**PICH Editorial Gastroenterology special edition**

**Challenges and opportunities for paediatric gastroenterology in low and middle income countries: high time to act.**

Paediatric gastroenterology remains a poorly developed area of subspecialty paediatrics in many low and middle income countries (LMIC)1,2. Here, general paediatricians and other health staff with no specialist training manage as best they can often complex paediatric gastroenterology conditions which often results in delayed diagnosis, complications and avoidable mortality.

In LMIC, there are few formally trained and certified paediatric gastroenterologists and few subspecialty training programmes.3,4 This contrasts sharply with well-structured and equipped centres in high-income countries (HIC) that support trainees in acquiring competence in enteral nutrition, endoscopy, endoscopic retrograde cholangiopancreatography, imaging and the use of bowel motility, immunology and genetic studies.

In Nigeria, like in many LMIC, most of the pioneers of this subspecialty were trained in the United Kingdom, Europe and North America and have since retired from practice either within or outside the country. Although the thinking then and lately is that LMIC require mainly the services of general paediatricians rather than subspecialists, however, these pioneers trained a cohort of subspecialists, though relatively few in numbers, who continue to train others. The Society of Gastroenterology, Hepatology and Nutrition in Nigeria,5 comprises of paediatricians, physicians, surgeons, radiologists and pathologists, has helped to promote the subspecialty. The MSc in Tropical Paediatrics at the University College Hospital, Ibadan, Nigeria has a module in Tropical Paediatric Gastroenterology and Nutrition and a new initiative led by the Postgraduate Medical Colleges in Nigeria aims to develop this subspecialty. In South Africa, paediatric gastroenterology has recently been registered as a subspecialty by the Health Professions Council1 and training opportunities are increasing; for example programmes offered by the University of Cape Town.6 However, there are few training programmes and fellowships in high-income settings that are accessible to LMIC practitioners.

In LMIC, national epidemiological data are not readily available to inform the development of paediatric gastroenterology services with information limited mainly to nutritional status and diarrhoeal disease. Information on less common diseases is mostly limited to case reports and single centre case series. However, as highlighted in this special issue of Paediatrics and International Child Health, gastrointestinal disorders such as coeliac disease and inflammatory bowel disease (IBD) which constitute a high proportion of the case load in HIC, are increasingly recognised in LMIC where there is sufficient awareness and also technology for diagnosis. In Liverpool, we have our own experience: a RCPCH Fellowship at Alder Hey Children’s NHS Foundation Trust for one of the authors (AA) resulted in the first diagnosis of ulcerative colitis in a child in over 30 years at the University College Hospital Ibadan, Nigeria. Subsequently, two other cases have been diagnosed probably due to increasing awareness and diagnostic capability.

Building the capacity of subspecialists in paediatric gastroenterology will improve the diagnosis of such diseases beyond that based on clinical diagnosis. The availability of paediatric endoscopy in LMIC is critical and growing as highlighted by Adeniyi et al in Lagos, Nigeria, where it is used mainly in the diagnosis of upper GI disorders with an overall endoscopic yield of 60.2%.7 In two tertiary centres in South-west Nigeria, paediatric endoscopy is performed by adult gastroenterologists.8 Although endoscopy services are more accessible for the general population in South Africa, there is a high case load and recurrent disruptions impact negatively on service delivery.9 These established adult services provide an infrastructure to develop endoscopy for children. However, in all settings, due consideration for creating a safe environment for children and developing the required support from multidisciplinary teams including paediatric dietetics, anaesthesia and histopathology is needed.10

Expansion of specialist training and international collaborations are needed not just to better diagnose and manage the full spectrum of paediatric gastroenterological disorders in LMICs, but also to capitalise on the renewed focus on the role that poor gut health plays in malnutrition. Slow progress in preventing malnutrition means that, currently, more than 1 in 5 under fives (150.8m worldwide) are stunted and wasting affects 7.5% of children (50.5m), of whom 16.4m have severe wasting.11 An aggregate measure of undernutrition that included fetal growth restriction, stunting, wasting, micronutrient deficiencies and suboptimal breastfeeding was estimated to account for a staggering 45% of all child deaths in 2011 (3.1m deaths).12 The little available evidence regarding the longer-term outcome of severe acute malnutrition indicates a high burden of chronic disease.13

