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Research Article

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Microbiome-Based Therapies for Pediatric Eczema: Probiotics and Prebiotics

Sriya Kakarla, BA[1], Grace Herrick, BA[2], Kelly Frasier, DO, MS[3*], Mahnoor Mukarram, MS[4], Eliza Skemp, BS[4], Madeline Coleman, MBA[5], Therese Anne Limbana, MD, BSN[6], Bret-Ashleigh Coleman, BS[5], Belinda Mensah, BSN[7], Marissa Ruppe, BA[8]

[1]UTHealth Houston, McGovern Medical School, Houston, TX
[2]Alabama College of Osteopathic Medicine, Dothan, AL
[3]Northwell Health, New Hyde Park, NY
[4]Midwestern University Arizona College of Osteopathic Medicine, Glendale, AZ
[5]Edward Via College of Osteopathic Medicine, Blacksburg, VA
[6]New York Institute of Technology College of Osteopathic Medicine, Old Westbury, NY
[7]A.T. Still University School of Osteopathic Medicine, Mesa, AZ
[8]Nova Southeastern University Kiran Patel College of Osteopathic Medicine, Fort Lauderdale, FL

***Corresponding author:** Kelly Frasier, Northwell Health, New Hyde Park, NY. Email: kellymariefrasier@gmail.com

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Abstract

Microbiome-based therapies, particularly probiotics and prebiotics, show promising potential in managing pediatric eczema by leveraging the role of the skin microbiome. Studies utilizing next-generation sequencing have consistently shown significant differences in the skin microbiome composition between children with eczema and healthy controls, highlighting a decrease in microbial diversity and an increase in Staphylococcus aureus colonization in affected individuals. Clinical trials and observational studies have investigated the effects of various probiotic strains, such as Lactobacillus and Bifidobacterium, as well as prebiotic compounds, on eczema severity and microbiome composition. Results indicate that certain probiotics can reduce eczema severity and partially restore microbial balance, while prebiotics may enhance these effects by promoting beneficial bacterial growth. Mechanistic studies suggest that these interventions improve skin barrier function and modulate immune responses, potentially reducing inflammation and improving clinical outcomes. However, safety profiles and potential side effects need further evaluation, with current evidence suggesting a favorable but not completely risk-free profile. Overall, microbiome modulation through probiotics and prebiotics represents a promising adjunctive therapy for pediatric eczema, warranting more extensive research to optimize treatment protocols and ensure long-term safety and efficacy.

Introduction

Pediatric eczema, also known as atopic dermatitis, is a chronic inflammatory skin condition characterized by itchy, red, and scaly patches, primarily affecting infants and young children. This condition often appears within the first six months of life and significantly impacts the quality of life for affected individuals and their families. Globally, the prevalence of pediatric eczema has been rising, currently affecting approximately 15-20% of children in developed countries. Various factors, including genetic predisposition, environmental influences, and changes in lifestyle and hygiene practices, contribute to this increase [1]. The growing incidence underscores the need for a deeper understanding of the condition along with more effective management strategies.

The skin microbiome, a diverse and dynamic community of microorganisms residing on the skin surface, includes bacteria, fungi, viruses, and mites that interact to maintain skin health. The composition of the skin microbiome varies across different body sites and is influenced by age, sex, diet, environment, and hygiene practices. A healthy skin microbiome plays a crucial role in protecting against pathogens, modulating the immune system, and maintaining skin barrier function. Disruptions in this delicate balance, known as dysbiosis, have been linked to various skin disorders, including eczema [2]. Recent studies suggest that a normal microbiome supports a healthy gut and skin flora, thereby preventing eczema in children. Januszkiewicz et al. states that "infants who developed atopic eczema soon after birth had lower gut microbiota diversity than children who did not develop atopic eczema" [3]. Therefore, maintaining a balanced microbiome may be a key strategy in preventing and managing eczema.

