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Clinical and epidemiological characteristics of children with mosquito-borne diseases in a tertiary hospital, Buenos Aires, Argentina, 2023

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ABSTRACT

Introduction. Arboviruses, such as dengue and chikungunya, have caused multiple epidemics in the Americas. They are transmitted through mosquito bites; *Aedes aegypti* is their main vector. As of January 2023, coinciding with the fourth dengue outbreak in Argentina, a new dengue outbreak was observed in the Americas, coincident with the presence of chikungunya.

We considered it essential to describe the demographic, epidemiological, clinical, and evolutionary characteristics of dengue/chikungunya patients seen in a tertiary pediatric hospital in the Autonomous City of Buenos Aires in 2023.

Population and methods. Descriptive, observational, retrospective cohort study. Includes children of 0 to 16 years with compatible symptomatology and positive PCR or IgM for dengue or chikungunya from February 1, 2023, through May 31, 2023.

Results. A total of 168 patients were identified, with a median age of 138 months (IQR: 107-164). The diagnosis of dengue was confirmed in 140 and of chikungunya in 28. Ninety-eight percent were autochthonous cases.

In 85% of the cases, PCR was used to make the virological diagnosis of dengue, and in the remaining 15%, IgM was used. PCR diagnosed chikungunya in 61% of cases.

Patients with dengue fever had a longer duration of fever, abdominal pain, headache, myalgias, and retroocular pain. Exanthema and arthralgias were associated with chikungunya.

***Conclusions*.** The epidemiology of mosquito-borne diseases is dynamic and is related to what happens in the rest of the countries of South America; knowledge of it is essential to predict the etiological risk and prevalence.

Keywords: *dengue; chikungunya virus; pediatrics; epidemiology; fever.*

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INTRODUCTION

Arboviruses, such as yellow fever, dengue (DEN), Zika, and chikungunya (CHIK), have caused multiple epidemics in the Americas. These diseases are transmitted through mosquito bites—the *Aedes aegypti* is their primary vector -with household and per domiciliary habits and predominantly domestic transmission.

The DEN virus belongs to the *Flaviviridae* family with four variants: serotypes 1, 2, 3, and 4. It is a growing problem for global public health.[1] In 2019, the World Health Organization (WHO) included it among the "Top Ten Global Health Threats".[2] Since its introduction in Argentina in 1998, it has occurred in epidemic outbreaks; the fourth is for 2022-2023. These outbreaks show an increase in the number of cases and a decrease in the interepidemic interval in each episode.

CHIK virus belongs to the *Togaviridae* family and was first identified in Tanzania in the early 1950s.[2] Since then, it has affected millions of people worldwide and continues to cause epidemics in several countries. It is endemic in Southeast Asia, Africa, and Oceania, and in late 2013, it entered the Americas region, causing major epidemics.[3]

From the clinical aspect, they are acute, febrile, and exanthematous diseases that share some clinical manifestations that are often indistinguishable. The virological laboratory provides diagnostic confirmation. They can present in asymptomatic forms to severe cases with high morbimortality, so diagnostic suspicion and adequate management are determining factors in the evolution.[1,3]

As of January 2023, coinciding with the fourth dengue outbreak, the presence of CHIK was observed in Argentina in simultaneous epidemics. A total of 129 857 DEN cases and 2344 CHIK cases between epidemiologic weeks 1 and 31 of 2023.[4]

Given the preceding, we consider it essential to describe the demographic, clinical, and evolutionary characteristics of patients with DEN/CHIK seen in a high-complexity pediatric hospital in the Autonomous City of Buenos Aires in 2023. Likewise, we describe the clinical-evolutionary differences and severity markers between DEN and CHIK that circulated simultaneously in the same period.

POPULATION AND METHODS

Observational, descriptive, and retrospective cohort study including children from 0 to 16 years who consulted the Hospital de Pediatría SAMIC Prof. Dr. Juan P. Garrahan with compatible symptomatology and in whom positive PCR or IgM for DEN or CHIK was found from February 1, 2023, to May 31, 2023.

Demographic, clinical, laboratory, and evolutionary characteristics were recorded.

The variables recorded were age, sex, origin, history of travel 14 days before the onset of symptoms, presence and type of comorbidity, clinical signs and symptoms, presence and type of alarm signs, main reason for hospitalization, general laboratory, specific diagnosis, and evolution.

