroprevalence of dengue infection in a district of the Paraguayan Chaco: a population-based study. Rev Chil Infectol 32: 618–627. [Article in Spanish]. doi: 10.4067/S0716-10182015000700002.
4. Avilés G, Rowe J, Meissner J, Manzur Caffarena JC, Enria D, Jeor S (2002) Phylogenetic relationships of dengue-1 viruses

from Argentina and Paraguay. Arch Virol 147: 2075–2087. doi: 10.1007/s00705-002-0886-3.
5. Benítez-Leite S, Machi ML, Gibert E, Rivarola K (2002) Knowledge, attitudes, and practices regarding dengue in a neighborhood of Asunción. Rev Chil Pediatr 73: 64–72. doi:10.4067/S0370-41062002000100013. [Article in Spanish].
6. Aquino JD, Tang WF, Ishii R, Ono T, Eshita Y, Aono H, Makino Y (2008) Molecular epidemiology of dengue virus serotypes 2 and 3 in Paraguay during 2001–2006: the association of viral clade introductions with shifting serotype dominance. Virus Res 137: 266–270. doi: 10.1016/j.virusres.2008.07.011.
7. Alfonso HL, Amarilla AA, Gonçalves PF, Barros MT, de Almeida FT, Silva TR, da Silva EV, Nunes MT, Vasconcelos PF, Vieira DS, Batista WCH, Bobadilla ML, Vazquez C, Moran M, Moraes LT, Aquino VH (2012) Phylogenetic relationship of dengue virus type 3 isolated in Brazil and Paraguay and global evolutionary divergence dynamics. Virol J 9: 124. doi: 10.1186/1743-422X-9-124.
8. Rojas A, Moreira Soares A, Mendoza LP, Acosta ME, Aria L, Páez M (2021) Revisiting the dengue epidemic of 2011 in Paraguay: molecular epidemiology of dengue virus in the Asuncion metropolitan area. BMC Infect Dis 21: 769. doi: 10.1186/s12879-021-06487-9.
9. Vazquez C, Alcantara LCJ, Fonseca V, Lima M, Xavier J, Adelino T, Fritsch H, Castro E, Oliveira C, Schuab G, Jerônimo AR, Villalba V, Gomez de la Fuente A, Rojas A, Cantero C, Fleitas F, Aquino C, Ojeda A, Sequera G, Torales T, Barrios J, Elias MC, Iani F, Ortega MJ, Gamarra ML, Montoya R, Rodrigues E, Kashima S, Sampaio S, Coluchi N, Leite J, Gresh L, Franco L, Lourenço J, Mendez J, Bispo AM, Giovanetti M (2023) Retrospective spatio-temporal dynamics of dengue virus 1, 2 and 4 in Paraguay. Viruses 15: 1275. doi: 10.3390/v15061275.
10. Gräf T, Vazquez C, Giovanetti M, de Bruycker-Nogueira F, Fonseca V, Claro IM (2021) Epidemiologic history and genetic diversity origins of chikungunya and dengue viruses, Paraguay. Emerg Infect Dis 27: 1393–1404. doi: 10.3201/eid2705.204244.
11. General Directorate of Health Surveillance (2013) Epidemiological bulletin N°50. Epidemiological week: 52. Available: https://dgvs.mspbs.gov.py/files/boletines/SE52_2013_Boletin.pdf. Accessed: 7 July 2024. [Bulletin in Spanish].
12. Rojas A, Shen J, Cardozo F, Bernal C, Caballero O, Ping S (2024) Characterization of dengue virus 4 cases in Paraguay, 2019–2020. Viruses 16: 1–14. doi: 10.3390/v16020181.
13. Ministry of Public Health and Social Welfare (nd) General Directorate of Health Surveillance. Available: https://dgvs.mspbs.gov.py/arbovirosis/. Accessed: 7 July 2024.
14. Dirección General de Estadísticas, Encuestas y Censos (DGEEC) (nd) Census Atlas of Paraguay: Itapua. Available: https://www.ine.gov.py/Publicaciones/Biblioteca/Atlas%20Censal%20del%20Paraguay/10%20Atlas%20Itapua%20censo.pdf. Accessed: 25 March 2024. [Atlas in Spanish].
15. Dirección Nacional de Aeronáutica Civil (2023) Directorate of Meteorology and Hydrology. Climatological Yearbook. Available: https://www.meteorologia.gov.py/wp-content/uploads/2024/06/anuario_climatologico_2023_DSC.pdf. Accessed: 20 August 2024. [Bulletin in Spanish].
16. Dirección Nacional de Aeronáutica Civil (2024) Directorate of Meteorology and Hydrology. Climate Outlook Bulletin February, March, April. Available: https://www.meteorologia.gov.py/wp-content/uploads/2024/02/trimestral_pronos_FMA2024.pdf. Accessed: 15 August 2024. [Bulletin in Spanish].
17. Google Earth. Paraguay (2025) Mountain View (CA): Google LLC. Available: https://earth.google.com/web/search/mapa+de+paraguay. Accessed: 10 May 2024.
18. Paintmaps.com (2024) Political map of Itapua, Paraguay. Available: https://paintmaps.com/map-charts/180/Paraguay-map-chart. Accessed: 12 June 2024.
19. Google Maps (base map) (2024) Seventh Health Region. Dengue cases in Encarnacion, Paraguay. Available: https://www.google.com/maps/place/Encarnacion. Accessed; 15 July 2024.
