

2023 epidemic dengue fever outbreak: the experience of a pediatric hospital in the City of Buenos Aires

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ABSTRACT

Introduction. Dengue is a viral infection that may be asymptomatic or include severe manifestations. This study aims to describe the characteristics of a pediatric population during the epidemic outbreak in 2023.

Population and methods. This cross-sectional study included patients with probable or confirmed dengue fever who were seen from March 13, 2023, to May 19, 2023, in a pediatric hospital in the Autonomous City of Buenos Aires.

Results. A total of 112 patients were included. The median age was 12 years; 58% were male. Seventy-six percent of them came from the City of Buenos Aires. Twenty-five percent had cohabitants with symptoms compatible with a suspected case. The most frequent clinical manifestations were fever, headache, retro-ocular pain, myalgia, and arthralgia. The most frequent laboratory alterations were leukopenia (65%) and elevated transaminases (60%). Twenty-one percent (24/112) presented alarm signs and required hospitalization. Leukopenia, plateletopenia, and elevated transaminases were associated with the presence of alarm signs. RT-PCR was detected in fifty-three patients; serotype 2 was the most frequent. Twenty-one patients had positive NS1 tests, 18 patients had positive IgM, and 20 patients with clinical and epidemiological links were assumed to be probable dengue cases. There were no cases of severe dengue.

Conclusion. Early clinical suspicion and recognition of laboratory parameters associated with alarm signs are essential for an adequate approach to the disease and early supportive treatment during dengue infection.

Keywords: dengue; arbovirus infections; pediatrics.

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INTRODUCTION

Dengue is a systemic and dynamic infectious disease. The infection may be asymptomatic or manifest with a broad clinical spectrum, including severe and non-severe manifestations.¹

The disease is caused by a virus transmitted through the bite of a mosquito belonging to the *Aedes* genus, mainly *Aedes aegypti*, the vector of this disease. Dengue virus belongs to the *Flaviviridae* family, and there are four serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. Any serotype can produce severe forms of the disease, although serotypes 2 and 3 have been associated with the highest number of severe cases.²

According to the Pan American Health Organization (PAHO), in 2023, between epidemiological weeks (SE) 1 and 24, a total of 2 102 848 cases of dengue were reported in the Americas region, with a cumulative incidence rate of 214 cases per 100 000 population. In Argentina, during 2023, up to SE 24, 114 680 cases of dengue were reported. The cases reported up to week 24 of 2023 are 153 times higher than the same period in 2022 and 7 times higher than the average of the last five years.³

In the Americas, all four dengue virus serotypes circulate. In Argentina, up to SE 24, 2023, serotypes 1, 2, and 3 were circulating.³ Several studies have shown that the frequency of severe cases depends on the virus strain; therefore, monitoring the temporal distribution of serotypes and subtypes in endemic areas provides information on the risk of severe dengue. DENV-2 is the serotype that most frequently produces severe cases, followed by DENV-3, DENV-1 and DENV-4.⁴

This study aims to describe the clinical, epidemiological, laboratory, and evolution characteristics of patients with dengue fever seen in a tertiary pediatric hospital during SE 11 to 20 of the 2023 epidemic outbreak.

POPULATION AND METHODS

Descriptive, cross-sectional study. The study included patients who were seen in the pediatric infectious disease outpatient clinic and inpatient wards of the Hospital General de Niños Ricardo Gutiérrez (third-level pediatric hospital of the Autonomous City of Buenos Aires) during the period between March and May 2023. Demographic, epidemiological, clinical, diagnostic, and evolutionary data were obtained using a collection form and digital upload.

Inclusion criteria: Patients between 0 and 18 years of age who met the criteria of a probable or confirmed case of dengue.

Exclusion criteria: Patients who, during their evolution, presented another alternative diagnosis that allowed ruling out dengue.

Definitions¹

A suspected case of dengue: a person who lives in or has traveled in the last 14 days to areas with dengue transmission and presents acute fever, usually 2 to 7 days, and two or more of the following manifestations:

- nausea, vomiting
- exanthema
- myalgia, arthralgia
- headache, retro-orbital pain
- petechiae or positive tourniquet test - leukopenia

Any child coming from or residing in an area with dengue transmission, with acute febrile symptoms, usually lasting 2 to 7 days and with no apparent etiology, may also be considered a suspected case.

Dengue with alarm signs: Any case of dengue that presents, close to the onset of fever or at the onset of fever or in the following hours, one or more of the following signs:

- severe and continuous abdominal pain or pain on palpation of the abdomen,
- persistent vomiting,
- fluid accumulation (ascites, pleural effusion, pericardial effusion),
- mucosal bleeding,
- lethargy or irritability,
- postural hypotension (lipotimia),
- hepatomegaly greater than 2 cm,
- progressive increase in hematocrit.

Severe dengue fever: Any case of dengue fever that has one or more of the following manifestations:

- shock or respiratory distress due to plasma extravasation,
- bleeding considered clinically significant by the treating physicians (examples: hematemesis, melena, voluminous metrorrhagia, central nervous system bleeding),
- severe organ involvement (myocarditis, hepatitis [elevated transaminases ≥ 1000 IU/L], encephalitis, or other organs).