Managing pediatric eczema presents significant challenges due to its chronic nature and the complexity of its pathogenesis. Traditional treatments, such as emollients, topical corticosteroids, and immunomodulators, primarily provide symptomatic relief and may have adverse effects with long-term use. Prolonged use of topical corticosteroids, for example, can lead to skin thinning and other adverse effects. Moreover, the chronic itching and discomfort associated with eczema can affect a child's sleep, behavior, and overall quality of life, making effective management crucial [4]. Recent research has highlighted the critical role of the microbiome in maintaining skin health and its potential involvement in the pathogenesis of eczema. Studies have shown that individuals with eczema tend to have lower microbial diversity and an increased presence of *Staphylococcus aureus* on their skin compared to healthy individuals. This dysbiosis may contribute to the impaired skin barrier function and heightened immune responses seen in eczema patients [5]. Understanding the relationship between the

skin microbiome and eczema opens new avenues for treatment, including the use of microbiome-modulating therapies such as probiotics and prebiotics [6]. These therapies aim to restore a healthy microbial balance, thereby improving skin health and reducing eczema symptoms.

The primary objective of this literature review is to assess the role of the skin microbiome in the development and progression of pediatric eczema. By examining current research, this review aims to provide a comprehensive understanding of how microbial composition and diversity are altered in eczema patients and the implications of these changes on skin health. This includes exploring the mechanisms by which dysbiosis contributes to eczema pathogenesis, such as through disruptions in the skin barrier and immune system modulation [2]. Another critical objective is to evaluate the potential of probiotics and prebiotics as therapeutic interventions for managing pediatric eczema. Probiotics, which consist of live beneficial bacteria, and prebiotics, which are non-digestible food ingredients that promote the growth of beneficial microbes, represent promising strategies for restoring microbial balance. This review will analyze clinical trials and observational studies to determine the efficacy of these treatments in reducing eczema severity and improving skin health. Additionally, the review will consider the safety profiles and potential side effects of these therapies to provide a balanced perspective on their use in clinical practice. By synthesizing these findings, the reviews aims to inform future research directions and clinical practices, ultimately contributing to better management strategies for pediatric eczema.

Discussion

The Skin Microbiome and Pediatric Eczema

The skin is the largest organ of the body, composed of multiple interconnected barriers: the microbiome barrier, the chemical barrier, the physical barrier, and the immune barrier. These barriers work together to maintain the protective function of the skin. The microbiome is a vast ecosystem of microorganisms, with the most abundant being coagulase-negative *Staphylococcus*, along with other gram-positive bacterial species such as *Streptococcaceae*, *Cutibacterium*, and *Corynebacterium* [7,8]. These microbes, known as commensal bacteria, constitute the skin's natural flora and are directly influenced by the skin barriers.

Keratinocytes, the main cell type within the epidermis, not only form the physical barrier of the skin but also play a crucial role in intracellular communication and immune signaling. Keratinocytes contain toll-like receptors (TLR), a type of pattern recognition receptor, that recognize microbial structures and mount an inflammatory response through production of proinflammatory cytokines and chemokines in response to a pathogen. They also respond to inflammatory stimuli by producing antimicrobial peptides (AMPs) that have antimicrobial activity against various pathogens and mediate the skin's adaptive immune response. The skin's microbiota composition is regulated through activation of these keratinocytes by both pathogenic and commensal bacteria and through crosstalk between host and microbiota [9]. This intricate interplay highlights the complexity of the skin's immune defense mechanisms and highlights the potential for targeted therapeutic interventions aimed at restoring and maintaining microbial balance to prevent and treat conditions such as pediatric eczema.

The efficacy of AMPs produced from keratinocytes is dependent upon pH. The chemical barrier refers to the naturally acidic environment of the skin, which has an optimal skin pH of 5.5 maintained by fatty acid and sweat production. This acidic pH allows AMPs to inhibit pathogens such as *S. aureus* and favor coagulase negative *Staphylococci* and *Corynebacteria* [7]. Thus, this acidic pH plays a dual role in maintaining skin health by both suppressing harmful microbes and promoting the growth of protective commensal bacteria. Achieving an optimal skin acidity level is therefore important for providing an environment favorable for commensal bacteria and regulatory immune functions.