For the definition of DEN/CHIK, DEN with alarm signs, and severe DEN, the definitions established by the Guidelines for the health team of the Argentine Ministry of Health for both diseases were used.[4]

For virological diagnosis, polymerase chain reaction (PCR) or serology with detection of specific immunoglobulin M (IgM) were used. As for laboratory findings, leukopenia was defined as leukocyte count <4500/ mm^3, plateletopenia as platelet count <150 000/mm^3, increased hematocrit >43%, and increased liver enzymes (glutamic oxaloacetic transaminase [GOT] and glutamic pyruvic transaminase [GPT]) >40 UI/l. These alterations were noticed at the onset of symptoms and during evolution.

Ethical considerations

The Juan P. Garrahan Hospital Teaching and Research Committee approved the research protocol, which was prepared based on the Good Clinical Research Practice Guidelines. Our institution's standards of care were followed for diagnosis and treatment per the Pan American Health Organization (PAHO) recommendations. The results were reported to each patient, parents, and guardians; the corresponding treatment or follow-up was indicated.

Access to the information in this study complies with the requirements established by the ethical and legal norms that protect confidentiality (Law 25326 on the Protection of Confidentiality of Personal Data). The data obtained may not be used for purposes other than those for which they were received.

Statistical analysis

A data collection form belonging to the Juan P. Garrahan Hospital was created in the RedCap database. Categorical variables are described in

number and percentage, and continuous variables in the median and the interquartile range (IQR). An univariate analysis was performed, comparing the variables of patients with a confirmed diagnosis of DEN and CHIK. The chi-square test was used to compare categorical variables and, depending on the distribution of continuous variables, the rank sum test or t-test. A *p*-value <0.05 was considered statistically significant. Data processing was performed using the R i386 3.5.0 program.

RESULTS

During the study, 168 patients were identified with confirmed DEN or CHIK. The median age was 138 months (IQR: 107-164). Only 2 patients were younger than 12 months. The diagnosis of DEN was confirmed in 140 children, and CHIK in 28. A total of 89 cases (53%) resided in Greater Buenos Aires (*Figure 1*). Ninety-eight percent (n = 164) were autochthonous cases. Travel history was present in 3 children with CHIK (Paraguay) and 1 with DEN (Misiones).

Seventeen percent (n = 29) had some form of comorbidity. The most frequent were congenital heart disease (n = 8), immunocompromised (n = 7), asthma (n = 6) and obesity (n = 4).

The virological diagnosis of DEN was made by PCR in 85% (n = 119) and by the presence of IgM in the remaining 15% (n = 21). DEN-2 infections were confirmed in 106 patients (75%). In CHIK, the diagnosis was made by PCR in 61% (*Table 1*).

CHIK cases were identified from epidemiological week 6 (onset 02/05/2023) and DEN cases from week 9 (onset 02/26/2023) (*Figure 2*).

All presented with fever. Comparing the characteristics of patients with DEN vs. CHIK, patients with DEN had a longer duration of fever, abdominal pain, headache, myalgias, and retroocular pain. Exanthema and arthralgias were statistically associated with the diagnosis of CHIK (*Table 1*).

Patients were classified as DEN without comorbidity or warning signs (n = 72; 51%), patients with alarm signs and no comorbidities (n = 45; 32%), with comorbidities and alarm signs (n = 12; 9%) and with comorbidities without alarm signs (n = 11; 8%). Hospitalization was required for 52/140 (37%) children with DEN and 5/28 (18%) with CHIK. The median duration of hospitalization was 2 days (IQR: 1-3) (*Table 2*). In the former, the leading cause was the presence of alarm signs 44/52, and in the latter, the general condition compromised 3/5.

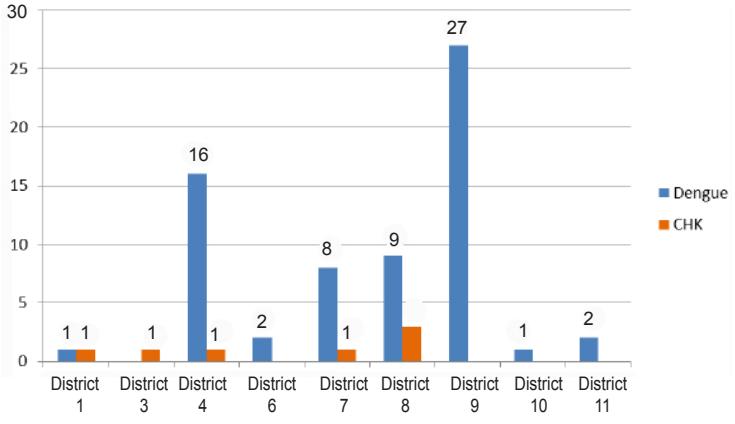
The evolution was favorable in all cases.

