Zika Virus Infection during Pregnancy and Early Childhood Development, French Polynesia, 2013–2016

Technical Appendix

Technical Appendix Table 1. Anthropometry and comparison between Zika virus seropositive and Zika virus seronegative controls*									
		Zika seropositive,	Zika seronegative,						
	All, n = 107 (n,% or	n = 81 (n,% or median,	n = 26 (n,% or median,						
Data	median, range)	range)	range)	p value†					
Child corrected age [‡] (months)	22.5 (13.4–28.3)	23.2 (13.6–28.3)	19.1 (13.4–25.4)	0.0046					
12–14.9	17 (16)	13 (16)	4 (15)	0.009					
15–17.9	13 (12)	5 (6)	8 (31)						
18–20.9	12 (11)	10 (12)	2 (8)						
21–23.9	35 (33)	26 (32)	9 (35)						
24–30.9	30 (28)	27 (33)	3 (12)						
Anthropometry at birth	n, % or median, IQR	n, % or median, IQR	n, % or median, IQR						
Weight (kg)	3.254 (2.950-3.682)	NA	NA						
Weight Z score§	1.26 (0.68–2.01)	1.43 (0.81–2.03)	0.99 (0.39-2.01)	0.14					
Underweight (Z <u><</u> 2 SD)	0 (0)								
Length (cm)	49 (47–50)	NA	NA						
Length Z score	1.01 (0.43–1.64)	1.09 (0.43–1.72)	0.84 (0.00-1.48)	0.19					
Stunted (Z <u><2</u> SD)	1 (1)	1 (1)	0 (0)	NA					
Head circumference Z score	1.14 (0.44–2.16)	1.16 (0.45–2.28)	0.99 (0.37-1.80)	0.36					
Microcephaly (Z <u><</u> 2 SD)	0 (0)								
Anthropometry at enrollment	n, % or median, IQR	n, % or median, IQR	n, % or median, IQR						
Weight (kg)	12.0 (10.8–13)	NA	NA						
Weight for age (Z score)	0.46 (-0.17 to 1.07)	0.52 (-0.21 to 1.18)	0.32 (0.01–0.81)	0.61					
Underweight (Z <u><</u> 2 SD)	0 (0)	NA	NA						
Height/length (cm)	84 (80-87.5)	NA	NA						
Height/length for age (Z score)	-0.05 (-0.89 to 0.69)	-0.06 (-0.89 to 0.62)	0.17 (-0.19 to 0.87)	0.66					
Stunted (Z<2 SD)	0 (0)								
Weight for height/length (Z score)	0.63 (-0.12 to 1.28)	0.62 (-0.12 to 1.33)	0.66 (-0.12 to 1.14)	0.54					
Wasted (Z<-2 SD)	0 (0)		,						
Head circumference (cm)	48 (47–49)	NA	NA						
Head circumference for age (Z score)	0.57 (0.04–1.33)	0.63 (0.11–1.33)	0.41 (0.04–0.89)	0.38					
Microcephaly (Z<2SD)	0 (0)	. ,	. ,						

*IQR, interquartile range; NA, not applicable; SD, standard deviation

 $\dagger\,^a\text{Pearson}\,\chi^2$ test for proportions and Mann-Whitney test for means

‡ Theoretical age if children were born at term.

§ Z-scores were generated using Intergrowth-21st for anthropometry at birth (1) and using the WHO 2005 growth charts (2) for anthropometry during the visit. A Z-score is defined as the deviation from the mean value of the gender-specific and age-specific reference populations, divided by the standard deviation for the reference population.

Technical Appendix Table	2. Early childhood development scores for French Polynesian children a	and reference children aged 12–30
months*		-

	Reference	(n = 269)	Study particip		
ECD domain	Mean score	SD	Mean score	SD	p value†
Socioemotional	90	10	92	10	0.69‡
Cognitive	64	19	57	26	0.001
Motor	64	20	60	20	0.08

*ECD, early childhood development; SD, standard deviation

†t-test unless specified.