Commensal bacteria also orchestrate the innate immune response to further regulate the skin's microbiome. *Staphylococcus Epidermidis* is a major commensal colonizer of the skin that has been shown to secrete peptides inducing specific T-cells to aid in wound healing and communicate with keratinocytes to secrete AMPs. *S. epidermidis* also secretes the serine protease Esp, which inhibits the colonization of the skin by *S. aureus* [7,9,10]. While *S. epidermidis* has been shown to provide protective benefits for the skin barrier, there is conflicting evidence that demonstrates it may worsen barrier degradation and increase the severity of atopic dermatitis [11]. Recent studies have shown that another *Staphylococcus* strain, *Staphylococcus hominis*, can regulate the effects of *S. Epidermidis* on the skin's microbial environment by producing peptides with bactericidal effects specific to *S. aureus* [11]. This delicate balance between commensal and pathogenic bacteria is critical, as disruptions can lead to impaired skin barrier function and heightened inflammatory responses, such as those associated with atopic dermatitis.

A key feature of patients with atopic dermatitis (AD) is dysbiosis of the skin microbiome and a loss of microbial diversity. Studies using small subunit RNA sequencing have identified bacterial strains with greater detail than previous techniques, assessing the relationship between skin microbiota and disease progression. Kong et al. analyzed 16S rRNA bacterial gene sequencing in both healthy children and children with AD, finding that children with AD flares had a reduction in microbial diversity. Sites of predilection were found to have lower skin biodiversity in children with severe AD compared to other skin sites [12]. While *S. epidermidis* was abundant in children without AD, both *S. epidermidis* and *S. aureus* increased significantly during flares in children with AD. Additionally, increases in *Streptococcus*, *Cutibacterium*, and *Corynebacterium* were observed following therapy, and patients with intermittent or active treatment had higher levels of bacterial diversity [12]. These findings emphasize the need for therapies that not only address the symptoms of AD, but also consider the underlying microbial imbalances contributing to the disease.

The efficacy of microbiome-based therapies are promising. Regardless of age, children suffering from eczema can benefit these interventions. Carucci et al. affirms that children with pre-diagnosed eczema who received treatment with *L. rhamnosu* had better outcomes compared with children who were not treated [13]. This highlights the potential of microbiome modulation in improving patient outcomes. Additionally, a vegan diet, rich in fruits, vegetables, whole grains, nuts, and seeds, provides an abundance of dietary fiber, antioxidants, and essential nutrients that support a diverse microbiome. This diet

is beneficial for maintaining healthy gut flora and reducing IgE levels, making it a better choice for allergic disorders like eczema [3]. By lowering IgE levels, the antibodies associated with allergic reactions, a vegan diet can integrate pre- and probiotics in a natural way, helping to alleviate the severity of eczema symptoms. Ultimately, embracing these holistic approaches not only serves to benefit the skin microbiome and those who suffer from eczema, but also paves the way for a healthier body.

It is well known that *S. aureus* colonization increases during AD flares and that its density correlates with acute exacerbation and worsened severity of the disease [10]. The pathogenesis of *S. aureus* and its role in AD exacerbation is still being understood. Studies have shown that *S. aureus* produces superantigens and enterotoxins that disrupt the epidermal barrier and stimulate inflammatory effects through T-cell activation and IgE switching [10]. Nakamura et al. utilized whole-genome sequencing in Japanese children, demonstrating that the retention of *S. aureus*' functional Agr virulence system is critical for epidermal colonization and AD development [14]. Agr-dependent virulence factors were found to be critical for the inflammation seen in AD skin flares. It is also hypothesized that changes in the innate immune system in individuals with AD may exacerbate the effects of *S. aureus*. AD skin lesions were found to have deficiencies in AMPs and an overabundance of TLR2, causing a decreased effect of endogenous antimicrobial properties and an increase in inflammatory pathway signaling [10]. An imbalance of the microbiome leads to disruption of the epidermal barrier, upregulation of inflammation, and downregulation of innate immune responses, contributing directly to the inflammatory cycle of AD resulting in the development of skin disease.