Interventions such as micronutrients during pregnancy, exclusive breastfeeding, safe complementary feeding and improvements to water, sanitation and hygiene practices, even with high levels of compliance, have not had the desired impact on improving growth.14,15 It was estimated that achieving 90% coverage with the best ten evidence-based nutrition-specific interventions would reduce stunting by only 20%16 thereby achieving only half of Sustainable Development Goal 2 - a 40% reduction in the prevalence of stunting by 2025.17

New insights into the role that environmental enteric dysfunction (EED; previously “tropical” or “environmental” enteropathy), plays in growth faltering present new opportunities. EED is a sub-clinical condition characterized in small intestinal biopsies by chronic inflammation, villous atrophy, and a “leaky” mucosa.18 EED is universal in people living with poor sanitation and hygiene and occurs early in life despite exclusive breastfeeding; >80% of infants in an urban slum in Bangladesh had evidence of EED by age 12 weeks despite exclusive breastfeeding for an average 120 days.19 The main manifestation of EED is impaired linear and ponderal growth resulting from impaired nutrient digestion and absorption and increased systemic inflammation. Studies demonstrating growth faltering associated with enteropathy, diarrhoea and asymptomatic gut infections20-21 have built on early work in The Gambia that attributed 40% of linear growth faltering to enteropathy.23

A composite of three domains for the diagnosis of EDD in therapeutic trials have been proposed: 1) age, linear growth failure, negative coeliac disease testing; 2) gut histopathology consistent with EED or at least two intestinal deficits assessed by less invasive biomarkers; 3) biomarkers nonspecific to enteric dysfunction but representing consequences of EED.24 Although small intestinal biopsy remains the gold standard for diagnosis, further evaluation of biomarkers of systemic and intestinal inflammation and mucosal integrity in stool and blood will facilitate community-based studies.25,26

The MAL-ED studies (8 sites across Southern Asia, Latin America and sub-Saharan Africa)27 and a study in Bangladesh28 have highlighted the role of subclinical enteric infection, especially with bacteria that damage the intestinal mucosa, in causing EED. As well as a greater understanding of the pathogenesis of EED, molecular techniques have offered new insights into gut microbiome development in early life and how this affects gut health and development. With the onset of breastfeeding, lactobacilli and bifidobacteria that are highly adapted to metabolise human glycans (human milk oligosaccharides and intestinal mucin) flourish and become abundant. From the minimal microbial colonisation at birth, there is a gradual diversification of the microbial community to resemble the adult microbiota by age 2-3 years.29 Bifidobacteria, as “primary microbial degraders”, are thought to play a key role in facilitating gut colonisation by a diverse range of anaerobes , cross-feeding other organisms through hydrolysing complex carbohydrates and producing organic acids. Some strains also have direct immune-modulatory, anti-inflammatory and anti-pathogen effects.29,30

This pattern of colonisation observed in healthy, breastfed infants is adversely affected by common environmental factors such as Caesarian section delivery, feeding and hygiene practices and exposure to antibiotics.29,30 Several studies have reported delayed maturation of the gut microbiome and a deficiency of *Bifidobacterium* in children with malnutrition.31 This growing body of research evidence suggests that modulating the gut microbiome in early life to boost colonisation resistance against enteropathogens may provide a new approach to preventing or ameliorating EED.

As evidenced in this special issue, paediatric gastroenterologists worldwide know all too well the severe adverse effects of an unhealthy gut whether this occurs in IBD, coeliac disease, food intolerances or malnutrition. Paediatric gastroenterologists can lead in bringing together expertise from many different disciplines to improve gut health and, thereby, overall health and well-being in some of the world’s most disadvantaged children – those living with poor hygiene and sanitation.

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