Probable case of dengue: Any suspected case of dengue that has a positive result of IgM or NS1 or clinical-epidemiological nexus (defined as a case with epidemiological nexus as any

person who lives or has been in the same area as a confirmed case of dengue within 30 days).

Confirmed case of dengue: Any laboratory-confirmed case of dengue (molecular techniques: real-time RT-PCR or others; seroconversion of paired IgM or IgG or fourfold increase in IgG).

Statistical analysis

Numerical variables were described using mean and standard deviation (SD) or median and interquartile range (IQR); categorical variables were expressed as numbers and percentages. The Mann-Whitney test was used to compare means. The chi-square or Fisher's exact test was used to compare nominal variables. Any p-value <0.05 was considered statistically significant. The data were analyzed using the SPSS® version 25.0 statistical package.

Ethical considerations

The study was approved by the Ethics and Research Committee of the Hospital General de Niños Ricardo Gutiérrez (registration code: 9778) on 5/18/23.

RESULTS

During the period analyzed, 773 patients were seen in the Pediatric Infectious Diseases outpatient clinic. One hundred seventy-four patients corresponded to suspected dengue fever cases, representing 27.9% of the consultations. In this group of patients, 112 patients (64%) were diagnosed with probable or confirmed dengue according to PAHO microbiological or clinical-epidemiological criteria.¹ The epidemiological and clinical characteristics of the population studied are summarized in *Table 1*.

According to the PAHO definitions above,¹ confirmed case of dengue was assumed in 53 patients (47.3%) with detectable RT-PCR technique. Serotype 2 was predominant, detected in 44 patients (83% of all positive RT-PCR), while 9 presented serotype 1. On the other hand, 59 patients were assumed to be probable cases: 21/59 (19%) with positive NS1 test, 18/59 (16%) with positive IgM serology for dengue, and 20/59 (18%) with epidemiological nexus in whom no laboratory diagnostic tests were performed. All confirmed or probable dengue patients received the same clinical follow-up and treatment.

The median age was 12 years (IQR: 9-14); 58% were male. Seventy-six percent of the patients were from the Autonomous City of Buenos Aires, while 24% were from Greater

Buenos Aires.

No patient reported travel prior to consultation. Nineteen percent (21/112) had had contact with a suspected case of dengue in the last 15 days. Twenty-five percent (28/112) had cohabitants with symptomatology compatible with a suspected case. Twenty-one percent (24/112) reported suspected dengue cases in their school and neighborhood. None of the patients had associated comorbidities.

All patients consulted for the presence of symptoms; the delay between the onset of symptoms (first day of fever) and the first consultation had a median of 2 days (IQR: 1-4 days). Fever was present in 100% of cases, with a median duration of 3 days (IQR: 1-9 days). Headache with retro-ocular pain, myalgia, and arthralgia were the most frequent symptoms, occurring in 93% of cases, followed by abdominal pain, vomiting, and skin rash.

Of all patients with probable or confirmed dengue fever, 21% (24/112) had alarm signs. Mucosal bleeding was the most frequent alarm sign in 50% of these patients. Of all patients with alarm signs, 16 were hospitalized in the pediatric clinic ward, with a median duration of 2 days (IQR: 1-4 days). The rest of the patients presented intolerance to the oral route that required observation and on-call treatment for less than 12 hours.

Regarding laboratory parameters, leukopenia (leukocytes <4000/mm³) was present in 65% (73/112) and was the most frequent laboratory alteration. The median white blood cell (WBC) count was 3600/mm³, ranging from 1800 to 17 300/mm³. Twenty-one percent of patients (23/112) had plateletopenia (<100 000 platelets [PT]) with a median platelet count of 178 000/mm³ (range: 19 000-447 000/mm³). Leukopenia and plateletopenia were significantly associated with the presence of alarm signs ($p = 0.002$ and $p < 0.001$, respectively). Mean WBC and PT counts were lower in patients with alarm signs (mean WBC: 3337/mm³; mean PT: 131 958/mm³) than in dengue cases without alarm signs (mean WBC: 4830/mm³; mean PT: 192 284/mm³) ($p < 0.006$ for both cases). Epistaxis was significantly associated with the finding of plateletopenia in the hemogram ($p = 0.006$). According to normal hematocrit values for sex and age, only 7/112 patients presented hemoconcentration. Sixty percent (67/112) of the patients had increased transaminases, with a median glutamic oxaloacetic transaminase (GOT)

TABLE 1. Epidemiological and clinical characteristics of the population studied (N = 112)