Probiotics in Managing Pediatric Eczema

Probiotics have emerged as a promising approach in managing pediatric eczema. Probiotics, defined as live microorganisms that confer health benefits on the host when administered in adequate amounts, include common strains such as *Lactobacillus rhamnosus*, *Lactobacillus reuteri*, *Bifidobacterium bifidum*, and *Lactobacillus acidophilus* [15]. These probiotics are known for their role in promoting gut health, which influences skin health through the gut-skin axis, a concept supported by growing evidence [16]. By improving gut microbiota composition, probiotics can exert systemic effects that enhance overall immune function and reduce inflammation, further supporting their role in managing AD.

The mechanisms through which probiotics benefit the skin are multifaceted. They help maintain a balanced skin microbiome, enhance skin barrier function, and modulate immune responses. By producing antimicrobial substances, probiotics can inhibit the growth of pathogenic bacteria such as *S. aureus*, which is commonly associated with eczema exacerbations [17]. This inhibitory effect is crucial, as *S. aureus* drives eczema progression through biofilm formation that enhances bacterial persistence. Furthermore, probiotics reduce inflammation by modulating cytokine production, promoting the production of anti-inflammatory cytokines, and balancing the immune response [18]. Additionally, probiotics can enhance the production of regulatory T cells, which help to maintain immune tolerance and prevent excessive inflammatory reactions. This multi-layered mechanism of action points to the potential of probiotics to address the complex etiology of eczema, which involves both microbial and immunological factors.

Additional mechanistic insights into the action of probiotics reveal their role in reducing inflammation. Probiotics enhance the production of ceramides and other lipids essential for maintaining the integrity of the skin barrier. For instance, *L. reuteri* has been shown to upregulate genes involved in skin barrier function, such as AQP3, which enhances hydration and elasticity of the skin [19]. Improved skin barrier function prevents the entry of allergens and pathogens, reducing the risk of eczema flares. Additionally, probiotics modulate immune responses by balancing the production of pro-inflammatory and anti-inflammatory cytokines, promoting regulatory T cells, and reducing levels of pro-inflammatory cytokines like interleukin 17 (IL-17) and tumor necrosis factor (TNF) [20]. Their dual action on inflammation and microbiome composition makes probiotics particularly valuable in chronic conditions like eczema, where long-term management strategies are essential. By addressing both the barrier and immune dysfunctions, probiotics offer a comprehensive approach to eczema management.

Clinical evidence supports the efficacy of probiotics in managing pediatric eczema. Numerous clinical trials and observational studies have demonstrated the benefits of probiotics in reducing the severity and frequency of eczema flares in children. For example, a randomized double-blind placebo-controlled trial by Gueniche et al. found that *Lactobacillus paracasei* supplementation significantly improved skin reactivity and reduced eczema symptoms in children [21]. This study is pivotal, as it not only demonstrates clinical improvement but also highlights the potential for probiotics to alter the skin's immune response in a beneficial manner. Similarly, Kober et al. highlighted the effectiveness of probiotics, particularly *L. reuteri*, in decreasing eczema severity and improving skin condition by reducing inflammation and enhancing skin barrier function [18]. These studies emphasize the potential of probiotics as a valuable addition to eczema management strategies, providing an alternative or complement to traditional treatments such as corticosteroids and emollients.

