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Rotavirus-Specific IgG Antibodies from Mothers' Serum may Inhibit Infant Immune Responses to the Pentavalent Rotavirus Vaccine

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To the Editors

Rotavirus vaccines have lower effectiveness in low and middle income countries (LMICs). One possible explanation is vaccine inhibition by rotavirus-specific antibodies present in mothers' sera or breast milk. IgG antibodies in maternal sera are transferred through the placenta and may inhibit vaccine-elicited immune responses, as recently reported for the 116E rotavirus vaccine (1). Also, breast milk IgA and neutralizing antibodies (NA) may directly inhibit the oral vaccine upon administration (2,3). Breast milk from LMIC mothers has higher levels of rotavirus-specific antibodies as compared to mothers from high income countries (3,4), indicating a greater potential for inhibition. We examined the association between rotavirus-specific antibodies in maternal sera and breast milk and immunogenicity to the first dose of the pentavalent rotavirus vaccine (RV5, Rotateq®) in respective infants.

Mother-infant pairs were recruited in León, Nicaragua in 2012. Eligibility criteria included: normal birthweight, gestational age > 35 weeks, currently breastfeeding > four times daily, and mother and infant without known immune disorder or blood transfusion. We measured

rotavirus-specific antibodies in maternal and infant serum at the time of RV5 immunization, and in infant serum four weeks following the first dose (post-dose 1) by EIA (2,4). Breast milk samples of mothers collected at the time of immunization were assayed for rotavirus-specific IgA and NA (2). For IgA and IgG assays, we started dilutions at 1:10, while for breast milk NA assays, we started dilutions at 1:2. Pre-immunization seropositivity was defined as pre-immunization rotavirus-specific IgA titers > 40 (5). Seroconversion was defined as > four-fold increase in rotavirus-specific IgA titers in the infant between the pre-immunization and post-dose 1 serum samples. Spearman's rank correlation coefficients were estimated to examine associations between rotavirus-specific IgG antibodies in maternal serum and infant pre-immunization serum. Wilcoxon rank sum tests were used to compare antibody titers between groups.

The 45 infants enrolled had a median pre-immunization rotavirus-specific IgA titer of 10 and post-dose 1 titer of 80. Among all infants, 22.2% were seropositive prior to immunization. There was a positive association between rotavirus-specific IgG titers in maternal serum and pre-immunization infant serum ($r=0.57$, $p<0.0001$).

Sixty-nine percent of infants met the seroconversion definition post-dose 1. Infants who did not seroconvert had mothers with higher serum rotavirus-specific IgG titers as compared to mothers of infants who did seroconvert (median 5120 in non-seroconverters vs. 2560 in seroconverters, $p=0.02$) (Table 1). Also, seroconversion occurred among 30% of infants who were IgA seropositive prior to immunization vs. 80% of infants who were not IgA seropositive prior to immunization ($p=0.005$). There was no significant difference in breast milk rotavirus-specific IgA titers between infants who did and did not seroconvert, although our sample size may not have been large enough to detect a small difference.

This study suggests that high titers of maternal rotavirus-specific IgG antibodies at the time of immunization may inhibit RV5-elicited immune responses. It is unclear whether these infants will be protected through active immunization from the remaining RV5 doses. Also, infants who were IgA seropositive prior to immunization were less likely to seroconvert. The clinical importance of pre-immunization IgA seropositivity in terms of vaccine immunogenicity and protection from rotavirus disease warrants further investigation.

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References

1. Appaiahgari MB, Glass R, Singh S, et al. Transplacental rotavirus IgG interferes with immune response to live oral rotavirus vaccine ORV-116E in Indian infants. *Vaccine*. 2014; 32(6):651–6. [PubMed: 24374502]
2. Moon SS, Wang Y, Shane AL, et al. Inhibitory effect of breast milk on infectivity of live oral rotavirus vaccines. *Pediatr Infect Dis J*. 2010; 29(10):919–23. [PubMed: 20442687]

3. Moon SS, Tate JE, Ray P, et al. Differential Profiles and Inhibitory Effect on Rotavirus Vaccines of Nonantibody Components in Breast Milk From Mothers in Developing and Developed Countries. *Pediatr Infect Dis J.* 2013; 32(8):863–870. [PubMed: 23584581]
4. Wang Y, Azevedo M, Saif LJ, Gentsch JR, Glass RI, Jiang B. Inactivated rotavirus vaccine induces protective immunity in gnotobiotic piglets. *Vaccine.* 2010; 28(33):5432–6. [PubMed: 20558244]
5. Groome MJ, Moon SS, Velasquez D, et al. Effect of breastfeeding on immunogenicity of oral live-attenuated human rotavirus vaccine: a randomized trial in HIV-uninfected infants in Soweto, South Africa. *Bull World Health Organ.* 2014; 92(4):238–45. [PubMed: 24700991]

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Table 1

Comparison of baseline rotavirus-specific antibody titers between infants who seroconverted* and infants who did not seroconvert (median titers [interquartile ranges])

	Seroconverters n=31	Non-seroconverters n=14	p-value[†]
IgA in infant sera (pre-immunization)	10 [1, 10]	30 [10, 80]	0.02
IgG in infant sera (pre-immunization)	1280 [640, 2560]	2560 [1280, 5120]	0.11
IgA in mother's sera	640 [320, 1280]	640 [320, 2560]	0.80
IgG in mother's sera	2560 [2560, 5120]	5120 [5120, 10240]	0.02
IgA in breast milk	160 [80, 320]	320 [160, 320]	0.20
Neutralizing antibody in breast milk	1 [1, 4]	1.5 [1, 4]	0.53

* Seroconversion definition: Four-fold increase in rotavirus-specific IgA titers in postdose 1 serum as compared to pre-immunization sera

[†] Wilcoxon ranksum tests were used to compare titers between seroconverters vs. nonseroconverters.