The Gut Microbiome in Child Malnutrition

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Undernutrition affects almost 25% of all children under the age of 5 worldwide and underlies almost half of all child deaths. Child undernutrition is also associated with long-term growth deficits, in addition to reduced cognitive potential, reduced economic potential, and elevated chronic disease risk in later life. Dietary interventions alone are insufficient to comprehensively reduce the burden of child undernutrition and fail to address the persistent infectious burden of the disease. Although the role of infections is well recognized in the pathogenesis of undernutrition, an emerging body of evidence suggests that commensal microbial communities, known as the microbiome, also play an important role [1].

Succession of the early-life gut microbiome critically regulates the structuring of the intestinal barrier, energy harvesting from nutrients, growth hormone signaling, colonization resistance, and immune tolerance against pathogens, among other pathways critically associated with healthy child growth. Hence, disturbance of the normal gut microbial ecosystem via undernourished diets or unhygienic environments, especially in the early phases of life, may perturb these critical pathways associated with child growth, thereby contributing to child undernutrition. Indeed, the programmed maturation of the gut microbiome in the first 2 years of life, as measured by the microbiome-for-age Z-score (MAZ), is highly predictive of healthy child growth [2]. Gut microbiome “immaturity” during this early life period is associated with undernutrition.

Stunting, a chronic form of undernutrition characterized by low height-for-age, is associated with compartmentalization of the intestinal tract, whereby commensal microbial taxa of oropharyngeal origin are found lower in the gastrointestinal tract [3]. It is hypothesized that the presence of these microbes outside of their ecological niche may stimulate a chronic inflammatory cascade leading to environmental enteropathic dysfunction (EED) and growth faltering. Preclinical studies have also demonstrated the essential role of the gut microbiome in linear growth via interaction with insulin-like growth factor 1 (IGF-1) and growth...
hormone [4]. Wasting, a more acute form of child undernutrition, does not present with a consistent gut microbiome profile; however, a reduced MAZ is associated with severe wasting. MAZ fails to persistently recover following standard therapeutic feeding for severe wasting, suggesting that current feeding protocols are insufficient to restore the gut microbiome to a healthy state [2].

Interventions to target the gut microbiome in child undernutrition have yet to yield convincing beneficial effects. Antibiotics appear to exert beneficial effects for linear growth; however, their benefits for growth recovery following severe wasting remain inconclusive [5]. Furthermore, the threat of antimicrobial resistance limits the future potential for mass antibiotic usage for child growth. Some probiotics pose potential to reduce undernutrition-associated diarrhea and increase weight; however, future interventions must consider timing of probiotic interventions, colonization potential, and strain specificity. Fecal microbiome transplantation poses potential as a novel therapy to tackle severe wasting; however, it remains untested.

Research into the gut microbiome has led to novel therapies that have significantly improved both survival and quality of life in patients with chronic intestinal and metabolic disorders in high-income settings. This wealth of knowledge must now be applied with a global health perspective in LMIC in order to improve child mortality and undernutrition, both of which remain unacceptably high. With expanding knowledge from preclinical and observational studies, future research must begin to investigate microbiota-directed therapies, which pose real potential to reduce the mortality and morbidity associated with child undernutrition.

References