 $\pm\chi^2$ -test using information on children with suspected "abnormal" development (7/107 among study participants and 21/248 among the reference population). The *t*-test was not done because socioemotional scores were not normally distributed.

	1. Socioemotional domain				2. Cognitive domain				3. Motor domain			
	A,	Q,	Ρ,	р	A,	Q,	Ρ,	р	А,	Q,	Ρ,	р
Mothers	n (%)	n (%)	n (%)	value†	n (%)	n (%)	n (%)	value	n (%)	n (%)	n (%)	value
All (N = 107)	100 (93)	3 (3)	4 (4)	NA	68 (64)	23 (22)	16 (15)	NA	81 (76)	20 (18)	6 (6)	NA
Zika virus												
seropositivity												
No	25 (96)	1 (4)	0 (0)	0.63	18 (69)	6 (23)	2 (8)	0.54	19 (73)	6 (23)	1 (4)	0.84
Yes	75 (93)	2 (2)	4 (5)	NA	50 (62)	17 (21)	14 (17)	NA	62 (76)	14 (17)	5 (6)	NA
History of Zika												
infection												
No infection	33 (97)	1 (3)	0 (0)	0.67	24 (71)	8 (24)	2 (6)	0.48	25 (74)	8 (24)	1 (3)	0.26
during												
pregnancy‡												
Asymptomatic	51 (91)	2 (4)	3 (5)	NA	33 (59)	12 (21)	11 (20)	NA	44 (79)	10 (18)	2 (4)	NA
(timing												
unknown)§												
Symptomatic	16 (94)	0 (0)	1 (6)	NA	11 (65)	3 (18)	3 (18)	NA	12 (71)	2 (12)	3 (18)	NA
during												
pregnancy¶												

Technical Appendix Table 3. Early childhood development and maternal Zika virus infection status, French Polynesia, 2013–2016*

*A, Adequate; NA, not applicable; Q, Question; P, Problem †P values obtained using Fisher's exact test.

¹Seronegative mothers and seropositive mothers who reported Zika-like illness outside pregnancy.

§ Seropositive mothers who did not report Zika-like illness during or outside pregnancy.

Seropositive mothers who reported Zika-like illness during pregnancy.

Technical Appendix	Table 4. Crude OR for the association of ECD b	y domain wi	th Zika	virus infection	, French Polynesia, 20	13–2016*

			Cognitive de	omain	Motor domain		
	 Socioemotional 	domain†	(ordered logistic re	gression,	(ordered logistic regression,		
	(logistic regression,	Adequate	Adequate vs. Que	estion vs.	Adequate vs. Question vs.		
	vs. Question/Pr	oblem)	Problem)	Problem)		
	Crude OR LRT		Crude OR	LRT	Crude OR	LRT	
Category	(95% CI) p-value		(95% CI)	p-value	(95% CI)	p value	
Zika virus seropositivity	2.00 (0.23-17.4)	0.50	1.51 (0.60–3.81)	0.37	0.87 (0.32-2.36)	0.74	
History of Zika virus infection							
Asymptomatic (timing unknown)‡	3.24 (0.36-28.9)	0.50	1.55 (0.60-4.00)	0.66	0.77 (0.27–2.17)	0.63	
Symptomatic during pregnancy§	2.06 (0.12-35.1)	NA	1.37 (0.38–4.89)	NA	1.37 (0.35–5.31)	NA	

*CI, confidence interval; LRT, likelihood ratio test; OR, odds ratio

+Because of the limited number of observations in the socioemotional domain, Question and Problem categories were grouped together and logistic regression was performed.

\$ Seropositive mothers who did not report Zika-like illness during or outside pregnancy.

§Seropositive mothers who reported Zika-like illness during pregnancy.

References

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- 2. de Onis M, Garza C, Victora CG, Onyango AW, Frongillo EA, Martines J. The WHO Multicentre Growth Reference Study: planning, study design, and methodology. Food Nutr Bull. 2004;25(Suppl):S15-26. PubMed http://dx.doi.org/10.1177/15648265040251S103