

LETTERS

Congenital Zika infection: neurology can occur without microcephaly

The fetal repercussions of Zika virus (ZIKV) infection during pregnancy is of interest for maternal and child health.¹ Studies on the psychomotor and neurodevelopment of children exposed in utero to arboviruses, especially non-microcephalic children, are lacking. At a maternity university hospital in Brazil, we started following the development of children, without microcephaly, born to mothers infected with ZIKV during pregnancy, searching for early warning signs of abnormalities. A normal head circumference for term newborns was defined, according to the 2016 WHO recommendation, as higher than 31.9cm for boys and higher than 31.5cm for girls.² We used the Alberta Infant Motor Scale for the evaluation of motor development, and the Denver II test for tracking development in personal/social, fine motor/adaptive, language and gross motor areas. Muscle tone was assessed by a modified Ashworth Scale, and the degree of child

Table 1 Basal characteristics of the study population

No.	Type of maternal infection	Trimester of maternal exposure	GA at birth (weeks)	Sex	HC (cm)	BW (g)	Appgar (1 min/5 min)
001	ZIKV	3	41	M	35.7	3850	9/9
002	ZIKV	3	39	M	35	2995	8/9
003	ZIKV	3	38	F	34	2670	9/9
004	ZIKV	1	40	F	36	3570	9/9
005	ZIKV	2	40	F	33.5	3340	9/9
006	ZIKV	2	32	F	30	1805	8/8
007	ZIKV	2	32	F	30	1650	3/8
008	ZIKV	3	31	M	28.5	1620	9/9
009	ZIKV	2	39	M	34	3540	9/9
010	ZIKV	1	38	M	32	2160	9/9
011	ZIKV	2	39	F	36	4130	9/9
012	ZIKV	3	39	F	NI	3090	NI
013	ZIKV	1	38	F	33	3080	9/10
014	ZIKV	1	38	M	34	2785	4/7
015	ZIKV	1	40	F	34	3535	9/9
016	ZIKV	2	38	F	38.5	3055	9/9
017	ZIKV	1	37	M	36	3200	8/9
018	ZIKV	1	38	F	35	3220	9/9
019	ZIKV	2	38	M	35	3530	8/9

NI, birth weight; F, female; HC, head circumference at birth; GA, gestational age; M, male; NI, not informed; ZIKV, Zika virus.

irritability was classified according to the evaluator's observation on the day of the consultation in a quiet room, in a special carpet area with age-appropriate toys. This actively searched for: clonus, tremor, nystagmus, circular movements of the arms, vermiform or choreic movements,

closed fist, extensor spasms of the lower limbs, asymmetry, tongue protrusion, persistence of the asymmetrical tonic neck reflex and opisthotonus.³

The baseline characteristics of 19 children from the ZIKV group are shown in table 1. Only one child had a normal

Table 2 Neuromotor development of children born to mothers infected with Zika virus during pregnancy

