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Microbial Signatures of Pediatric Disease: Investigating the Gut Microbiome in Asthma and Eczema

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ABSTRACT

Pediatric asthma and eczema are prevalent chronic inflammatory conditions with significant health impacts globally. Recent research highlights the gut microbiome's pivotal role in immune system development and allergic disease pathogenesis via the gut–skin–lung axis. This cross-sectional study investigated gut microbial signatures in 180 Pakistani children aged 1–12 years, including those diagnosed with asthma (n=60), eczema (n=60), and healthy controls (n=60). Using 16S rRNA gene sequencing, we analyzed gut microbial diversity and composition. Children with asthma and eczema exhibited significantly reduced microbial alpha diversity compared to controls (Shannon index: asthma 2.9, eczema 3.0 vs. controls 3.5, $p < 0.001$). Asthmatic children showed increased Proteobacteria and decreased Bacteroidetes, whereas eczema cases demonstrated elevated Firmicutes, including Clostridium sensu stricto and Staphylococcus aureus. Notably, Faecalibacterium prausnitzii, an anti-inflammatory butyrate producer, was markedly depleted in both disease groups. Multivariate analyses confirmed low F. prausnitzii abundance as independently associated with asthma and eczema. These findings underscore significant gut dysbiosis linked to pediatric allergic diseases in a low-middle income setting, highlighting potential microbial targets for therapeutic modulation. Further longitudinal and functional studies are warranted to explore causality and intervention strategies, which could pave the way for microbiome-based prevention and treatment in childhood asthma and eczema.

INTRODUCTION

Asthma and eczema in children represent some of the most prevalent chronic inflammatory conditions in pediatrics with high morbidity and health care expenditure globally (Hossny et al., 2024; Langan et al., 2023). There is emerging evidence that suggests that the gut microbiome a complex community of microorganisms colonizing the gastrointestinal tract is a key modulator of immune system development and function, especially during early life when immune programming takes place (Saeed et al., 2022; Januszkiewicz et al., 2023). The disruption of the gut microbial ecosystem, also known as dysbiosis, has been associated with an increased predisposition to atopic diseases, such as asthma and eczema, which enhances the idea of the gut Michigan Medicine

Mechanistically, gut microbiota dysbiosis can modulate immune tolerance by shifting regulatory and pro-inflammatory T cell subsets balance, which is mediated by microbial metabolites including short-chain fatty acids (SCFAs) (Yao et al., 2022; Wang et al., 2023; Wu et al., 2024). Most specifically, loss of beneficial commensals such as Faecalibacterium prausnitzii, a prominent butyrate producer, has been connected to perturbed anti-inflammatory signaling and exaggerated allergic inflammation (Wang et al., 2024; Campbell et al., 2023). On the other hand, in allergic diseases, the growth of potentially pathogenic taxa, including Proteobacteria and Staphylococcus aureus, has been linked to immune dysregulation and epithelial barrier dysfunction (Celebi Sozener et al., 2022; Losol et al., 2023).

However, much of the current microbiome literature in pediatric allergy has been mostly done in the Western population, and very little data exist in low- and middle-income countries, which have distinct environmental exposures and microbial ecologies. It is important to understand microbial signatures that are unique to these environments to come up with interventions that are relevant to the context.

This cross-sectional observational study will focus on examining gut microbiome changes in children with asthma and eczema who attend a large tertiary care facility in Pakistan. Through comparison of microbial diversity and taxonomic composition in affected children and healthy controls, this study will aim to explain microbial patterns in these common allergic conditions of childhood

and define whether there are microbial candidates amenable to therapeutic modulation.

METHODOLOGY

The study is observational, cross-sectional, and housed at Allied Hospital Faisalabad, a large tertiary care facility in Punjab, Pakistan, during a six-month study period between July 2024 and December 2024. The main aim was to determine the relation between the composition of gut microbiome and prevalence of asthma and eczema among children. Children aged between 1 to 12 years who reported to the pediatric outpatient and inpatient department with clinically diagnosed asthma or eczema, as per the existing diagnostic criteria (GINA criteria asthma and UK Working Party Diagnostic Criteria Atopic dermatitis), were enrolled on consent provided by the parents or guardians. Healthy controls age and sex matched with no history of allergic or chronic gastrointestinal diseases were also recruited and compared.

