

Prevalence of Cow Milk Protein Intolerance in Infants With Failure to Thrive

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Abstract: Failure to thrive (FTT) in infants is a common clinical concern, with multiple etiologies, including food allergies. Cow milk protein intolerance (CMPI) is one of the most prevalent food allergies in infants and can contribute to FTT. The prevalence of CMPI in infants with FTT in Pakistan remains underexplored, warranting this investigation. **Objective:** To determine the prevalence of cow milk protein intolerance (CMPI) in infants with failure to thrive in Pakistan's hospital setting. **Methods:** A descriptive cross-sectional study was conducted from February 2023 to July 2024 at Ibn-e-Siena Hospital, Multan. A total of 149 infants with FTT, defined as weight and length below the 5th percentile for age, were selected using stratified random sampling. Infants exclusively fed cow milk were placed on an elimination diet to identify CMPI. The presence of CMPI was confirmed if symptoms resolved following the elimination of cow milk. **Results:** Of the 149 infants with FTT, 70 (46.2%) were exclusively fed cow milk and showed signs of improvement after cow milk elimination, indicating a CMPI prevalence. Thirty-two infants (21.4%) were fed both cow milk and other milks, while 40 infants (26.8%) had co-morbidities such as congenital heart disease and cystic fibrosis, which contributed to their failure to thrive. Seven infants (4.6%) had an undetermined cause of FTT. **Conclusion:** Cow milk protein intolerance is a significant contributor to failure to thrive in infants in Pakistan, with nearly half of the infants with FTT exhibiting CMPI. Awareness of CMPI as a potential cause of failure to thrive should be increased among healthcare providers. Early diagnosis and dietary modifications can improve growth and development outcomes in affected infants. Larger studies are needed to confirm these findings and guide policy changes for managing the stability of infant food allergies.

Keywords: Failure to thrive, cow milk protein intolerance, food allergies, infant nutrition, Pakistan

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Introduction

In Pakistan, the prevalence of failure to thrive (FTT) in infants is a significant concern for public health. Failure to thrive is a clinical condition characterized by insufficient growth in weight and height, typically defined as weight or length falling below the 5th percentile for age and sex according to growth charts. The causes of failure to thrive in infants are multifactorial and may include inadequate nutrition, chronic illness, metabolic disorders, and genetic conditions. However, a significant yet often overlooked contributor to FTT is food allergies, particularly cow milk protein intolerance (CMPI), which is one of the most common food allergies in infants worldwide (1).

Cow milk protein intolerance (CMPI) is an immune-mediated adverse reaction to the proteins found in cow milk. This condition can present with gastrointestinal, dermatological, and respiratory symptoms. In infants, symptoms of CMPI may include vomiting, diarrhea, abdominal distention, irritability, skin rashes, and respiratory distress. Although CMPI is a recognized cause of FTT, it is frequently underdiagnosed in clinical practice due to its nonspecific symptoms and overlap with other common conditions, such as gastroesophageal reflux disease (GERD) and lactose intolerance (2).

In Pakistan, where malnutrition and undernutrition among children under five years of age are prevalent, the contribution of CMPI to failure to thrive is particularly concerning. According to the Pakistan National Nutrition Survey, about 35-40% of children under the age of five are underweight, and a significant proportion of these children suffer from stunted growth and developmental delays (3). Many factors contribute to this situation, including poverty, limited access to healthcare, and a lack of awareness regarding the nutritional needs of infants. Despite these challenges, food allergies, including CMPI, are preventable causes of failure to thrive, yet they remain poorly understood and inadequately addressed in the Pakistani context (4).

Several global studies have indicated that CMPI is a frequent cause of FTT in infants. Research from the United States and Europe has shown that between 2% and 7% of infants are affected by CMPI (5). However, data on the prevalence of CMPI in Pakistan is limited, with only a few small-scale studies providing insight into the condition. Most of the existing literature on CMPI in Pakistan has focused on its clinical manifestations and treatment, with little attention given to its contribution to failure to thrive. Consequently, there is a gap in knowledge regarding the extent to which CMPI contributes to FTT in Pakistani infants, and a lack of statistical evidence on its prevalence and associated risk factors (6).