Identification	Group	Head circumference	Age at evaluation (months)	AIMS	Denver II	Ashworth Scale	Abnormalities in movement control				
							Tone alteration	Signs of ataxia	Dyskinesia	Posture	Irritability
001	ZIKV	N	1	Suspect	Suspect	2	Hypertonia	Tremor	Absent	Symmetric	Irritated
002	ZIKV	N	4	Normal	Normal	2	Hypertonia	Appendicular	Absent	Symmetric	Absent
003	ZIKV	N	2	Normal	Normal	1	Hypertonia	Absent	Ballistic	Symmetric	Absent
004	ZIKV	N	2	Normal	Normal	1+	Hypertonia	Appendicular	Choreic	Symmetric	Motivated crying
005	ZIKV	N	1	Normal	Normal	2	Hypertonia	Absent	Absent	Symmetric	Motivated crying
006	ZIKV	N	1	Delay	Suspect	2	Hypertonia	Absent	Absent	Asymmetric	Irritated
007	ZIKV	N	1	Normal	Normal	00	Hypotonia	Tremor	Absent	Asymmetric	Irritated
008	ZIKV	N	4	Normal	Normal	1+	Hypertonia	Appendicular	Tongue athetosis	Symmetric	Absent
009	ZIKV	N	4	Normal	Normal	2	Hypertonia	Appendicular	Absent	Symmetric	Inconsolable
010	ZIKV	N	2	Normal	Suspect	2	Hypertonia	Tremor	Tongue athetosis	Asymmetric	Motivated crying
011	ZIKV	N	1	Suspect	Suspect	2	Hypertonia	Tremor	Choreic	Asymmetric	Absent
012	ZIKV	N	7	Normal	Normal	0	Normal	Absent	Absent	Symmetric	Absent
013	ZIKV	N	4	Normal	Normal	1+	Hypertonia	Absent	Absent	Symmetric	Motivated crying
014	ZIKV	N	4	Delay	Suspect	00	Hypotonia	Axial	Absent	Symmetric	Inconsolable
015	ZIKV	N	2	Normal	Normal	1+	Hypertonia	Absent	Absent	Symmetric	Absent
016	ZIKV	N	2	Suspect	Normal	1	Hypertonia	Tremor	Tongue athetosis	Symmetric	Absent
017	ZIKV	N	2	Suspect	Suspect	1+	Hypertonia	Absent	Choreic	Asymmetric	Irritated
018	ZIKV	N	1	Normal	Normal	1	Hypertonia	Absent	Absent e	Symmetric	Motivated crying
019	ZIKV	N	1	Delay	Suspect	2	Hypertonia	Absent	Ballistic	Asymmetric	Inconsolable

The scale classification is as follows: 5% percentile=delay; 10%=suspect; and >25%=normal. Denver II test: scores according to less than 2 faults=normal; and 2 faults or more=suspect. Ashworth Scale: 00= hypotonia; 0=no increase in muscle tone; 1=slight increase in muscle tone (increased tone at the beginning or at the end of the movement arc), 1+=slight increase in muscle tone (increased tone in less than half of the movement arc); 2=more marked increase in muscle tone (increase of tone in more than half of the movement arc), 3=considerable increase in muscle tone (parts in flexion or extension and moved with difficulty); and 4=rigid parts in flexion or extension.; Irritability classification: (1) absent: when the child remained calm throughout the evaluation; (2) motivated crying: where the child was easily comforted after the crying episodes; (3) irritated: when the child spent most of the time crying and was difficult to comfort; (4) inconsolable: when the child cried all the time and only stopped when he or she slept. Abnormal responses were classified as 3 and 4.

AIMS, Alberta Infant Motor Scale; N, normal; ZIKV, Zika virus.

evaluation. All others had some signs of developmental abnormality (table 2), 2 had hypotonia and the other 16 hypertonia. Half had signs of ataxia, eight had some form of dyskinesia and six had some degree of asymmetry. Irritability was detected in eight children.

Most of the evaluated children had changes in muscle tone, with a predominance of hypertonia. Both hypertonia or hypotonia can be warning signs for central disorders, with possible damages to the pyramidal or extrapyramidal pathways, requiring early physiotherapeutic interventions to minimise their negative impacts.³ Among the signs related to hypertonia are the presence of extensor spasms of lower limbs, compatible with that observed in children with cerebral palsy. Ballistic, choreic and tremor movements also indicate suspected abnormalities. These findings suggest that ZIKV infection in pregnancy can lead to neurodevelopmental abnormalities, even in children without microcephaly.

One previous study of intrauterine ZIKV exposure has reported the development of children with normal head circumference at birth.⁴ The authors reported postnatal development of microcephaly in 11 of 13 infants and all had reduced brain volume on neuroimaging. The clinical findings were similar to ours, since all children had some degree of hypertonia, and some had dysphagia, irritability, a diagnosis of epilepsy, dystonia and spastic hemiparesis.⁴

In congenital Zika syndrome, irritability is reported as one of the most frequent symptoms,⁵ and we found it present in about half of the patients. These findings, even in children without microcephaly, were compatible with those observed in children with cerebral palsy,³ and prognosis may be compromised. Therapeutic actions should begin early to reduce possible sequelae.

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