

TITLE: *Campylobacter jejuni* virulence traits associations with growth impairment in children from Northeastern Brazil.

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ABSTRACT

Campylobacter spp. are well-recognized as being important causes of diarrhea worldwide, whereas *C. jejuni* is the leading pathogenic species. Recent studies have shown remarkable associations between *Campylobacter* infections and anthropometric Z-score decrements even without the presence of diarrhea, but none have investigated potential virulence strategies more associated with these outcomes. This study aimed to investigate whether specific *Campylobacter jejuni* virulence factors are associated with malnutrition in children from Northeastern Brazil. A case-control design was undertaken at the city of Fortaleza, Ceara, Brazil. Children aging 6-24 months were enrolled from August 2010 to June 2013. Malnourished children (cases) were characterized by weight-for-age Z-score (WAZ) ≤ 2 ; and controls by WAZ ≥ 1 . Feces were collected at the enrollment time and were processed for DNA extraction. DNA samples previously diagnosed positive for *C. jejuni/coli* by Real-Time PCR were further analysed for targeting *C. jejuni* by detection of *hipO* (hippurate hydrolase) gene using conventional PCR. A total of 33 samples (12 cases and 21 controls) was evaluated for the presence of a diverse panel of 18 *C. jejuni* virulence genes by four conventional Multiplex PCRs. Data analysis was made by investigating gene combinations with CART (Classification and Regression Tree) software. *CadF* (adhesion), *iamA* (invasion), *cheW* (chemotaxis) and *sodB* (survival to oxidative stress) genes were the most prevalent genes in this population (100%, 90.9%, 87.9% and 75.8%, respectively). None individual virulence gene was associated with case or control groups. The CART tree provided a specific group of DNA samples associated with malnutrition, being characterized by the absence of *cdtB* gene and the presence of *flgE* gene (P = 0.0272 OR = 8.125, 95% CI 1.4 to 47.0 by Fisher's exact test). CdtB is the active subunit of the cytolethal distending toxin complex and is often associated with diarrhea, whereas FlgE is the flagellar hook protein which may be related to persistent colonization. *C. jejuni* strains lacking CdtB and harboring flgE might lead to a less diarrheagenic and more chronic infection, which contributes to a poorer intestinal absorptive capacity and subsequent malnutrition. These data reinforce the impact of *Campylobacter* for enteropathy and highlights the contribution of specific virulence genes for pathobiology.

Keywords: *Campylobacter jejuni*, virulence, malnutrition, children.

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