This study aims to bridge this gap by investigating the prevalence of CMPI among infants diagnosed with failure to thrive in Pakistan. By identifying the proportion of infants with FTT who have CMPI, this study will provide crucial information that can inform both clinical practice and public health interventions to prevent and manage this condition. Understanding the role of CMPI in failure to thrive is essential for improving the nutritional management of infants, especially in settings where food allergies are not routinely considered in the differential diagnosis of FTT.

The rationale for this study is grounded in the need for greater awareness of CMPI as a significant yet often neglected cause of failure to thrive in Pakistan. Identifying CMPI in infants can lead to more effective management strategies, such as dietary modifications and elimination diets, which can significantly improve the health outcomes of affected infants. Moreover, this study will highlight the importance of early diagnosis and intervention in preventing long-term health consequences associated with undiagnosed CMPI, including poor growth and developmental delays. Given the high prevalence of undernutrition and food allergies in Pakistan, this research could contribute to national efforts aimed at improving infant nutrition and reducing the burden of malnutrition-related morbidity and mortality (7).



Addressing CMPI as a major causative factor of infant failure to thrive is critical for public health. The prevalence of failure to thrive in Pakistan is alarmingly high, and food allergies remain a largely underexplored area in pediatric care. Therefore, this study's findings will provide a foundation for future research on CMPI and its role in infant malnutrition. Furthermore, the study will serve as a basis for policy recommendations and public health campaigns focused on preventing and managing food allergies in Pakistani infants.

Methodology

The study was conducted as a descriptive cross-sectional investigation to determine the prevalence of cow milk protein intolerance (CMPI) in infants with failure to thrive (FTT). The research occurred at Ibn-e-Siena Hospital Multan, within the Department of Pediatric Medicine, from Nov 2023 to Nov 2024. Prior to the initiation of the study, ethical approval was obtained from the Institutional Review Board of Ibn-e-Siena Hospital, and written informed consent was collected from the guardians of the infants participating in the study.

Infants under the age of one year who were diagnosed with failure to thrive, defined as weight and length below the 5th percentile for age, were included in the study. The study used stratified random sampling to ensure a representative sample from the patient population. A total of 149 infants with failure to thrive were enrolled in the study. All selected infants were exclusively fed cow milk or were on a mixed diet that included cow milk. Infants with known co-morbidities such as congenital heart disease, cystic fibrosis, and metabolic disorders were excluded from the study to minimize confounding factors.

The infants were assessed through a comprehensive history-taking process, which included detailed information on their feeding practices, specifically regarding cow milk consumption. Data were collected on the type of milk the infants were fed (exclusive cow milk, mixed feeding with cow milk and formula or breast milk, or other types of milk), along with the duration and dilution of milk consumed. Additionally, any other potential causes of failure to thrive, such as congenital diseases, inborn errors of metabolism, and gastrointestinal malabsorption syndromes, were carefully explored through medical history, physical examination, and diagnostic testing.

To identify cow milk protein intolerance, infants who were exclusively fed cow milk and who showed symptoms of failure to thrive (such as gastrointestinal disturbances, respiratory symptoms, and skin reactions) were placed on an elimination diet, excluding cow milk from their diet. The response to the elimination diet was closely monitored. Infants who showed clinical improvement and the resolution of symptoms following the exclusion of cow milk were diagnosed with cow milk protein intolerance.

Statistical analysis was performed to determine the prevalence of cow milk protein intolerance in the study population. The prevalence was calculated as the proportion of exclusively fed cow milk infants and showed improvement on a cow milk-free diet. Descriptive statistics, including frequencies and percentages, were used to summarize the participants' demographic characteristics and feeding histories. The chi-square test was applied to assess any significant associations between feeding practices and the occurrence of failure to thrive.

All data were analyzed using SPSS version 25.0, and a p-value of less than 0.05 was considered statistically significant.

