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## Intestinal Permeability in Normally Nourished and Malnourished Children with and without Diarrhea

We evaluated the association between diarrhea, malnutrition and intestinal function using the lactulose-mannitol test. Our study showed that a third of all children have abnormal intestinal permeability, there was an expected increase of permeability in children with acute diarrhea and alteration in intestinal permeability was greater in children with concurrent malnutrition and diarrhea.

**Key words:** *Diarrhea, Intestinal permeability, Lactulose-mannitol test.*

**A**cute and persistent diarrhea have been associated with increased intestinal permeability, and repeated episodes of diarrhea result in malnutrition in children [1-3]. To study the association between diarrhea, malnutrition and intestinal function we evaluated intestinal permeability in children admitted with acute gastroenteritis and controls with no gastrointestinal illness.

All children aged 6-59 months, hospitalized for management of acute gastroenteritis, without co-morbid conditions and with a weight >5 kg, were eligible for recruitment as cases. For each case, a child admitted at the same time for an illness other than severe infection or gastrointestinal disease was recruited. Written informed consent was obtained from parents and the study was approved by the institutional review board. Clinical management was according to regular protocols, with oral or intravenous rehydration as indicated. All children had anthropometric measurements recorded using calibrated weighing scales and infantometer and underwent the lactulose-mannitol test for intestinal permeability.

Malnutrition was defined as a weight for age Z score

below -2SD by WHO Anthro [4]. For the lactulose-mannitol test, after a 3-hour fast, children were given 2 mL/kg body weight of test solution containing 50mg/ml of mannitol and 250 mg/mL of lactulose. The entire volume of urine passed in the 5 hour period following the test solution was collected using adhesive urine bags in a container with 1 mL of chlorhexidine. The volume was measured and a 10 mL aliquot stored in a sterile 15 mL polypropylene tube at -20°C until testing. The ratio of urinary excretion of lactulose to mannitol was measured by high performance liquid chromatography (Ultra Fast Liquid Chromatography System, Shimadzu, Spinco Biotech, Chennai) with evaporative light scatter detection using melibiose as an internal standard. The values of lactulose mannitol in urine are expressed as the ratio % excretion of lactulose / % excretion of mannitol (or LM ratio) during the 5 hours, and a ratio of greater than or equal to 0.089 indicates increased permeability [5,6]. Fischer's exact test was used to compare proportions between groups

A total of 64 children were enrolled, with 34 cases and 30 controls. Ten children were excluded, five because of inadequate sample collection and five because of problems with determining the LM ratio. Thus, data from 54 children were analysed, with 26 cases and 28 controls. There were differences in age, weight and height in children enrolled as cases and controls, with controls being older (mean age of 28 months vs. 19 months), and consequently taller (mean height 84.7 cm vs. 79.1 cm) and heavier (10.7 kg vs. 8.8 kg), but there were no differences in the gender distribution (67% male vs. 73% male) or nutritional status (mean WAZ score -1.5 vs. -1.8). The LM test showed increased

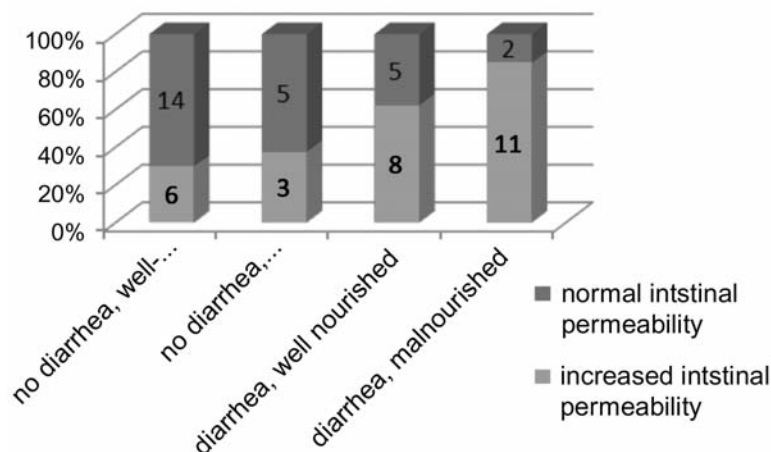


FIG. 1. Distribution of children in each category.

permeability in 61.5% of children with acute diarrhea and 32.2% of children without diarrhea ( $P=0.01$ ). When the children were stratified by nutritional status, 78.6% of children with malnutrition and acute diarrhea and 37.5% of malnourished controls had increased intestinal permeability.

Mannitol is absorbed transcellularly and lactulose has a paracellular route of absorption. Reduction in mannitol absorption shows reduced surface area and increased lactulose absorption indicates a leaky gut [7]. In this study, use of the LM test in a south Indian population showed that a third of all children have abnormal intestinal permeability, there was an expected increase of permeability in children with acute diarrhea and alteration in intestinal permeability was greater in children with concurrent malnutrition and diarrhea. We acknowledge the limitations of small numbers and differences between cases and controls.

Malnutrition and diarrhea form a vicious cycle leading to worsening of the malnutrition state and outcome of diarrheal infections [8], which may potentially be prevented with better nutrition or mechanisms such as by tightening cell junctions or promoting rapid repair of intestinal epithelium.

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