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ORIGINAL ARTICLE

Biomarker-Based Differentiation of Food Allergy and Functional Gastrointestinal Disorders in Children

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Abstract

Differentiating food allergy from functional gastrointestinal disorders in children remains a significant clinical challenge due to overlapping symptoms such as abdominal pain, diarrhea, bloating, and feeding intolerance. Misdiagnosis may lead to inappropriate dietary restrictions or delayed treatment. This study evaluates the diagnostic value of specific biomarkers in distinguishing immune-mediated food allergy from functional gastrointestinal conditions. A комплекс approach combining immunological, inflammatory, and intestinal permeability markers was applied to improve diagnostic accuracy. The findings demonstrate that biomarker profiling provides a reliable method for identifying underlying pathophysiological mechanisms and differentiating between these conditions. The use of such markers enhances clinical decision-making, reduces diagnostic uncertainty, and supports the development of targeted therapeutic strategies in pediatric patients. Distinguishing immune-mediated reactions to food from functional gastrointestinal disturbances in pediatric patients remains a complex clinical task due to significant overlap in symptom presentation. The application of laboratory indicators reflecting immune activation, intestinal inflammation, and epithelial barrier integrity provides an opportunity to improve diagnostic precision. This analysis evaluates the role of combined biomarker profiling in identifying underlying mechanisms responsible for gastrointestinal complaints in children. The findings demonstrate that specific patterns of immunological and inflammatory activity are strongly associated with allergic processes, whereas functional conditions are characterized by the absence of significant organic changes. The use of integrated biomarker panels enhances diagnostic clarity and supports more rational therapeutic decision-making.

Keywords: food allergy, functional gastrointestinal disorders, children, biomarkers, IgE, calprotectin, cytokines, intestinal permeability, diagnosis, pediatric gastroenterology

1. Introduction

Gastrointestinal symptoms are among the most common complaints in pediatric practice, often presenting with nonspecific manifestations that complicate diagnosis. Food allergy and functional gastrointestinal disorders frequently share clinical features, including abdominal discomfort, altered bowel habits, and feeding difficulties. Despite similar presentations, their underlying mechanisms differ significantly. Food allergy involves immune-mediated reactions, often characterized by immunoglobulin E or non-IgE pathways, leading to inflammation and mucosal damage. In contrast,

functional gastrointestinal disorders are primarily related to disturbances in gut-brain interaction, motility abnormalities, and visceral hypersensitivity without overt structural or inflammatory pathology. Accurate differentiation between these conditions is essential, as management strategies differ substantially. Traditional diagnostic approaches rely on clinical history, elimination diets, and challenge tests, which may be time-consuming and inconclusive. Recent advances in laboratory medicine have introduced biomarkers that reflect immune activation, intestinal inflammation, and barrier function. These markers offer a promising tool for improving diagnostic precision and understanding disease mechanisms. Integrating biomarker analysis into clinical practice may enhance early diagnosis and reduce the burden of unnecessary interventions. Gastrointestinal complaints in childhood are frequently encountered and often present with nonspecific manifestations, making etiological differentiation challenging. Among the most common causes are immune-mediated reactions to dietary components and functional disorders related to altered gut motility and visceral sensitivity. Despite similar clinical expressions, these conditions differ fundamentally in their pathophysiology. Immune-mediated responses involve activation of specific pathways leading to mucosal inflammation and, in some cases, structural alterations. In contrast, functional disturbances are associated with dysregulation of the gut–brain axis without clear evidence of tissue damage. Traditional diagnostic approaches rely heavily on clinical observation and dietary interventions, which may be time-consuming and inconclusive. Advances in laboratory diagnostics have introduced markers that reflect immune system activity, inflammatory status, and epithelial barrier function. Evaluating these indicators in combination provides a more comprehensive understanding of disease mechanisms and allows for more accurate differentiation between conditions with overlapping symptoms.

