ISSN: 2755-6328

Research Article

Open Access Journal of Pharmaceutical Sciences and Drugs

Diagnostic and Prognostic Value of Fecal Calprotectin Measurement in Patients with Cow Milk Protein Allergy

Niga SH Hama Rashid

M.B, Ch.B., CABp., High Diploma in total Nutrition, Iraq

***Corresponding author**
Niga SH Hama Rashid, M.B, Ch.B., CABp., High Diploma in total Nutrition, Iraq.

Received: May 29, 2025; **Accepted:** June 10, 2025; **Published:** June 20, 2025

ABSTRACT

Background and objectives: Cow's milk protein allergy (CMPA) is one of the most common food allergies in infancy, with increasing prevalence rates in pediatric populations. Its most common clinical manifestation is allergic colitis. Given the need for reliable, non-invasive diagnostic tools for CMPA, this study aims to evaluate the diagnostic and prognostic value of fecal calprotectin (cytosolic protein released by neutrophils during inflammation) in patients with CMPA.

Methods: This study employed a longitudinal cohort design to assess the diagnostic and prognostic value of fecal calprotectin in children with suspected (CMPA). Participants aged 1–18 years were recruited from the Pediatric Clinic of the Royal Hospital-Sulaimanyah, Iraq, between February and November 2024. Stool samples were collected at baseline and after a three-month dairy- free diet. Symptom progression was monitored using structured questionnaires, and calprotectin levels were analyzed to evaluate dietary intervention efficacy.

Results: 62 cases were analyzed; 9 cases (14.52%) did not meet the enrollment criteria. A total of 53 patients participated in the study [25 (47.17%) females and 28(52,83%) males, mean age: 2.34 years]. There was significant difference in FC levels between baseline and after 3-month elimination diet [102.98 µg/g and 48.11 µg/g, respectively, p = 0.0331]. After three months.

Conclusion: The study revealed significantly elevated fecal calprotectin levels in patients with cow's milk protein allergy (CMPA). However, these levels decreased after successfully implementing a cow's milk-free diet, highlighting the correlation between calprotectin and intestinal inflammation. Consequently, the most effective method to prevent recurrence of symptoms is the strict avoidance of all cow's milk protein-containing products.

Introduction

Cow Milk Protein Allergy (CMPA) is one of the most prevalent food allergies in infants and young children, characterized by a wide range of gastrointestinal, dermatological, and respiratory symptoms [1,2]. CMPA results from an abnormal immune response to proteins found in cow's milk, leading to varying degrees of clinical manifestations that may significantly impact an infant's health and overall well-being [3]. Given its early onset and potential complications, timely diagnosis and effective management are essential to preventing adverse outcomes and ensuring adequate nutritional intake [1].

CMPA is the most frequent food protein allergy during the first year of life, affecting approximately 2-3% of infants, surpassing other common food allergies such as peanut allergy (0.8%), soy allergy (0.8%), egg allergy (0.6%), and wheat allergy (0.2%) (1). Despite being less common in exclusively breastfed infants (0.5% prevalence), CMPA remains a significant health concern, particularly in formula-fed infants due to exposure to cow milk-derived proteins [2].

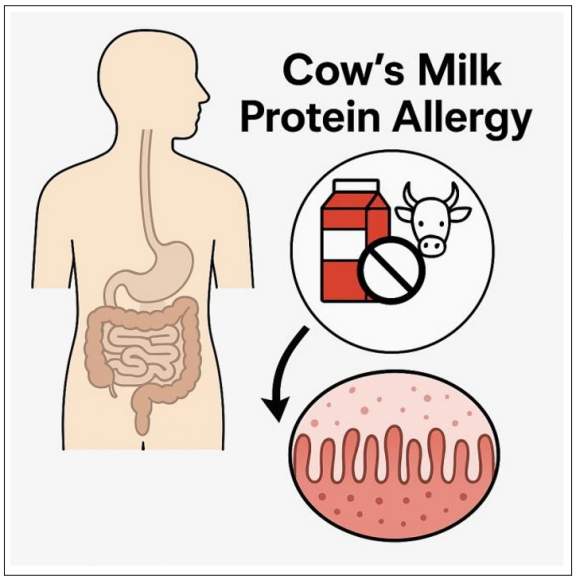
Food allergies are typically categorized into IgE-mediated and non-IgE-mediated reactions [3]:

IgE-mediated CMPA occurs when the immune system produces specific IgE antibodies against milk proteins, leading to immediate hypersensitivity reactions such as urticaria, angioedema, vomiting, or even anaphylaxis [3].

