

TITLE: ENTEROAGGREGATIVE *Escherichia coli* CAUSES SUBCLINICAL INFECTION IN MALNOURISHED C57BL / 6 MICE BY REGIONAL BASIC DIET

AUTHORS: RIBEIRO, S. A.; PEREIRA, J. M.; MEDEIROS, P.H.Q.S.; AMARAL, M.S.M.G; VERAS, H.N.; GUANABARA JÚNIOR, M. F. A.; RODRIGUES, F.A.P.; HAVT, A.; LIMA, A.A.M.

INSTITUTION: Departamento de Fisiologia e Farmacologia, Universidade Federal do Ceará, Fortaleza, CE, Brasil.

ABSTRACT:

The vicious cycle of enteric infections-malnutrition affects about one-third of children in developing countries, being able to cause physical and cognitive impairments. In this context, enteroaggregative *Escherichia coli* (EAEC) infections are important because they cause persistent diarrhea in malnourished children and show high prevalence in communities with low socioeconomic status from Fortaleza, Brazil. The objective of this study was to evaluate the intestinal barrier modulation by EAEC in mice malnourished by a regional basic diet that resembles malnutrition from children from northeastern Brazil. C57BL / 6 mice (21 days old) were submitted to malnutrition by the regional basic diet and after 14 days received orally the EAEC 042 strain inoculum of 5×10^8 CFU (ethics committee nº 17/15). Animals were evaluated daily for weight, water and diet consumption for a period of 21 days post-infection. Feces were collected for pathogens quantification and portions of the jejunum were collected for morphological and myeloperoxidase (MPO) analysis. Parametric data were analyzed by ANOVA followed by *Bonferroni* post-test, whereas non-parametric data were analyzed by ANOVA followed by *Kruskal-Wallis* test. The results were considered significant at $P < 0.05$. Infection with EAEC 042 strain did not cause a significant reduction ($P > 0.05$) on weight gain when compared to controls, and did not induce diarrhea. Food and water intakes in the infected groups were slightly higher than the controls, but without significant difference ($P > 0.05$). When evaluating pathogen load in the stools, EAEC was detected up to 21 days post-infection. Infection affected mainly malnourished animals, with a significant reduction ($P < 0.05$) in the crypt of malnourished/infected animals when compared to the malnourished group, as well significantly reduction the villus ($P = 0.003$) and consequent reduction in villus/crypt ratio ($P < 0.005$), when compared to nourished/infected animals. Morphometric changes appeared independently of inflammatory processes elicited by EAEC infection, as there was no significant difference ($P < 0.05$) between the groups infected. EAEC is able to colonize the intestine of nourished and malnourished mice, altering intestinal morphology mainly of malnourished animals, however without causing clinical manifestations such as reduction of weight gain or presence of diarrhea.

Keywords: enteroaggregative *Escherichia coli*, infection, malnutrition

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