DISCUSSION

The global incidence of DEN has increased considerably over the last two decades and is a major public health challenge in tropical and subtropical regions.

Between 2000 and 2019, the WHO documented that the number of cases reported worldwide increased tenfold, from 500 000 to 5.2 million. In 2019, an unprecedented peak was reached, with cases reported in 129 countries.

Figure 1. Origin of dengue and chikungunya cases by districts of the City of Buenos Aires



CHK: chikungunya.

Table 1. Characteristics of the study population

Variable		Total n = 168	Dengue n = 140	Chikungunya n = 28	*p* value
Median age in months (RIC)*		138 (107-164)	139 (106-165)	135 (112-149)	0.4
Male sex, % (n)		60 (100)	60 (84)	57 (16)	0.8
Origin, % (n)	CABA	43 (73)	47 (66)	25 (7)	0.001
	Buenos Aires	53 (89)	50 (70)	68 (19)	0.01
	Others	4 (6)	3 (4)	7 (2)	0.3
Sick cohabitant, % (n)		32 (53)	30 (42)	39 (11)	0.3
Baseline disease, % (n)		17 (29)	16 (23)	21 (6)	0.4
Immunosuppressed host, % (n)		4 (7)	4 (5)	7 (2)	0.5
Days of fever until diagnosis, median (IQR)		1 (1-3)	2 (1-3)	1 (0-1)	0.005
Total fever duration, median (IQR)		3 (2-5)	4 (3-5)	3 (2-3)	0.001
Signs and symptoms, % (n)	Abdominal pain	45 (76)	49 (68)	29 (8)	0.005
	Exanthema	54 (90)	51 (71)	68 (19)	0.01
	Headache	62 (105)	66 (92)	46 (13)	0.01
	Myalgias	47 (79)	51 (72)	25 (7)	0.002
	Arthralgias	29 (48)	24 (33)	54 (15)	0.001
	Nausea/vomiting	61 (103)	61 (86)	61 (17)	1
	Diarrhea	23 (38)	22 (31)	25 (7)	0.7
	Retroocular pain	23 (38)	26 (36)	7 (2)	0.005
Diagnosis % (n)	PCR	81 (136)	85 (119)	61 (17)	0.002
	Serology	19 (32)	15 (21)	39 (11)	0.002

CABA: Autonomous City of Buenos Aires, PCR: polymerase chain reaction, IQR: interquartile range, n: number.

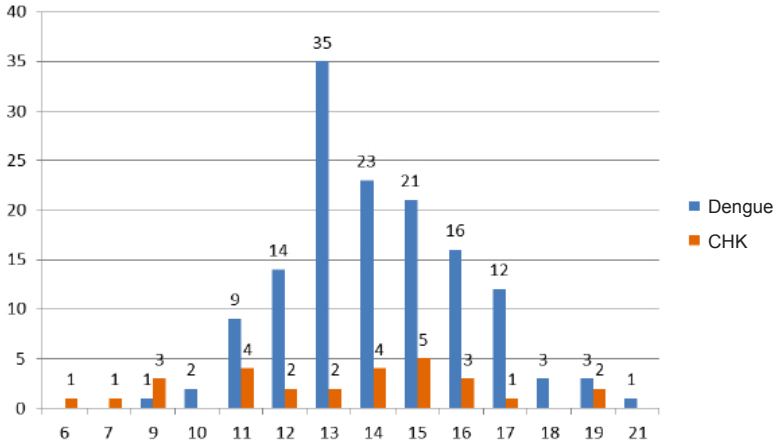
Nearly 80% of these cases (4.1 million) have been reported in the Americas region.[5] DEN is the most widespread and causes the highest number of cases.

Since its reintroduction in Argentina in 1998, from 2008 to 2009 onwards, there have been five epidemic outbreaks with an exponential increase in cases and increasingly shorter inter-epidemic periods.