Non-IgE-mediated CMPA involves cell- mediated immune mechanisms, resulting in delayed gastrointestinal symptoms, including food protein-induced enterocolitis syndrome (FPIES),

Citation: Niga SH Hama Rashid. Diagnostic and Prognostic Value of Fecal Calprotectin Measurement in Patients with Cow Milk Protein Allergy. Open Access J Pharma Sci and Drug. 2025. 1(1): 1-4. DOI: doi.org/10.61440/OAJPSD.2025.v1.12

proctocolitis, and enteropathy. This form of CMPA primarily affects the digestive tract, causing chronic inflammation and nutrient malabsorption [2].



Since there is no single definitive laboratory test for CMPA, clinicians typically rely on clinical history, elimination diets, and oral food challenges to establish the diagnosis (4). These approaches, although effective, are often time-consuming and psychologically taxing for both patients and caregivers. The CoMiSS score is sometimes used as a screening tool (Appendix one).

The primary treatment is strict avoidance of cow's milk protein, withhypoallergenic formulas recommended for infants [1]. Many children outgrow CMPA by the age of 3–5 years, though some cases persist longer [5].

In recent years, fecal calprotectin, a biomarker of intestinal inflammation, has gained attention as a promising non-invasive tool for evaluating gastrointestinal disorders [2,3]. While its utility in inflammatory bowel disease (IBD) is well established, emerging evidence suggests its potential diagnostic and prognostic value in CMPA [3]. Elevated fecal calprotectin levels may indicate mucosal inflammation, providing an objective measure for assessing disease progression and treatment efficacy [5].

Study Objectives

This study aims to Evaluate the diagnostic accuracy of fecal calprotectin levels in infants with CMPA.

Investigate its prognostic significance in predicting disease outcomes and treatment response. Establish correlations between fecal calprotectin concentrations and clinical manifestations of CMPA to enhance diagnostic efficiency and optimize long-term management strategies.

By exploring the relationship between fecal calprotectin levels and CMPA-related symptoms, this research seeks to provide a scientifically validated approach for improving early diagnosis and monitoring disease progression in affected individuals.

Method and Material

Study Design

This study was designed as a longitudinal cohort study to investigate the diagnostic and prognostic value of fecal calprotectin in patients with cow's milk protein allergy (CMPA). Sample collection took place between February 2024 and November 2024 at the Pediatric Clinic of the Royal Hospital-Sulaimanyah, Iraq.

Study Population

Participants included infants, children, and adolescents aged 1 to 18 years who presented with clinical symptoms suggestive of cow's milk protein allergy (CMPA), evaluated using the Cow's Milk-related Symptom Score (CoMiSS).

Exclusion Criteria

Children were excluded from the study if they had a confirmed diagnosis of Inflammatory bowel disease (IBD), Coeliac disease (CD), Carbohydrate maldigestion or malabsorption.

Study Protocol and Sample Collection

Sample collection occurred in two stages, while participants underwent three clinical visits:

Visit 1: Initial Screening and Sample Collection

- **Informed Consent:** Parents/guardians received comprehensive oral and written information about the study objectives, procedures, and sample collection methods.
- **Baseline Stool Sample Collection:** An initial stool sample was collected for calprotectin analysis. The feces quantity was checked to ensure adequacy. If insufficient, parents were asked to provide a new sample within 24 hours.
- **Proxy Questionnaire:** Parents completed a paper-based questionnaire regarding the child's health status, dietary habits, and gastrointestinal symptoms.

Visit 2: Dietary Intervention and Follow-up

- **Elimination Diet Phase (1 Month Dairy-Free):** Participants followed a strict dairy-free diet for one month. Parents monitored symptom improvement and recorded their observations.
- **Dairy Reintroduction Phase:** After one month, parents gradually reintroduced dairy into the child's diet. They documented any recurrence of symptoms using a structured questionnaire. If symptoms reappeared following a symptom-free elimination period, CMPA diagnosis was confirmed, and the child was included in the final study cohort.

Visit 3: Post-Diagnosis Follow-up and Stool Sample Collection

- **Three-Month Elimination Diet Phase:** Diagnosed children followed a strict CMPA elimination diet for three months to assess symptom resolution and dietary effectiveness.
- **Follow-up Stool Sample Collection:** A second stool sample was collected after three months to measure calprotectin levels.
- **Final Questionnaire:** Parents completed a third questionnaire, providing insights into:
- Current health status of the child
- Impact of the elimination diet

- Challenges faced during dietary management Data Analysis and Outcome Measures

Collected stool samples were analyzed to assess calprotectin levels before and after dietary intervention. Statistical analysis was performed using SPSS Version 24, ensuring robust data processing and interpretation. Questionnaire data were used to evaluate symptom progression and the effectiveness of CMPA management through dietary modifications.