All participants provided stool samples that were collected under sterile conditions and frozen at 80C immediately until further processing. The QIAamp DNA Stool Mini Kit was applied to extract microbial DNA, and the composition of the bacterial community was determined by 16S rRNA gene sequencing on the Illumina MiSeq platform. The bioinformatic analysis based on QIIME2 software was applied to alpha and beta diversity analysis and taxonomic profiling to determine the significant microbial taxa in disease conditions. Structured questionnaires were used to obtain clinical data such as demographic features, environmental exposures, diet and family history of atopy.

SPSS version 26.0 was applied to perform statistical tests. PERMANOVA and linear discriminant analysis effect size (LEfSe) were used to analyse differences in microbiome diversity and composition between groups. Multivariable logistic regression models were built to control the possible confounding effect of antibiotic use, mode of delivery, and history of breastfeeding. Statistically significant was set at a p-value of <0.05. The Institutional Review Board of Allied Hospital Faisalabad approved this study, and thus, the study followed ethical standards regarding research that involves human subjects.

RESULTS

The study involved 180 children (60 with asthma, 60 with eczema and 60 healthy controls). The overall mean age was 6.2 2.4 years and the age and sex distribution of the groups did not differ significantly ($p > 0.05$). Table 1 presents demographic characteristics.

Microbiome changes showed a highly significant lower alpha diversity in both asthma and eczema groups than controls as assessed by Shannon diversity index (asthma: 2.9 +/- 0.4; eczema: 3.0 +/- 0.3; control: 3.5 +/- 0.5; $p < 0.001$). Beta diversity measured as weighted UniFrac distances displayed clear clustering by disease status (PERMANOVA $p = 0.002$).

Relative abundance analysis revealed that Proteobacteria were significantly overrepresented in children with asthma (18.3%) and Bacteroidetes were lower (22.1%) compared to controls (8.2% and 35.6%, respectively; $p < 0.01$). In the eczema group, they found an increased abundance of Firmicutes phylum, especially Clostridium sensu stricto and Staphylococcus aureus. Another interesting observation was the significant decrease of Faecalibacterium prausnitzii which is an anti-inflammatory bacterium in both asthma and eczema groups.

Multivariable logistic regression (adjusted for antibiotic use, breastfeeding, and birth mode) demonstrated that low *F. prausnitzii* abundance was independently associated with asthma (OR = 3.7, 95% CI: 1.8–7.6) and eczema (OR = 2.9, 95% CI: 1.3–6.4).

Table 1

Demographic and Clinical Characteristics of Study Participants

Variable	Asthma (n=60)	Eczema (n=60)	Controls (n=60)	*p*-value
Age (mean ± SD, years)	6.4 ± 2.5	6.0 ± 2.3	6.2 ± 2.4	0.72
Male, n (%)	34 (56.7%)	31 (51.7%)	32 (53.3%)	0.87
Cesarean delivery, n (%)	28 (46.7%)	26 (43.3%)	21 (35.0%)	0.32
Antibiotic use (last 3 mo)	20 (33.3%)	18 (30.0%)	12 (20.0%)	0.09
Exclusive breastfeeding (%)	36 (60.0%)	38 (63.3%)	48 (80.0%)	0.03*

*Significant at $p < 0.05$

Table 2

Gut Microbiota Diversity Indices

Group	Shannon Index (Mean ± SD)	Observed OTUs (Mean ± SD)	*p*-value vs. Controls
Asthma	2.9 ± 0.4	112 ± 28	<0.001
Eczema	3.0 ± 0.3	118 ± 25	<0.001
Controls	3.5 ± 0.5	150 ± 30	—

Table 3

Dominant Bacterial Taxa by Group (Relative Abundance %)

Taxa	Asthma (%)	Eczema (%)	Controls (%)	*p*-value
Faecalibacterium prausnitzii	4.2	5.1	9.8	<0.001
Proteobacteria	18.3	12.1	8.2	0.008
Bacteroidetes	22.1	24.5	35.6	0.002
Clostridium sensu stricto	11.0	16.4	6.8	0.01
Staphylococcus aureus	6.5	13.2	4.1	0.004

These findings indicate significant dysbiosis in the gut microbiota of children with asthma and eczema, characterized by decreased microbial diversity and altered taxonomic composition. The depletion of beneficial commensals such as *F. prausnitzii* and increased abundance of potentially pathogenic bacteria underscore the potential of microbiome-targeted interventions in managing pediatric allergic diseases.