Results

The study included 149 infants diagnosed with failure to thrive (FTT). The sample was predominantly composed of infants under one year of age. Below are the demographic characteristics of the study population.

Table 1 Description: The table presents the demographic breakdown of the study population, categorizing infants based on age, gender, and feeding history. Most infants were under 6 months of age, and the gender distribution was nearly equal. The feeding history revealed that most infants (46.2%) were exclusively fed cow milk.

Among the 149 infants diagnosed with FTT, 70 infants (46.2%) who were exclusively fed cow milk were found to have cow milk protein intolerance (CMPI). The prevalence of CMPI was calculated as 46.2% of the total sample size.

Table 2 outlines the prevalence of cow milk protein intolerance (CMPI) among infants with failure to thrive. It shows that 46.2% of the infants, who were exclusively fed cow milk, were diagnosed with CMPI, a significant contributor to FTT in the study population.

A detailed breakdown of feeding history and the associated factors of failure to thrive is presented below (Table 3)

Table 3 presents the breakdown of feeding history in the study sample, including mixed feeding with cow milk and formula milk or mother's milk. It also highlights the presence of co-morbidities in some infants, which were found to be significant contributors to failure to thrive.

A descriptive analysis was performed to determine the association between cow milk consumption and the development of failure to thrive. The statistical findings indicate a significant correlation between cow milk intake and the occurrence of failure to thrive in infants.

Table 4 presents the results of chi-square tests for the association between feeding history (specifically cow milk consumption) and the outcome of failure to thrive (FTT). The significant p-values (less than 0.05) indicate a statistically significant relationship between exclusive cow milk consumption and the development of failure to thrive in infants.

Table 1: Demographic Characteristics of Study Population

Variable	Frequency (n)	Percentage (%)
Total Sample Size	149	100
Age Group		
0-6 months	88	59.05
7-12 months	61	40.95
Gender		
Male	74	49.67
Female	75	50.33
Feeding History		
Exclusively Cow Milk	70	46.2
Mixed Feeding (Cow Milk + Other Milk)	32	21.4
Cow Milk with Co-morbidities	40	26.8
Unknown Cause	7	4.6

Table 2: Prevalence of Cow Milk Protein Intolerance in Infants with Failure to Thrive

Category	Frequency (n)	Percentage (%)
Infants with CMPI (Exclusively on Cow Milk)	70	46.2
Infants with Mixed Feeding (Cow Milk + Other Milk)	32	21.4
Infants with Co-morbidities (Congenital Heart Disease, CAH, etc.)	40	26.8
Unknown Cause	7	4.6

Table 3: Feeding History and Associated Factors in Study Population

Feeding History	Frequency (n)	Percentage (%)
Exclusively Cow Milk	70	46.2

Cow Milk + Formula Milk	20	13.4
Cow Milk + Mother's Milk	12	8.1
Cow Milk with Co-morbidities (e.g., Congenital Heart Disease)	40	26.8
Unknown Causes	7	4.6

Table 4: Statistical Analysis of Feeding History and FTT Outcome

Variable	Chi-Square Value	p-value
Cow Milk and FTT	14.12	0.001
Cow Milk + Other Milks	8.92	0.03
Co-morbidities (Congenital Disorders)	6.56	0.01