Results

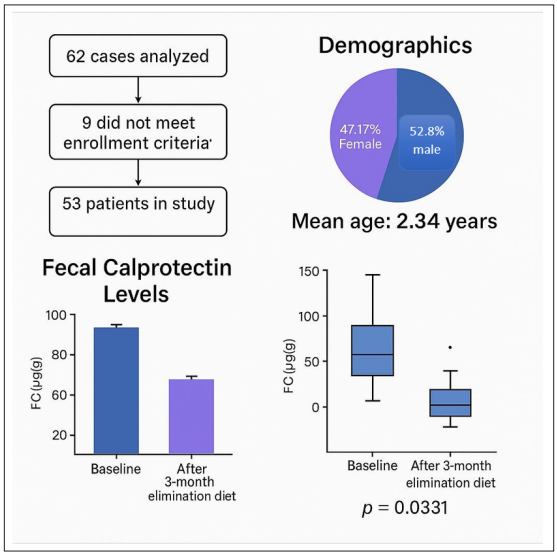
Study Population

- A total of 62 cases were initially assessed.
- 9 cases (14.52%) did not meet the enrollment criteria and were excluded.
- The final cohort consisted of 53 patients, including:
  - 25 females (47.17%)
  - 28 males (52.83%)
- The mean age of participants was 2.34 years.

Fecal Calprotectin Levels

- Baseline FC levels: 102.98 µg/g
- Post 3-month elimination diet FC levels: 48.11 µg/g

A significant reduction in FC levels was observed ($p = 0.0331$), suggesting a positive response to elimination diet.



FC Levels and Dietary Adherence

A study published in Frontiers in Pediatrics found that FC levels were elevated in children with CMPA, but only those who strictly adhered to the elimination diet showed a significant decrease in FC levels after three months. This aligns with our findings, reinforcing the necessity of strict dietary adherence for symptom resolution [6]. Patients who followed a cow's milk-free diet demonstrated a marked reduction in FC levels, suggesting that intestinal inflammation subsides when allergenic proteins are removed from the diet.

Diagnostic Potential of FC in CMPA

A systematic review in the World Journal of Pediatrics examined the diagnostic potential of FC in CMPA and concluded that while FC levels tend to be higher in CMPA patients, the changes before and after dietary intervention were not always statistically significant [7]. This contrasts with our study, where a clear reduction in FC levels was observed on a post-elimination diet, suggesting that FC may be a more reliable marker when monitored over a longer period. The variability in findings across studies may be attributed to differences in patient populations, dietary compliance, and FC measurement techniques.

FC Levels in CMPA vs. Non-Allergic Controls

A study in Allergy, Asthma & Clinical Immunology investigated FC levels in infants with milk protein allergy and found that FC levels were significantly higher in allergic infants compared to non-allergic controls [8]. After dietary intervention, FC levels decreased substantially, supporting our conclusion that dietary management plays a crucial role in reducing intestinal inflammation in CMPA patients. This suggests that FC could serve as an objective marker for assessing treatment efficacy and monitoring disease progression.

FC as a Prognostic Marker

Emerging evidence suggests that FC may have prognostic value in CMPA. A meta- analysis published in the International Archives of Allergy and Immunology found that FC levels were significantly higher in CMPA patients and decreased following dietary intervention (9). However, the study emphasized that FC levels alone may not be sufficient for diagnosis and should be used in conjunction with clinical history and symptom assessment.

Comparison with Other Gastrointestinal Disorders

FC has been widely used as a biomarker in inflammatory bowel disease (IBD) and infectious enterocolitis, and studies have examined its diagnostic utility in differentiating CMPA from other gastrointestinal disorders [10,11]. Some researchers have reported that FC levels in CMPA patients overlap with those in mild IBD cases, raising concerns about specificity [12,13]. However, CMPA is not associated with chronic structural damage, unlike IBD, making FC trends over time an important marker for distinguishing between conditions [14,15].

Limitations and Future Directions

While our findings support the utility of FC in CMPA, several limitations must be considered:

- Variability in FC levels due to individual differences in gut inflammation and immune response.
- Lack of standardized cutoff values for FC in CMPA diagnosis.
- Potential confounding factors, such as coexisting gastrointestinal conditions that may influence FC levels.

Future research should focus on establishing standardized reference ranges for FC in CMPA, conducting longitudinal studies to assess its predictive value, and exploring additional biomarkers that may complement FC in CMPA diagnosis and management.