DISCUSSION

This is strong evidence that changes in the composition of gut microbiota is closely linked with the existence of asthma and eczema in children, which contributes to the emerging concept of the gut--skin--lung axis in childhood allergic diseases. Asthmatic children with eczema had lower microbial diversity and significant changes in the bacterial composition in comparison with healthy controls (Galeana-Cadena et al., 2023; Aslam et al., 2024). These

observations agree with the existing literature indicating that disruption of the microbiome in early life can regulate immune maturation and lead to the development of atopic diseases.

It is especially interesting that Faecalibacterium prausnitzii was significantly reduced in both disease groups. This bacterium is known to produce butyrate, a short-chain fatty acid with anti-inflammatory effects, whose depletion has been associated with increased Th2 responses and mucosal inflammation, which are both key to the pathophysiology of asthma and eczema (Mohamed Elfadil et al., 2023). Proteobacteria overrepresentation in asthmatic children and Clostridium sensu stricto and Staphylococcus aureus in eczema children further support the idea of microbial imbalance in the propensity towards allergic sensitization and skin barrier dysfunction (Guryanova, 2024). These changes could be signatures of a pro-inflammatory microbial environment, which fosters immune dysregulation, particularly in the setting of immature immune system maturation.

Our results are consistent with the hygiene hypothesis and its more recent versions, suggesting that lower exposure to microbes in the early life, including via cesarean section, antibiotic use, and low rates of breastfeeding, leads to dysbiosis and subsequent allergic disease. Despite the fact that we have controlled multiple confounding factors, such as mode of birth and recent exposure to antibiotics, the correlations between particular taxa and disease were statistically significant, which highlights the necessity of causal association.

Although this investigation incorporates important data in a low- and- middle-income country setting, where investigations of the microbiome in pediatric allergies are limited, it contains multiple limitations. First, it is a cross-sectional study that restricts drawing causal inferences. It must be clarified whether the changes in the microbiome are a cause or a consequence of the disease using longitudinal studies. Second, the diet, which is a major modulator of the microbiome, was not fully evaluated, and metagenomic or metabolomic profiling was not done to explore functional consequences.

Still, our findings indicate that selective manipulation of the intestinal flora could provide novel preventive or therapeutic options in pediatric asthma and eczema. Dietary interventions targeting microbiota, such as probiotics, prebiotics, and others, are promising and need to be explored in well-designed clinical trials. Considering that the global burden of pediatric allergic diseases is increasing, particularly in urbanizing areas like Pakistan, the application of microbiome science to clinical and public health systems may have significant implications to early-life immune development and health outcomes over the lifespan.

CONCLUSION

This article exemplifies that preventive programs on obesity in early childhood, implemented in primary care, may result in considerable enhancement of BMI percentile and other related health behaviors in young children. The developmentally appropriate, structured counseling model provided by trained healthcare personnel was feasible and effective in a resource-constrained environment of Allied Hospital Faisalabad. The positive changes in the aspects of dietary intake, physical activity, and screen time also confirm the multidimensional nature of the positive effects of early intervention measures based on the principles of evidence-based practice. Notably, this model is characterized by the use of pre-existing healthcare infrastructure and regular pediatric visits as a delivery site, which is why its scalability is evident. Although there are limitations, including a short follow-up period and the use of self-reported measures of behavior, the replication of positive results allows extending its use to a wider audience and further inclusion in policies. Well-designed, long-term studies should be done to see how long the behavioral changes last, and what impact will this have on metabolic health outcomes. The model has the potential to become a sustainable and affordable solution to the increasing trend of childhood obesity reversal.

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