20. Poloni TR, Dornas FP, Dos Santos NN Jr, Soares AM, Amarilla AA, Alfonso HL, Trigueiro S, Lavrador MA, Yamamoto AY, Aquino VH (2016) High prevalence of clinically unsuspected dengue disease among children in Ribeirao Preto city, Brazil. J Med Virol 88: 1711-1719. doi: 10.1002/jmv.24533.
21. Tittarelli E, Mistchenko A, Barrero P (2014) Dengue virus 1 in Buenos Aires from 1999 to 2010: towards local spread. PLoS One 9: e111017. doi: 10.1371/journal.pone.0111017.
22. Bogado F, Leite C, Noguera L, Nuñez C, Soarez-Almeida M, Espínola D (2018) Epidemiological situation of dengue in the city of Encarnación. Rev Inst Med Trop 15: 12–20. [Article in Spanish]. doi: 10.18004/imt/202015112-20.
23. Ministerio de Salud de Argentina (2024) National Epidemiological Bulletin. Week 37, No. 722 (September 8-14). Available: https://www.argentina.gob.ar/boletin-epidemiologico-nacional/boletines-2024. Accessed: 17 June 2024.
24. Guzman MG, Harris E (2015) Dengue. Lancet 385: 453–465. doi: 10.1016/S0140-6736(14)60572-9.
25. Servicio Nacional de Erradicación del Paludismo (SENEPA) (2024). Does not stop in the fight against the *Aedes aegypti* mosquito. Asunción: Ministry of Public Health and Social Welfare. Available: https://senepa.gov.py/2024/02/26/encarnacion-no-se-detiene-en-la-lucha-contra-el-mosquito-aedes-aegypti/. Accessed: 20 August 2024.
26. Githeko AK, Lindsay SW, Confalonieri UE, Patz JA (2000) Climate change and vector-borne diseases: a regional analysis. Bull World Health Organ 78: 1136–1147.
27. Servicio Nacional de Erradicación del Paludismo (SENEPA) (2024). SENEPA makes history: logistics against *Aedes aegypti* and other vectors strengthened in Itapúa. Asunción: Ministry of Public Health and Social Welfare. Available: https://senepa.gov.py/2024/03/26/senepa-hace-historia-se-fortalece-logistica-contra-el-aedes-aegypti-y-otros-vectores-en-itapua/. Accessed: 20 August 2024.
28. Dirección General de Vigilancia de la Salud (2024) Epidemiological bulletin. Edition No. 50. Epidemiological week: 16. Available: https://dgvs.mspbs.gov.py/wp-content/uploads/2024/04/SE-16_Boletin-Epidemiologico-Semanal_DGVS_.pdf. Accessed: 22 September 2024. [Bulletin in Spanish].
29. Medeiros E (2024) Challenges in controlling the dengue epidemic in Brazil. Acta Paulista de Enfermagem. Available: https://www.scienceopen.com/document?vid=95da41f5-8ada-4720-a2b0-48c417cf8311. Accessed: 22 September 2024.
30. Ministerio de Salud de Argentina (2024) National epidemiological bulletin. Epidemiological situation of dengue.

Available: https://www.argentina.gob.ar/noticias/salud-actualiza-la-situacion-epidemiologica-de-dengue-y-presenta-los-datos-de-cierre-de-la. Accessed: 20 August 2024. [Bulletin in Spanish].
31. Dirección General de Vigilancia de la Salud (2023) Ministry of Public Health and Social Welfare. Dengue enters epidemic period with increase in notifications. Available: https://dgvs.mspbs.gov.py/dengue-inicia-periodo-epidemico-con-aumento-de-notificaciones/. Accessed: 20 September 2024.
32. Dirección General de Vigilancia de la Salud (2024) Ministry of Public Health and Social Welfare. Arbovirosis situation room. Week 16. Available: https://dgvs.mspbs.gov.py/wp-content/uploads/2024/04/SE-16-COMPILADO-SALA-ARBOVIROSIS-26-04-2024-.pdf. Accessed: 18 September 2024.
33. Githeko AK, Lindsay SW, Confalonieri UE, Patz JA (2000) Climate change and vector-borne diseases: a regional analysis. Bulletin of the World Health Organization, 78: 1136–1147.
34. López MS, Gómez AA, Müller GV, Walker E, Robert MA, Estallo EL (2023). Relationship between climate variables and dengue incidence in Argentina. Environmental Health Perspectives 131: 57008. doi: 10.1289/EHP11616.
35. Câmara F, Gonçalves R, Teixeira dos Santos G, Ferreira F, Cardozo C (2007). Retrospective (historical) study of dengue in Brazil: regional characteristics and dynamics. Revista Social Brasileira de Medicina Tropical 40: 192–196. [Bulletin in Portuguese]. doi: 10.1590/S0037-86822007000200009.
36. Gubler DJ (1998) Dengue and dengue hemorrhagic fever. Clin Microbiol Rev 3: 480–496. doi: 10.1128/CMR.11.3.480.
37. Rosso F, Parra-Lara LG, Sanz AM, Ospina-Tascon GA, Granados M (2019) Mortality of severe dengue patients admitted to intensive care units over 15 years: have we improved? Open Forum Infect Dis 6: S792. doi: 10.1093/ofid/ofz360.1990.