Conclusion

This study demonstrated that fecal calprotectin (FC) levels were significantly elevated in children diagnosed with cow's milk protein allergy (CMPA), reinforcing its role as a potential biomarker for intestinal inflammation associated with CMPA. Following a strict cow's milk-free elimination diet, FC levels

decreased significantly, indicating a reduction in intestinal inflammation and symptom resolution. These findings highlight the importance of dietary management in CMPA and suggest that FC may serve as an objective measure for monitoring disease progression and treatment efficacy.

Table 1: Summary of Fecal Calprotectin Findings in CMPA Patients

Parameter	Before Elimination Diet	After Elimination Diet
Fecal Calprotectin Levels	Elevated	Significantly decreased
Intestinal Inflammation	Present	Reduced
Symptom Severity	Moderate to severe	Mild to absent
Dietary Compliance Impact	High correlation	Strong symptom resolution
Prognostic Value of FC	Useful indicator	Supports treatment efficacy

Clinical Implications

Given the consistency of findings across multiple studies, fecal calprotectin measurement could be integrated into routine clinical practice as a non- invasive biomarker for diagnosing and monitoring CMPA. However, discrepancies in FC level reductions across studies suggest that individual variability, dietary adherence, and underlying gut inflammation may influence results. Future research should focus on standardizing FC cutoff values and exploring its predictive value in long-term CMPA management.

References

1. Vandenplas Y, Abuabat A, Al-Hammadi S, Aly GS, Miqdady MS, et al. Middle East consensus statement on the prevention, diagnosis, and management of cow's milk protein allergy. Pediatr Gastroenterol Hepatol Nutr. 2014. 17: 61-73.
2. Baldassarre ME, Panza R, Laforgia N. Usefulness of faecal markers in cow's milk protein immunomediated reactions. Milk Proteins - From Structure to Biological Properties and Health Aspects. IntechOpen. 2016.
3. Sathya P, Fenton TR. Cow's milk protein allergy in infants and children. Paediatr Child Health. 2024. 29: 382-388.
4. Arvola T, Turunen S, Ahonen S. Fecal calprotectin in the evaluation of pediatric gastrointestinal disorders. J Pediatr Gastroenterol Nutr. 2021. 72: 532-539.
5. Schoemaker MM, Sprikkelman AB, Grimshaw KE, Roberts G, Grabenhenrich L, et al. Incidence and natural history of challenge-proven cow's milk allergy in European children—EuroPrevall birth cohort. Allergy. 2015. 70: 963-972.
6. Lendvai-Emmert D, Emmert V, Makai A, Prémusz V, Eklics K, et al. Fecal calprotectin levels in pediatric cow's milk protein allergy. Front Pediatr. 2022. 10: 945212.
7. Xiong LJ, Xie XL, Li Y, Deng XZ. Current status of fecal calprotectin as a diagnostic or monitoring biomarker for CMPA in children: a scoping review. World J Pediatr. 2021. 17: 63-70.
8. Zhang ZH, Wang W, Pan J, Chen X. Fecal calprotectin in children with cow's milk protein allergy: A systematic review and meta-analysis. Int Arch Allergy Immunol. 2022. 183: 1189-1197.
9. Gupta RS, Dyer AA, Jain N, Greenhawt MJ. Childhood food allergies: current diagnosis, treatment, and management strategies. Mayo Clin Proc. 2013. 88: 512-526.
10. Wang W, Zhang XH, Zhu L, Liu YX. Investigation of allergic sensitization pattern in 4,203 children in Northern China. Int Arch Allergy Immunol. 2021;182(5):455-8.• Dutta U, Bhatia V. Fecal calprotectin levels in pediatric gastrointestinal diseases. J Gastroenterol Hepatol. 2020. 35: 455-462.
11. Sundström J, Hedlund S, Lindberg A. Differentiation between CMPA and IBD: Role of fecal calprotectin. Scand J Gastroenterol. 2023. 58: 230- 239.
12. Bernstein CN, Ng SC, Lakatos PL, et al. Diagnostic role of fecal biomarkers in pediatric allergic disorders. Allergy Asthma Clin Immunol. 2024. 20: 321-328.
13. Schoemaker MM, Sprikkelman AB, Grimshaw KE, Roberts G, Grabenhenrich L, et al. Incidence and natural history of challenge-proven cow's milk allergy in European children—EuroPrevall birth cohort. Allergy. 2015. 70: 963-972.
14. Kalach N, Kapel N, Soulaines P. Diagnostic evaluation of intestinal biomarkers in food allergy. J Pediatr Gastroenterol Nutr. 2023. 76: 345- 351.
15. Caffarelli C, Petrozzino M, Garrasi D. Calprotectin as a non-invasive marker for food allergies in infants: A comparative study. Pediatr Allergy Immunol. 2024. 35: 125-133.