In 2023, the Northeast region of Argentina reported uninterrupted cases throughout the year, with no inter-epidemic intervals.

According to data from the National Ministry of Health, during the study period, 139 946 cases

Figure 2. Distribution of cases by epidemiological week



CHK: chikungunya.

Table 2. Laboratory and evolution of patients with confirmed dengue (n = 140)

Variable		% (n)
Type of dengue	DEN 1	9 (13/119)
	DEN 2	75 (106/119)
Warning signs		41 (57/119)
	Bleeding	61 (35/57)
	Drowsiness	2 (1/57)
	Severe abdominal pain	12 (7/57)
	Persistent vomiting	23 (13/57)
	Sudden increase in Ht with a concomitant decrease in platelet count	30 (17/57)
Hospitalization requirement		37 (52/140)
Duration of hospitalization in days, median (IQR)		2 (1-3)
Minimum value of platelets/mm^3, median (IQR)		94 000 (69 000-121 000)
Minimum value of white blood cells/mm^3, median (IQR)		3040 (2550-3490)

Ht: hematocrit, IQR: interquartile range, n: number.

of DEN were reported in Argentina, adding up to 2329 cases of CHIK,[4] which were the first reports of CHIK in the hospital.

Climate change, population growth, and precarious urbanization are reasons for the increase in cases,[2] as it occurs in the Autonomous City of Buenos Aires and Greater Buenos Aires, where the study population comes from.

According to what was published by Berberian et al.,[6] in the periods 2015-2016 and 2019-2020, 112 and 127 cases of dengue fever were diagnosed in the hospital, respectively, and 140 for the period 2022-2023. At the same time, we can observe a decrease in imported cases over the years and an increase in autochthonous cases, where the history of travel was present in 19% in the period 2015-2016, 5.5% in the period 2019-2020, and in only one patient in our series. Of note is the increase in the proportion of DEN cases with alarm signs, compared with publications from previous seasons.[6-8]

With the increase in the circulation of *Aedes aegypti* and coinciding with the presence of cases in neighboring countries, autochthonous cases of CHIK are beginning to be registered.[4]

PAHO recommends applying clinical and therapeutic management measures corresponding to DEN in all suspected mosquito-borne diseases (MBD) patients. This recommendation is because severe cases and mortality of MBD occur mainly with cases of DEN.

In our study, the median duration of fever at diagnosis was one day; therefore, it is important to emphasize early diagnosis since early consultation and clinical suspicion facilitate timely diagnosis and appropriate follow-up.[9]

In a study conducted in Thailand, leukocyte counts greater than 5000/mm^3, fever of less than two days duration, and exanthema were statistically associated with CHIK.[10] Other authors associate encephalitis and arthralgias with the diagnosis of CHIK.[11]

In our study, DEN 2 was the most dominant. This data coincides with what the Ministry of Health reported for the same period.[3]

A high proportion of patients diagnosed with DEN required hospitalization, mainly due to the presence of alarm signs. Identifying these signs and adequate hydroelectrolytic management reduce the mortality associated with DEN. In this study, no deceased patients were identified. The most frequent alarm signs were abdominal pain, bleeding, nausea, and vomiting, in agreement with other pediatric series of patients with DEN.[6,7] The duration of hospitalization was short in relation to the duration of the critical phase of the disease.

Infant mortality for children is higher in children under a year old and in those with comorbidities.[5] Despite being a tertiary care hospital, this study's proportion of patients with comorbidities was low.

Due to their sudden onset, high disease burden, varied and unpredictable evolution, and low mortality, DEN epidemics generate an overload in the health system. For all these reasons, it is essential to protocolize their management and organize the health systems based on the clinical manifestations, comorbidities, and alarm signs that guide whether hospitalization is necessary.

CONCLUSIONS

DEN is the arbovirosis with the highest number

of cases globally, with an evident expansion to non-endemic areas, as has occurred in the last 15 years in the central part of the country, of which Buenos Aires is part.

Fever is still the most frequent form of presentation, so its presence during times of viral circulation leads us to suspect the disease. DEN should be considered in those who also present abdominal pain, headache, myalgia, and retro-ocular pain, and CHIK should be considered in those with associated rash and arthralgias.

The etiological differentiation is made only with the microbiological laboratory results since their differential characteristics are indistinguishable from each other, especially in children. ■

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