	N	%
Median age in years (IQR)	12	(2-18)
Male	65	58
Origin		
CABA	85	76
PBA	27	24
Epidemiological link		
Contact with a confirmed case of dengue	21	19
Symptomatic cohabitants	28	25
Suspicious cases in neighborhood/school/workplace	24	21
Time from onset of fever to first visit (median)	2	(2-4)
Symptoms		
Fever	112	100
Retroocular headache/pain	104	93
Myalgia and arthralgia	104	93
Abdominal pain	75	67
Vomiting	56	50
Exanthema	55	49
Nausea	48	43
Diarrhea	34	30
Warning signs	24	21
Epistaxis	14	13
Gingivorrhagia	7	6
Petechiae	6	5
Pruritus	5	4
Duration of fever in days (range)	3	(1-9)
Warning signs	24	21
Mucosal bleeding	12	50
Severe or sustained abdominal pain	6	25
Persistent vomiting	3	12.5
Sudden drop in platelet value	3	12.5

N: number, CABA: Autonomous City of Buenos Aires (by its Spanish acronym), IQR: interquartile range, PBA: province of Buenos Aires (by its Spanish acronym).

of 42.5 IU/L (range: 7-401 IU/L) and glutamate pyruvate transaminase (GPT) of 30.5 (range: 6-299 IU/L). The elevation of transaminases was significantly associated with alarm signs ($p = 0.008$).

DISCUSSION

In the last 30 years, dengue in the region of the Americas has had an upward trend with epidemic peaks. Our country presented significant dengue outbreaks in 2016, with 40 072 cases, and in 2020, 50 385 cases. During 2023, 139 496 cases of dengue fever were reported, significantly higher than in previous outbreaks.^{3,5,6}

The causes of this upward behavior are multifactorial. They could be related to a higher vector density, the high number of susceptible people during these periods, the circulation of different viral serotypes, and phenomena specific to the circulating strains concerning its

virulence and pathogenicity. Environmental and socioeconomic changes, such as population growth, unplanned urbanization, increased poverty, and migration, contribute to this phenomenon.⁷ However, it is evident that dengue has become urbanized, causing an increase in cases in major cities such as the Autonomous City of Buenos Aires and the Buenos Aires metropolitan area.

In our study, most of the patients (76%) came from the Autonomous City of Buenos Aires and the rest from Greater Buenos Aires. There were no imported cases of dengue. In 65% (73/112) of the patients, there was some epidemiological link with the disease: contact with a person with confirmed dengue, symptomatic cohabitants, or suspected cases in the neighborhood and school. In line with other studies,⁸⁻¹⁰ all patients consulted within 48 hours of the onset of fever, and the most frequent symptoms were fever, headache,

myalgia, and arthralgia. Of the total number of cases, 21% (24/112) presented dengue with alarm signs, a higher percentage than that reported by Cazes et al. during the outbreak in the Autonomous City of Buenos Aires in 2016.¹⁰ In our study, serotype DENV-2 was predominant (83% of all positive PCRs), unlike what occurred during the 2016 and 2020 outbreaks in which serotype DENV-1 was the most frequent. According to the 2023 National Epidemiological Bulletin, up to SE 31 DENV-2 predominated in all provinces of northwestern Argentina (NOA) and the Central region.⁹⁻¹¹

Laboratory findings showed a high percentage of patients with leukopenia, similar to those reported in other studies.¹⁰ During dengue virus infection, early identification of warning signs is essential to establish early supportive treatment. In our work, leukopenia, plateletopenia, and elevated transaminases were significantly associated with the appearance of alarm signs. These parameters should alert and promote the exhaustive search for these signs during outpatient follow-up. In contrast, hemoconcentration was neither a frequent finding nor associated with disease severity and was present in a low percentage of patients (6%), similar to that reported in another recent study.⁹

One of the impact goals that PAHO set for the region is maintaining the dengue case fatality rate per 100 000 live births below 0.05%. One of the main challenges lies in distinguishing this arbovirolosis from other causes of acute febrile syndrome at an early stage.⁸ In our series, there were no deaths due to dengue. Since there is no specific treatment, timely clinical diagnosis, early identification of warning signs, and early supportive treatment are essential to avoid severe cases and deaths.

Disease prevention strategies are a fundamental pillar for disease control. It is necessary to continuously strengthen epidemiological surveillance, social communication strategies, and the promotion of environmental policies for vector control. Recently, Argentina approved the tetravalent attenuated virus vaccine from 4 years of age, another prevention tool. Although the mortality rate and the percentage of severe forms of dengue are low, PAHO considers its introduction in environments with high viral load and high transmission rates to maximize the health impact, thus reducing the disease burden and avoiding overloading the health system.¹²

The strengths of this study lie in the description of an extensive series of patients with dengue virus infection during the 2023 epidemiological outbreak in the Autonomous City of Buenos Aires. This series allows us to know the epidemiological characteristics of the disease and to study in depth the variation of the circulating serotypes and their different clinical manifestations and signs of severity.

CONCLUSION

Early clinical suspicion and recognition of laboratory parameters associated with alarm signs are essential for an adequate approach to dengue infection. This study highlights a high percentage of dengue patients with alarm signs, probably related to the predominance of DENV-2 during the 2023 epidemiological outbreak in the Autonomous City of Buenos Aires. ■

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