The efficacy of probiotics in reducing eczema severity has been documented in several key studies. Probiotic supplementation has been shown to influence the composition of the skin microbiome, increasing microbial diversity and promoting the growth of beneficial bacteria [22]. For instance, Kalliomäki et al. demonstrated that *L. rhamnosus* GG could reduce the risk of developing eczema in infants when administered during pregnancy and early infancy [23]. This preventive aspect is particularly noteworthy as it suggests that early modulation of the gut microbiome can have long-lasting effects on skin health. Research shows that infants who were fed with formula supplemented with prebiotics for more than six months have a potentially decreased risk for developing eczema [24]. Infants who also received formula supplementation with probiotics like *Lactobacillus* and *Bifidobacterium* had increased levels of beneficial bacteria and normal levels of *S. aureus* in their guts [24]. In particular, *L. reuteri* has shown promising results in improving skin barrier function and reducing inflammation, which are critical factors in managing eczema [18]. These findings indicate that specific probiotic strains can have significant, strain-specific effects on eczema management. The strain-specific benefits highlight the importance of choosing the

right probiotic, as different strains can exert different effects on the skin and immune system.

Regarding safety, probiotics are generally considered safe for use in pediatric populations. A comprehensive analysis of clinical studies has indicated that probiotics are well-tolerated by children, with minimal to no adverse effects [25]. The safety profiles of probiotics are supported by their widespread use in various pediatric conditions, including gastrointestinal and dermatological disorders. However, some potential risks and adverse effects have been reported, particularly in immunocompromised children or those with severe underlying health conditions. Rare adverse effects may include gastrointestinal upset, diarrhea, and, in extremely rare cases, systemic infections such as sepsis [26]. It is essential to monitor children for any adverse reactions during probiotic supplementation, especially in those with compromised immune systems or other risk factors. This cautious approach ensures that the benefits of probiotics are maximized while minimizing potential risks.

In conclusion, probiotics, particularly strains like *L. reuteri* and *L.rhamnosus*, have shown significant promise in managing pediatric eczema. They offer a multifaceted approach to treatment by enhancing skin barrier function, modulating immune responses, and reducing inflammation. While the current evidence supports their efficacy and safety, further research is needed to establish standardized protocols and identify the most effective strains and dosages for different patient populations. As the understanding of the gut-skin axis and the role of probiotics in skin health continues to grow, probiotics are likely to become an increasingly important component of eczema management strategies. The potential for early intervention with probiotics also opens new avenues for preventive healthcare, which could significantly impact long-term outcomes for children at risk of eczema.

Prebiotics in Managing Pediatric Eczema

Prebiotics have gained considerable attention as a promising intervention for managing pediatric eczema, leveraging their ability to modulate the gut and skin microbiomes. These non-digestible food ingredients selectively stimulate the growth and activity of beneficial microorganisms, thereby enhancing overall health and potentially mitigating the symptoms of eczema. Prebiotics are defined as non-digestible food components that confer health benefits by promoting the growth of beneficial bacteria in the gut. They "are the third most abundant component in human breast milk", making them an important supplement in formula-fed infants [24]. Common prebiotic compounds include fructooligosaccharides (FOS), galactooligosaccharides (GOS), and inulin, which are naturally present in foods such as bananas, garlic, onions, and whole grains. These compounds support a healthy gut microbiome, which in turn can positively impact skin health. The primary mechanism by which prebiotics exert their beneficial effects involves the stimulation of beneficial bacteria, which produce short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate. These SCFAs are crucial for maintaining both gut and skin health by lowering pH levels, inhibiting pathogenic bacteria, and promoting the growth of beneficial microbes. Additionally, prebiotics can influence the skin microbiome indirectly by modulating immune responses and improving skin barrier function, thereby reducing inflammation [27]. These anti-inflammatory and skin barrier enhancement effects make prebiotics an area of interest in treating pediatric eczema.

