Vibrio cholerae causes a spectrum of infection in humans ranging from asymptomatic colonization to rapidly fatal secretory diarrhea. Adaptive immune responses from previous exposure as well as innate genetic and nutritional characteristics are likely to influence susceptibility to V. cholerae infection and disease. To evaluate factors associated with susceptibility to V. cholerae, we prospectively observed a cohort of household contacts of patients with cholera in Bangladesh.

Household contacts of patients presenting to the ICDDR,B hospital with acute watery diarrhea due to V. cholerae were selected for inclusion in this study. Within 4 to 6 hours of presentation of the index case, a field team discussed enrollment with household contacts of the index patient, defined as individuals sharing the same cooking pot. Blood specimens for ABO typing and baseline measurements of cholera-specific immunologic measurement were collected immediately upon enrollment from consenting contacts. Contacts were visited on each of the next six days and on days 14 and 21. During these visits, contacts were questioned about diarrheal symptoms, and rectal swabs were obtained for V. cholerae culture. We compared the baseline characteristics of contacts that had a positive rectal swab for V. cholerae with contacts that had no evidence of V. cholerae infection.

Of the 1077 household contacts that were enrolled, 938 completed 21 days of observation. Of the 938 household contacts that were evaluated, 202 had a positive rectal swab for V. cholerae and 422 had no evidence of V. cholerae infection. In the assessment of baseline immunologic markers among contacts, we found that V. cholerae antigen-specific serum IgA levels predicted individual’s susceptibility to V. cholerae infection. Higher levels of IgA directed at the toxin coregulated pilus (TCP) and cholera toxin (CT) were associated with protection from infection with both the O1 and O139 serogroups V. cholerae. Higher serum levels of IgA specific to lipopolysaccharide (LPS) were associated with protection from infection with V. cholerae O1, but not with V. cholerae O139. Serum levels of these antibodies did not predict whether contacts developed symptoms if infected; a similar finding was observed for the vibriocidal titer. In contrast, serum CT, LPS and TCP specific IgG antibodies were not predictive of the likelihood of infection with V. cholerae in our cohort.

To explore the relationship between micronutrient levels and susceptibility to cholera, we also evaluated baseline zinc and retinol levels in a subset of our cohort. We did not find an association between serum zinc levels and susceptibility to cholera. Retinol deficiency was associated with an increased risk of infection with V. cholerae O1, and low retinol levels were also strongly associated with a higher likelihood of developing symptomatic disease if infected.

As we previously described in an initial subset of the current cohort, we found that individuals with blood group O were less likely to become infected with V. cholerae O1, but if infected had greater than twice the odds of developing symptomatic infection. Because we hypothesized that additional genetic factors contribute to host susceptibility to cholera, pedigree analysis demonstrated that household contacts who were first degree relatives (sibling, parent or child) of the index case had increased odds of being infected with V. cholerae compared to non-related or less closely related household contacts (OR 2.90, P=0.028, 95% CI 1.12-7.52). This suggests a genetic component of susceptibility to cholera that merits further study.