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Oral polio vaccine response in breast fed infants with malnutrition and diarrhea

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ABSTRACT

Oral vaccines for polio (OPV) and rotavirus are less effective in children in the developing world. The reasons for this are not well understood. We tested for risk factors for poor response to OPV in infants from an urban slum of Dhaka, Bangladesh. Diminished serum neutralizing response to OPV, but not failure of intramuscularly administered vaccines, was associated with malnutrition, diarrhea, and shorter breastfeeding duration. Children with malnutrition (WAZ <−2) had significantly lower OPV 3 titers ($p = 0.029$). Children who had 2 or more diarrhea episodes during the 1st months of life were more than twice as likely to experience OPV failure as those who had 1 diarrhea episode or no diarrhea ($p = 0.0245$). In contrast, each additional month in exclusive breastfeeding was associated with an increase in OPV 3 titer by 0.41 ($p = 0.0072$) and 0.16 ($p = 0.0065$) at the 25th and 50th percentiles of OPV 3 titers respectively. These data are consistent with a defect in induction of immunity in the gut for OPV but not parenteral vaccines, a defect that may be amenable to intervention in part via promotion of exclusive breastfeeding.

1. Introduction

Oral polio vaccine is less effective in children in the developing world [1]. The per dose efficacy of the trivalent OPV has been estimated to be 50% in the United States but only 21% in India [2]. Similarly, oral rotavirus vaccine was only half as effective at preventing severe rotavirus infection [3,4]. Hypotheses for this lower efficacy of oral vaccination in developing countries include malnutrition, diarrheal disease, and environmental enteropathy [5–12]. Environmental enteropathy is thought to be common in children in the developing world and is pathologically characterized by villous shortening with increased intraepithelial lymphocytes in the small intestine [9–12]. There is little data on the effectiveness of oral vaccines in children with environmental enteropathy, but it has been observed that OPV is less effective if given during episodes of diarrhea [13]. This suggested a potential link of enteric infection and enteropathy with vaccine failure, and led us to test for such an association in infants in Dhaka, Bangladesh.

2. Methods

2.1. Longitudinal birth cohort

The children studied were from an urban slum of the Mirpur Thana of Dhaka, Bangladesh. Subjects were identified by a census for pregnant women in the community, conducted by trained field research assistants. Children were enrolled within the first week of birth starting in January 2008 and followed by twice-weekly household visits until one year of age. A total of 435 children entered the cohort who received OPV (any number of doses). 314 children received at least three doses of OPV by 12 months, of whom 258/314 received 3 doses by 6 months of age. The median number of doses was 3 and the lower and upper quartiles were 3 and 4 respectively. Diarrhea was defined as three loose or unformed stools in 24 h, or by the mother's report in a breast fed infant under the age of one year. Exclusive breast feeding was defined by the mother's