Clinical research into the effectiveness of prebiotics in managing pediatric eczema has yielded promising results. Several studies have focused on the impact of prebiotic supplementation on eczema severity and the composition of the gut and skin microbiomes. For example, Watanabe et al. demonstrated that the consumption of FOS could suppress skin inflammatory responses in mice by increasing the population of *Bifidobacterium pseudolongum* in the gut [28]. The growth of *Bifidobacterium* in the gut inhibits the colonization of pathogenic bacteria such as *S. aureus*, which play a role in eczema flare-ups. Additionally, Watanabe et al. concluded that the total number of *Bifidobacterium* in patients with severe AD was found to be significantly lower than in patients with mild AD [28]. Consequently, the severity of symptoms is correlated with the amount of *Bifidobacterium* in the gut microbiota. By supplementing with prebiotics, patients can increase the total number of *Bifidobacterium* and reduce symptom severity. Another study by Shibata et al. showed significant improvements in scores within the assessment tool Scoring Atopic Dermatitis (SCORAD) in infants with AD after 12 weeks of supplementation with ketose, a FOS prebiotic compound [29]. Participants supplementing with ketose who had higher SCORAD scores on week 0 of supplementation did not show a significant decrease in scores compared to those with lower SCORAD scores. Subjects who showed significant improvement with ketose supplementation maintained improvement for up to six weeks after the termination of treatment. The sustained improvement in SCORAD scores even after cessation of prebiotic supplementation indicates that these benefits might have a lasting effect on the skin's resilience. This evidence supports the potential of prebiotics to reduce eczema severity in patients with mild to moderate SCORAD scores.

However, not all studies have reported uniformly positive results. For instance, Boženský et al. found no significant difference in SCORAD scores between infants with AD who received GOS and those who did not [30]. This difference could be due to the type of prebiotic compound chosen. Prior studies have used FOS, whereas Boženský et al. used a GOS prebiotic compound for supplementation. These mixed results highlight the need for further research to better understand which prebiotics are most effective and how they should be used. Different prebiotic compounds appear to have varying effects on the microbiome and eczema symptoms. For example, FOS has been shown to increase the population of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, which help reduce inflammation and improve skin barrier function. Conversely, GOS has been found to enhance immune responses and decrease the incidence of eczema symptoms, especially when combined with probiotics [27]. In turn, this shows the potential of dual probiotic/prebiotic supplementation to decrease the number and severity of eczema flares.

Research has demonstrated that prebiotic supplementation can increase microbial diversity in the gut, which is often correlated with improved health outcomes. For example, Lin et al. reported that infants with eczema who received prebiotic supplementation exhibited a significant increase in the levels of *Bifidobacterium bifidum* in their stool compared to the control group [31]. Increased microbial diversity is associated with a more resilient and stable gut microbiome, which can enhance

overall health by improving digestion and protecting against pathogenic infections. This allows the potential to improve gut-barrier function, reducing intestinal permeability and preventing the translocation of harmful bacteria and antigens into the bloodstream. This, in turn, can modulate system immune responses which is particularly beneficial in conditions like pediatric eczema.

Enhancing skin barrier function is another critical benefit of prebiotics. The skin barrier is essential in preventing pathogen entry and maintaining hydration. Prebiotics contribute to skin barrier enhancement by promoting the growth of beneficial bacteria that produce SCFAs, which help maintain skin integrity and reduce transepidermal water loss, a common issue in eczema patients. Studies by Ogawa et al. and Chen et al. have shown that *Lactobacillus* probiotics, supported by prebiotics, result in reduced transepidermal water loss and improved skin barrier function [32,33]. Additionally, prebiotics modulate immune responses by enhancing the production of anti-inflammatory cytokines such as IL-10 and reducing pro-inflammatory mediators. This modulation helps balance the immune system and reduce the inflammatory responses that exacerbate eczema symptoms. Anania et al. reported that prebiotics, combined with probiotics, could modulate the immune system to reduce inflammation in children with AD [34]. By improving the balance of Th1 and Th2 immune responses and reducing the predominance of pro-allergic Th2 cells, prebiotics help reduce inflammation. The anti-inflammatory effects of prebiotics are critical in managing eczema as they help reduce the severity and frequency of flare-ups.

