Clinical and laboratory features of fatal dengue fever in children: a case-control study

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Background

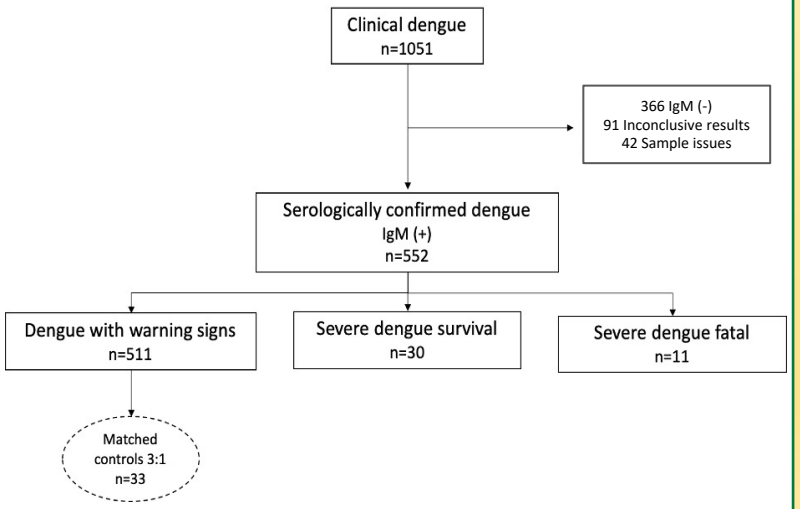
Dengue fever (DF) is a mosquito-borne illness that causes significant morbidity and mortality in tropical climates. Prompt recognition of warning signs, adequate monitoring and support can reduce progression to shock and mortality.

Objective

To compare the clinical features of fatal DF cases to severe non-fatal, and non-severe controls in pediatric patients in Guayaquil - Ecuador.

Methods

Retrospective case-control study of children (1 month to 15 years) hospitalized with serologically-confirmed DF in Guayaquil, Ecuador from 2013 to 2017. Cases of severe, fatal (SF) DF were compared to two control groups: (1) severe DF survivors (SS); and (2) patients with dengue with warning signs (DWS), matched 3:1 to cases for age, sex, and admission date.



Study profile

Results

Presentation		Severe, fatal (SF) n = 11	Severe, survived (SS) n = 30	Dengue with warning signs (DWS) n = 33
Baseline characteristics	Age (y), median (IQR)	9.6 (5.5 - 11.2)	8.1 (1.8 - 11.5)	9.7 (5.3 - 11.6)
	Female	4 (36)	13 (43)	12 (36)
	Weight (Kg)	42.0 (18.5 - 52.1)	25.5 (12 - 44)	**28 (17 - 37)***
	Previous encounters, median (IQR)	3 (2 - 4)	**2 (1 - 3)***	**2 (1 - 3)***
	Prior antibiotic use	7 (64)	20 (67)	20 (58)
History	Duration of fever (days), median (IQR)	3 (2-5)	5 (4-6)	5 (4 - 6)
	Headache/Ocular pain	3 (27)	12 (40)	14 (42)
	CNS symptoms [a]	9 (82)	15 (50)	**7 (21)****
	Muscular/joint pain	2 (18)	11 (37)	13 (39)
	Mucosal bleeding	5 (45)	14 (47)	7 (21)
	Nausea/vomiting	9 (82)	23 (77)	23 (67)
	Abdominal pain	8 (73)	23 (77)	25 (73)
	Diarrhea	4 (36)	7 (23)	13 (36)
Physical exam	Fever	4 (36)	10 (33)	10 (30)
	Altered level of consciousness [b]	9 (82)	**5 (17)****	**3 (9)****
	Tachycardia	8 (73)	**2 (7)*****	**3 (9.1)*****
	Tachypnea	5 (45)	**2 (7)****	**0*****
	Pulse pressure (mmHg), median (IQR)	36 (28 - 46)	30 (26 - 36)	30 (30 - 40)
	Rash	6 (55)	9 (30)	15 (46)
	Hepatomegaly	8 (73)	**5 (17)****	**8 (24)***
	Capillary refill (sec), median (IQR)	4 (3-4)	**3 (2-3)***	**2 (2-3)***
	Severe bleeding	2 (18)	4 (13)	1 (3)
Laboratory	WBC (x10^3/µl)	7.8 (5.3 - 17)	4.6 (3.7 - 8.6)	**4.5 (3.6 - 7.2)***
	ANC (x10^3/µl)	5.1 (3.2 - 8.5)	2.4 (1.8 – 2.9)	**2.1 (1.6 - 2.8)***
	Hematocrit (%)	37 (35 - 41)	37 (33 - 42)	38 (35 - 41)
	Platelets (x10^3/µL)	140 (100 - 160)	99 (71 - 160)	160 (90 - 180)
Ultrasound	Pleural effusion, n(%)	7 (64)	12 (40)	8 (24)
	Ascites, n(%)	4 (36)	8 (27)	12 (36)
	Gall bladder edema n(%)	1 (9)	5 (17)	3 (9)

WBC: White blood cells, ANC absolute neutrophil count
[a]: CNS: Lethargy, seizure, irritability, syncope.
[b]: Less than Alert on AVPU scale (A: alert V: response to verbal stimuli P: response to painful stimuli U: unresponsive)
Numbers represent n (%) unless otherwise specified
*p<0.05; ** p<0.01; ***p<0.001

Evolution	Severe fatal (SF) n = 11	Severe, survived (SS) n = 30	Dengue with warning signs (DWS) n = 33
Length of stay (days), median (IQR)	1.9 (0.8 - 4.0)[§]	10 (8.7 - 14)	5 (3.7 - 5.7)
PICU admission [c]	6 (45)	17 (77)	0
Mechanical ventilation (MV)	11 (100)	9 (30)	0
Intravenous dextrose	3 (27)	**21 (70)***	14 (44)
Supplemental oxygen	5 (45)	3 (10)	**1 (3)****
Inotropes	2 (18)	0 (0)	0
Blood products	1 (9)	4 (13)	0
Antibiotics	2 (18)	4 (13)	1 (6)
Chest tube	1 (9)	3(10)	0

PICU pediatric intensive care unit
Numbers represent n (%) unless otherwise specified
*p<0.05; ** p<0.01; ***p<0.001
[§] time to death in SF group
[c] PICU admission was indicated in 11/11 (100%) of SF cases and 22/30 (73%) of SS controls; however, lack of beds limited the management in critical care area.

Conclusions

Delayed recognition by healthcare workers, higher weight, vital sign abnormalities, hepatomegaly, neurological symptoms, leukocytosis, neutrophilia, and lack of dextrose in intravenous solutions were associated with mortality in children with DF. These findings have implications for optimizing the diagnosis and management of severe pediatric dengue infection.

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