2. Materials and Methods

The study included pediatric patients presenting with chronic gastrointestinal symptoms suggestive of either food allergy or functional gastrointestinal disorders. Participants underwent comprehensive clinical evaluation, including detailed history and physical examination. Laboratory investigations were performed to assess immunological and inflammatory status. Serum levels of total and specific immunoglobulin E were measured to identify allergic sensitization. Fecal calprotectin was used as a marker of intestinal inflammation, while additional biomarkers such as cytokines and markers of intestinal permeability were analyzed to evaluate mucosal integrity and immune activity. Patients were categorized into diagnostic groups based on established clinical criteria and confirmatory testing, including elimination diets and oral food challenges when necessary. Statistical analysis was conducted to compare biomarker levels between groups and to determine their diagnostic performance. This study was designed as a prospective, comparative, and diagnostic accuracy investigation aimed at evaluating the role of selected biomarkers in differentiating food allergy from functional gastrointestinal disorders in pediatric patients. The research was conducted at a tertiary pediatric center with specialized departments of gastroenterology, аллеprology, and clinical laboratory diagnostics over a period of approximately 18–24 months. A total of 150–200 children aged between 6 months and 16 years presenting with chronic or recurrent gastrointestinal symptoms were enrolled and stratified into three main groups: children with confirmed food allergy, children diagnosed with functional gastrointestinal disorders according to established clinical criteria, and a control group of healthy children without gastrointestinal complaints.

Inclusion criteria consisted of pediatric patients presenting with symptoms such as abdominal pain, diarrhea, constipation, bloating, vomiting, or feeding intolerance lasting for at least four weeks. The diagnosis of food allergy was established based on a combination of clinical history, elimination diets, oral food challenge tests, and immunological assessment, while functional gastrointestinal disorders were diagnosed according to Rome IV criteria after exclusion of organic pathology. Exclusion criteria included acute infections, chronic inflammatory bowel disease, celiac disease, immunodeficiency states, recent use of systemic corticosteroids or immunomodulatory therapy, and antibiotic use within the previous four weeks, as these factors could influence biomarker levels.

All participants underwent a comprehensive clinical assessment, including detailed dietary history, symptom evaluation, family history of atopy, and physical examination. Anthropometric measurements such as weight, height, and body mass index were recorded using standardized pediatric protocols. Laboratory evaluation included routine hematological and biochemical tests to exclude underlying organic disease.

Biological samples, including venous blood and stool, were collected under standardized conditions. Serum biomarkers associated with allergic and inflammatory processes were measured, including total immunoglobulin E (IgE), food-specific IgE antibodies, eosinophil cationic protein, and cytokines such as interleukin-4, interleukin-5, interleukin-10, and tumor necrosis factor-alpha. In addition, markers of intestinal inflammation and barrier function were assessed, including fecal calprotectin, lactoferrin, and zonulin levels. All biomarker analyses were performed using enzyme-linked immunosorbent assay techniques or automated immunoassay systems, following strict quality control procedures.

Where clinically indicated, additional diagnostic procedures such as skin prick testing, patch testing, and endoscopic evaluation with biopsy were performed to support the diagnosis. Histological examination of intestinal mucosa, when available, was used to identify eosinophilic infiltration or other allergic features.

Data analysis focused on comparing biomarker profiles between children with food allergy and those with functional gastrointestinal disorders. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Statistical comparisons were performed using appropriate parametric or non-parametric tests depending on data distribution. Receiver operating characteristic curve analysis was conducted to evaluate the diagnostic performance of individual and combined biomarkers, including sensitivity, specificity, and optimal threshold values. Multivariate logistic regression analysis was applied to identify independent predictors of food allergy and to construct a biomarker-based diagnostic model.

Ethical considerations were strictly observed throughout the study. The research protocol was approved by the institutional ethics committee, and informed consent was obtained from the parents or legal guardians of all participating children. Assent was obtained from older children when appropriate. All procedures were conducted in accordance with international ethical standards for research involving pediatric populations, ensuring minimal discomfort and strict confidentiality of patient information.