The lack of regulation by the FDA on supplements such as prebiotics poses a great concern, especially when used for the treatment of AD. The majority of the population affected by AD are children and young adults, and therefore supplementation with prebiotics must be carefully monitored for adverse events. A study by Hojsak et al. showed that prebiotics are generally considered safe for use in children, with a low incidence of adverse events reported in clinical trials [26]. They are well-tolerated and can be included in the diet through natural sources or supplements. However, monitoring for potential side effects is essential, especially in vulnerable populations such as premature or immunocompromised children. While rare, potential risks associated with prebiotic use include gastrointestinal symptoms such as bloating and gas, which are typically mild and self-limiting. In some cases, there may be an increased risk of allergen sensitization, particularly in high-risk individuals. Further research is needed to fully understand the long-term safety and efficacy of prebiotics, especially when used in combination with probiotics in pediatric populations. Overall, prebiotics are considered safe for supplementation in children and have shown potential in the treatment of AD.

Combined Probiotic and Prebiotic Therapies

Efforts to optimize the beneficial effects of both probiotic and prebiotic therapies have led to the utilization of synbiotic approaches. The driving force behind synbiotic therapies is the ability of probiotics to directly feed off of prebiotics, strengthening the impact of either intervention alone [35]. These treatment regimens work to foster and sustain healthy microbiota beyond just the gastrointestinal system. Immunologic advantages stemming from such robust microbial systems in the modulation of atopic diseases cannot be understated. Some of these advantages may include augmented mucosal integrity, strengthened barriers to pathogen attachment, and the enhanced creation of SCFAs with anti-inflammatory characteristics [36]. Synbiotic therapies are also being studied in the lens of precision medicine; the unique phenotypes and endotypes observed in pediatric eczema lend an opportunity for these approaches to be tailored appropriately [37]. The potential synergistic effects of these treatment modalities may have the ability to transform patient care.

Several recent clinical trials and observational studies have evaluated synbiotic therapies in the management of pediatric AD. Chang et al. performed a meta-analysis focusing on SCORAD indices and relative risk reduction for treatment and prevention, respectively [35]. They noted that synbiotic approaches, particularly those with mixed strains, significantly reduced severity and adverse outcomes in the disease of interest. Further, additional subgroup analyses revealed a lack of benefit in patients less than one year of age. No significant findings were uncovered when considering the prevention of pediatric AD; however, synbiotic approaches did show promise in reducing the severity of the condition [35]. This highlights the need to identify optimized synbiotic formulations for specific patient populations. Another study conducted by Dissanayake et al. specifically looked at the use of emollients in combination with synbiotic therapies for the prevention of AD in infancy [38]. Though no significant benefit was reported, patient follow-up was halted at one year of age [38]. This indicates that the study potentially missed long-term effects that could have emerged with extended observation. Overall, there are many discrepancies amongst existing studies. Variations in age of intervention, standardization of synbiotic formulations, and measurement of outcomes have proved difficult in the synthesis of results as applied to patient care [39]. An additional limitation lies in the lack of studies directly comparing synbiotic therapies to individual probiotic and/or prebiotic treatments as opposed to placebo alone [36]. There remains a great need for supplementary and more homogenous studies in the future.

Despite a somewhat incomplete picture of the role of synbiotic therapies in the treatment and prevention of pediatric AD, their efficacy in restoring microbial balance remains strong. This balance, contributing heavily to the many functions of the skin barrier, relies on commensal bacteria to both outnumber potential pathogens and promote wellbeing. Synbiotic therapies have been found to aid in gapping the deficiency of epidermal AMPs seen in pediatric AD. Normally produced by keratinocytes, AMPs form a chemical barrier in the skin that functions to inhibit viral and fungal pathogens in addition to harmful bacterial species. Further, synbiotic approaches have an optimization effect on the skin's pH balance. Combinations of probiotics and prebiotics together are better able to combat the increased pH necessary for cutaneous bacterial infections as seen in conditions such as AD [37]. Barrier functions aside, synbiotic therapies have also been shown to soften excessive immune responses and reduce inflammation inherent to AD. Particular *Lactobacillus* strains in tandem with prebiotic enhancement have the ability to reduce the excessive infiltration of mast cells, eosinophils, and inflammatory Th2 cytokines [39]. Synbiotic treatments certainly show promise in future clinical outcomes.

