Vibriocidal Titer and Protection from Cholera in Children

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Background

• Vibrio cholerae infection causes over 100,000 deaths each year from severe diarrhea/dehydration.
• There are two primary serogroups of V. cholerae.
  o O1: subdivided into Ogawa and Inaba serotypes.
  o O139
• Serum vibriocidal antibodies correlate with immunity.
  o Increased titers correlate with protection.
  o Baseline titers increase with age, likely due to recurrent exposure to V. cholerae in endemic areas.
• Oral cholera vaccination produces a robust vibriocidal response in all age groups, yet vaccine efficacy is lower and of shorter duration in children under 5 years.
• Do vibriocidal titers predict protection from V. cholerae in children as accurately as in adults?

Research Question

To assess whether vibriocidal titers are equally predictive of protection from V. cholerae infection across all age groups.

Methods

Vibriocidal antibody assay:
• Baseline vibriocidal titers were measured using guinea pig complement and the homologous Ogawa and Inaba serotypes.

Statistical analysis:
• Outcome of interest: infection with V. cholerae.
• Mean log vibriocidal titer stratified by infection and age.
• Logistic regression models generated for age groups.
• Generalized estimating equations with a compound symmetry correlation structure adjusted for household clustering. Age was modeled as a continuous and categorical variable. The goodness of fit was compared using Quasilikelihood under the Independence model Criterion (QIC).

Results

• Total enrolled household contacts: 1,741.
• Contacts excluded for:
  o Diarrhea during follow-up but negative rectal swabs (indeterminate result for infection).
  o Cholera symptoms in the week before enrollment or day of enrollment.
  o Fewer than three measured vibriocidal titers.
  • 826 household contacts included in final study.
  • The mean baseline titer was higher in uninfected household contacts in all age groups compared to contacts who developed V. cholerae infection during follow up (Figure 1).
  • No interaction between age and vibriocidal titer (age as continuous variable): P = 0.66

Discussion/Conclusions

We investigated whether vibriocidal titers uniformly predict protection from V. cholerae infection in different age groups. We found that the degree to which vibriocidal titers predict protection across age strata was uniform.

This suggests that how the vibriocidal titer relates to long-term memory B cell responses (the most likely mediator of long term protection) after V. cholerae infection differs between adults and children. This could be because children have less lifetime exposure to V. cholerae, resulting in less immunologic priming. Other host factors that vary between adults and children may also play a role, such as immunologic immaturity, malnutrition, enteric enteropathy, or gut microbiome differences.

Results indicate that the vibriocidal titer cannot be successfully used to distinguish between differences in protection afforded by cholera vaccines in adults compared to children. Improved markers of protective immunity are needed for measuring vaccine efficacy in children.

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