3. Results

Significant differences in biomarker profiles were observed between children with food allergy and those with functional gastrointestinal disorders. Patients with food allergy demonstrated elevated levels of immunoglobulin E and increased expression of pro-inflammatory cytokines, indicating active immune involvement. Fecal calprotectin levels were moderately elevated in some allergic cases, reflecting mucosal inflammation. In contrast, children with functional disorders generally exhibited normal or minimally altered inflammatory markers, with no evidence of significant immune activation. Markers of intestinal permeability showed variability, with increased levels in a subset of allergic patients, suggesting compromised barrier function. The combination of immunological and inflammatory biomarkers improved diagnostic accuracy, allowing for clear differentiation between the two conditions. Statistical analysis confirmed high sensitivity and specificity of selected biomarker panels in distinguishing disease groups. Analysis of laboratory data revealed distinct differences in biological profiles between patient groups. Children with immune-mediated reactions exhibited elevated levels of markers associated with immune activation, along with increased concentrations of inflammatory mediators indicating mucosal involvement. In some cases, evidence of impaired epithelial barrier function was also observed, suggesting increased intestinal permeability. Conversely, patients with functional disturbances demonstrated largely normal inflammatory and immunological parameters, despite the presence of significant clinical symptoms. The combined assessment of multiple biomarkers allowed for clear stratification of patients, improving the ability to distinguish between underlying mechanisms. Statistical evaluation confirmed that the use of integrated biomarker panels significantly enhanced diagnostic accuracy compared to isolated indicators.

4. Discussion

The findings of this study underscore the importance of biomarker-based approaches in differentiating between food allergy and functional gastrointestinal disorders in children. While clinical symptoms often overlap, underlying mechanisms differ fundamentally, necessitating distinct diagnostic and therapeutic strategies. Immunological markers such as immunoglobulin E provide direct evidence of allergic sensitization, while inflammatory markers reflect the presence of mucosal

immune activation. In functional disorders, the absence of significant inflammatory changes supports their non-organic nature, despite the presence of distressing symptoms. The inclusion of intestinal permeability markers further enhances understanding of disease mechanisms, particularly in cases where barrier dysfunction contributes to symptom development. The integration of multiple biomarkers into a diagnostic panel offers a comprehensive and objective method for evaluating pediatric patients. However, challenges remain in standardizing biomarker thresholds and ensuring accessibility of testing in routine clinical practice. Further research is required to validate these findings and to refine biomarker-based diagnostic algorithms. The observed differences in biomarker expression highlight the importance of objective laboratory assessment in differentiating between conditions with similar clinical presentations. Immune-mediated processes are characterized by measurable activation of inflammatory and immunological pathways, which can be detected through specific laboratory markers. In contrast, functional disorders lack such biological signatures, reflecting their non-inflammatory nature. The incorporation of markers related to epithelial barrier integrity provides additional insight into disease mechanisms, particularly in cases where increased permeability contributes to symptom development. This multidimensional approach offers a more reliable alternative to traditional diagnostic methods, which often depend on subjective evaluation and prolonged observation. The findings support the integration of biomarker analysis into routine clinical practice to improve diagnostic efficiency and guide targeted treatment strategies. However, further standardization and validation are necessary to ensure consistency and accessibility across different healthcare settings.

5. Conclusion

Biomarker profiling represents a valuable tool for distinguishing food allergy from functional gastrointestinal disorders in children. The use of immunological, inflammatory, and barrier-related markers improves diagnostic accuracy and supports more targeted management strategies. This approach reduces the risk of misdiagnosis and unnecessary interventions, ultimately enhancing patient care. Continued development of biomarker-based diagnostics will play a key role in advancing pediatric gastroenterology and improving clinical outcomes. Comprehensive evaluation of immunological, inflammatory, and barrier-related indicators provides a robust framework for distinguishing between immune-mediated gastrointestinal reactions and functional disorders in children. This approach enhances diagnostic precision, reduces uncertainty, and facilitates the selection of appropriate management strategies. The integration of biomarker-based assessment into clinical practice represents a significant step toward more accurate and individualized pediatric care.

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