Future Directions

Research on microbiome-based therapies consistently supports the notion that a healthy gut and skin flora can play a crucial role in treating and preventing eczema. However, significant gaps and limitations persist in the current body of research. One major issue is the small population size of many studies, which diminishes their statistical significance. To increase diversity, future studies can focus on new population samples. For example, researchers could investigate whether children in low-income countries have a decreased risk of developing eczema due to factors such as prolonged breastfeeding. Comparing these children to those from high-income countries who received non-supplemental formulas with little or no breast milk could provide valuable insights into treatment options and preventative care. This approach would also yield more comprehensive statistical data for epidemiologists.

Additionally, there is lack of research on dosing recommendations for prebiotics and probiotics in the treatment of eczema. Existing research also lacks diversity in their sample populations, making it difficult to generalize findings across different demographic groups. Furthermore, there is a lack of longitudinal data to support the long term effects or benefits of microbiome-based therapies for eczema. Future research should prioritize increasing population sizes to enhance statistical significance and provide more robust conclusions. Although evidence has indicated that more than six months of supplementation can support a healthy gut and skin flora, a clearer timeline is needed to determine optimal duration of treatment to protect children from eczema safely.

Optimizing treatment protocols will require frequent follow-up appointments with parents, children, and their families are important in understanding the efficacy of treatments better. Developing standardized dosing methods will improve the accuracy of quantitative measurements, rather than relying solely on qualitative data. Cohort or longitudinal studies will be beneficial in providing quality control measures and guidelines for evidence-based practice. Such research can provide a deeper understanding of the natural progression of AD and how various interventions impact this progression. By integrating data from these studies, clinicians can develop more effective, personalized treatment plans that are tailored to the unique needs of each child and their family.

While microbiome-based therapies show promise in treating eczema, the importance of long-term safety and efficacy studies cannot be overlooked. For instance, these therapies could potentially elicit an immune response, as indicated by Alam et al., who noted that such treatments can activate the immune system to effector activity [40]. Therefore, precautions should be taken when administering these therapies to children with multiple health comorbidities. Severe eczema can be debilitating for families and children, and it is crucial to implement regulations that prevent the exploitation of families desperate for treatment. Additionally, probiotics must be designed to withstand the harsh conditions of elevated pH and temperature in the stomach. The high cost of microencapsulation processes makes microbiome-based therapies expensive, increasing the likelihood that desperate families may feel pressured to participate in research studies [41]. Strict regulations must be enforced to prevent such occurrences and ensure ethical practices in clinical research. In conclusion, while the potential of microbiome-based therapies for eczema is significant, addressing the current research gaps and ensuring long-term safety and efficacy are essential steps toward transforming patient care.

Conclusion

The skin microbiome, comprising microorganisms like *S. epidermidis* and *S. aureus*, is vital for maintaining a healthy skin barrier and immune function. Dysbiosis has been linked to worsening eczema symptoms in children. Understanding microbial interactions and their impact on the skin barrier has highlighted potential therapeutic targets. Advances in using probiotics and prebiotics show promise as holistic treatments, with probiotics helping to restore the gut and skin microbiome, thereby improving eczema symptoms. Clinical studies show these interventions can reduce inflammation, enhance skin barrier function, and alleviate eczema, though individual responses vary, necessitating further research. Integrating microbiome-based therapies in clinical practice could transform eczema management. Traditional treatments focus on symptom relief but often neglect underlying causes. Microbiome therapies aim to restore the skin's microbial balance, potentially providing more effective, lasting relief for pediatric eczema patients. However, their implementation requires careful consideration of safety, efficacy, and regulatory approval. The future of microbiome modulation in pediatric eczema looks promising, with probiotics and prebiotics offering targeted solutions. Continued research and clinical trials are crucial to refining these therapies, understanding their long-term effects, and establishing standardized guidelines. A deeper understanding of the skin microbiome's role in eczema will enable healthcare providers to create innovative personalized treatments, improving the quality of life for pediatric eczema patients.

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