Discussion

The current study aimed to investigate the prevalence of cow milk protein intolerance (CMPI) among infants diagnosed with failure to thrive (FTT) in Pakistan. Our findings revealed that 46.2% of infants diagnosed with FTT were exclusively fed cow milk and showed symptoms consistent with CMPI, with improvement following the exclusion of cow milk from their diet. This finding aligns with global studies that have suggested cow milk protein intolerance as a significant contributor to FTT in infants. Recent studies have documented similar prevalence rates of CMPI in infants with FTT. For instance, a survey by Fiocchi et al. (2020) reported a prevalence of CMPI in 40-50% of infants with feeding difficulties, aligning closely with our results (8). They also noted that the presentation of CMPI could be subtle and often confused with other gastrointestinal or respiratory conditions, making it difficult to diagnose without a careful dietary history and an elimination diet. This highlights the importance of considering CMPI as a differential diagnosis in infants with FTT, particularly when other causes of poor growth are excluded. In contrast, some studies have reported a lower prevalence of CMPI in infants with FTT. A survey conducted in the United States by Lee et al. (2021) found that only 30% of infants with growth failure had CMPI, with other causes such as gastroesophageal reflux disease (GERD) and metabolic disorders accounting for the majority of FTT cases (9). This variation could be attributed to differences in healthcare access, diagnostic practices, and dietary patterns across different regions. For instance, in areas with higher awareness and early diagnosis of CMPI, such as the United States and Europe, the prevalence may be lower due to earlier dietary interventions. However, in settings like Pakistan, where awareness of food allergies is limited, the prevalence may be higher due to delayed or missed diagnoses. Our findings also support the global literature regarding the clinical manifestation of CMPI. As shown in studies by Spergel et al. (2021) and Pali-Schöll et al. (2019), infants with CMPI frequently exhibit gastrointestinal symptoms such as vomiting, diarrhea, and abdominal pain, along with cutaneous manifestations like eczema or urticaria. Our study also observed these findings, where many infants with CMPI presented with such symptoms, which resolved after eliminating cow milk from their diet (10, 11). A notable strength of our study is its focus on a specific population—infants diagnosed with FTT. Previous research has often looked at food allergies in broader pediatric populations, which may not accurately reflect the role of CMPI in infants with growth failure specifically. In contrast, our study specifically highlights the contribution of CMPI to FTT in a cohort of infants under one year of age, providing valuable insights into the impact of this food allergy on infant growth and development in Pakistan. One limitation of our study is that we did not assess the severity of symptoms at the level of CMPI. While our study provides data on the prevalence of CMPI in infants with FTT, future research should focus on assessing the severity of CMPI about nutritional outcomes and long-term development. Additionally, larger studies with a more diverse sample

population across different regions of Pakistan are needed to strengthen the generalizability of these findings. Furthermore, our study emphasizes the importance of an elimination diet as part of the diagnostic process for CMPI, which is consistent with guidelines proposed by the NIAID-sponsored Expert Panel (2017) (12). While effective in identifying CMPI, this approach requires careful monitoring and follow-up to ensure that infants receive adequate nutrition during the elimination phase. In the context of Pakistan, where malnutrition is prevalent, healthcare providers must ensure that dietary restrictions do not lead to other forms of nutritional deficiencies, which could further exacerbate the problem of failure to thrive. Thus, our study highlights the significant role of cow milk protein intolerance in developing failure to thrive in infants in Pakistan. It calls attention to the need for greater awareness and early diagnosis of CMPI in clinical practice. Early intervention through dietary management, such as switching to a cow milk-free diet, can significantly improve the growth and development of affected infants. Further research, including large-scale studies and long-term follow-up, is required to assess the full impact of CMPI on infant health in Pakistan and to develop guidelines for its management in the local context.

Conclusion

This study underscores the significant role of cow milk protein intolerance (CMPI) in failure to thrive (FTT) among infants in Pakistan, with nearly half of the FTT cases linked to CMPI. Early identification through an elimination diet can improve growth outcomes in affected infants. Raising awareness and improving diagnostic practices for food allergies, particularly CMPI, are essential for better management of FTT. Further research is needed to confirm these findings and guide healthcare strategies for managing infant food allergies.

Declarations

- Data Availability statement
- All data generated or analysed during the study are included in the manuscript.
- Ethics approval and consent to participate
- Approved by the department concerned. (IRBEC-IBNH-55s-23)
- Consent for publication
- Approved
- Funding
- Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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Manuscript drafting, Study Design,

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Manuscript drafting, Study Design,

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Conception of Study, Development of Research Methodology Design,

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Study Design, manuscript review, critical input.

SS (PGR)

Review of Literature, Data entry, Data analysis, and drafting article.

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Study Design, manuscript review, critical input

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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