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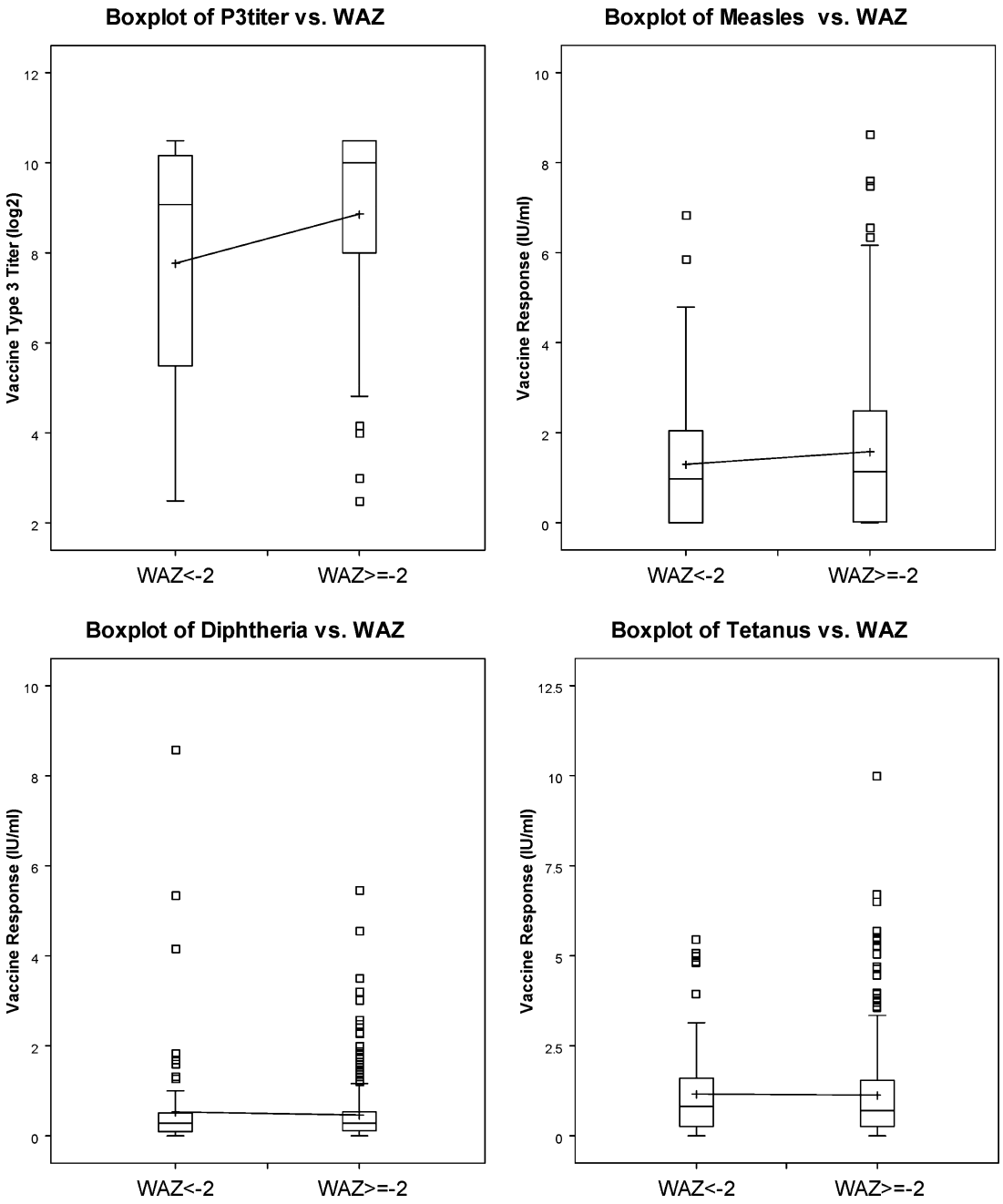

Fig. 1. Oral polio vaccine type 3 and parenteral vaccine responses in well and malnourished children. The titers of serum neutralizing antibody responses to OPV type 3 and parenterally-administered vaccines at 12 months of age for children with WAZ scores of <−2 were compared to those with WAZ >−2 at 6 months of age ($n = 314$; $p = 0.0289$ for OPV; $n = 435$ and $p =$ NS for diphtheria, tetanus, and measles vaccine responses; Kolmogorov–Smirnov rank order test).

monthly report of her child's consumption of human milk without supplementation (including water but excluding medications). The study was approved by the Research and Ethical Review Committees of the International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, and the Institutional Review Board of the University of Virginia. There have been two previous reports from this cohort on enteric infections [14,15].

2.2. Anthropometry

Weight and length of the children were assessed using electronic scales and length boards precise to 10 g and 1 mm respectively (SECA Gmbh & Co, Hamburg, Germany). The mean of two consecutive measurements were recorded. These were converted to weight for age (WAZ) and length for age (LAZ) using the WHO Multicenter Growth Reference Study child growth standards [16]. Underweight was defined as WAZ <−2 and stunting as LAZ <−2.

2.3. Vaccine history and immunogenicity

Immunization histories were obtained from the infants' mothers, and only children with a minimum of three OPV immunizations were included in the analyses. Serum neutralizing antibodies to the type 1–3 polio strains were measured at the CDC, Atlanta as previously described [17,18]. The $\log_2$ based titer was used in all OPV analyses. Tetanus, measles, and diphtheria serum IgG levels were expressed in IU/ml and were measured by ELISA as directed by the manufacturer's instructions (Virion/Serion GmbH, Germany).