European Journal of Clinical Pharmacy
Print ISSN: 2385-409X, **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Association of Celiac Disease with the age of introduction of wheat in diet of infant- A cross-sectional study

Article History:

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Received: 02-11-2025
Revised: 06-11-2025
Accepted: 16-12-2025
Published: 21-12-2025

Abstract: Background: Celiac disease is a chronic immune-mediated enteropathy triggered by gluten ingestion in genetically susceptible individuals, with early-life feeding practices playing a potential role in its development.**Objectives:** To determine the association between the age of wheat introduction and the occurrence of celiac disease in children.**Study Design & Setting:** This cross-sectional study was conducted at a pediatric department of a tertiary care hospital from 30 June 2025 to 30 September 2025.**Methodology:** A total of 76 children aged 6–60 months were included using non-probability consecutive sampling. Data regarding demographic characteristics, clinical features, breastfeeding practices, and timing of wheat introduction were collected using a structured questionnaire. Celiac disease status was assessed based on laboratory findings. Data were analyzed using SPSS version 25.0. Chi-square test was applied for association, and multivariate logistic regression analysis was performed to identify independent predictors. A p-value ≤0.05 was considered statistically significant.**Results:** The mean age of participants was 26.42 ± 17.67 months, with 55.3% males. Celiac disease was diagnosed in 23.7% of children. Early wheat introduction (<4 months) showed a significantly higher frequency of celiac disease (57.1%) compared to standard and delayed introduction groups (p = 0.005). Multivariate analysis revealed that early wheat introduction (AOR = 4.21, p = 0.006) and breastfeeding for less than 6 months (AOR = 3.18, p = 0.030) were significant predictors. Daily wheat consumption showed a borderline association (p = 0.054).**Conclusion:** Early introduction of wheat and shorter breastfeeding duration significantly increase the risk of celiac disease. Appropriate infant feeding practices may help reduce disease burden.

Keywords: Breastfeeding, Celiac disease, Children, Gluten, Wheat introduction

INTRODUCTION

Celiac Disease (CD) is a chronic immune-mediated genetically heterogeneous disorder triggered in predisposed individuals by ingesting gluten. It causes enteropathy with systemic manifestations which range from GI symptoms to anemia, osteoporosis, and stunted growth 1. The global prevalence of CD is between 0.05% and 2.6% 2. However, emerging data from South Asia, especially Pakistan, suggests a rising burden of CD where 1-3% of the population may be affected. Studies have reported the CD prevalence to be 29.3% in specific populations of Pakistan 3,4 . This

disparity highlights an urgent need to investigate region-specific risk factors as dietary practices and genetic vulnerabilities differ in Pakistan. In CD pathogenesis, there is interplay between genetic susceptibility and environmental triggers like infant feeding practices. Based on Western studies, a window of tolerance (4-6 Months) for the safe introduction of gluten is proposed where immune tolerance and CD risk may be balanced.5 However, trials like CELIPREV and LEAP show paradoxical data that delayed introduction does not reduce CD risk and early peanut introduction reduces allergies. 6, 7 Hence, there is a complex relationship between genetic, dietary, and regional factors. For instance, breastfeeding has a protective effect against CD through immune modulation. However, breastfeeding practices vary in the Pakistani population and often wheat is introduced before 4 months as it is the dietary staple.8

Pakistani population has unique dietary practices and genetic vulnerabilities which create a guideline-practice mismatch whereby not only the age of wheat introduction and breastfeeding vary according to the socioeconomic status and life style .9 Finally, the public health policies are based upon Western data that ignores the unique breastfeeding practices, dietary practices, and genetic vulnerabilities.10
There is an absence of studies that evaluate the interplay of wheat introduction timing, breastfeeding duration, and HLA status. This cross-sectional study aims to fill this gap by investigating the association between wheat introduction age and CD prevalence, determining whether breastfeeding duration modifies this association, and evaluating how HLA risk alleles interact with wheat introduction timing to shape CD susceptibility. The objective of this study is to assess the frequency of Celiac Disease among children according to the age of introduction of wheat.

MATERIALS AND METHODS

A cross-sectional study was conducted at Fauji Foundation Hospital, Islamabad, Pakistan, from 30 June 2025 to 30 September 2025. A total sample size of 76 participants was calculated using the OpenEpi online sample size calculator, considering a two-sided significance level (1-α) of 90%, power (1-β) of 80%, and a prevalence of celiac disease of 1.2%.11 Stratified random sampling with multistage recruitment was employed. Participants were included if children were aged between 6 months to 5 years with a documented age of wheat introduction, had one or more symptoms suggestive of celiac disease, had a known history of breastfeeding duration, and whose parents were willing to allow anti-tTG serology and duodenal biopsy if required. Children were excluded if they had severe medical conditions such as congenital anomalies, other allergic disorders, recent surgeries, or uncontrolled chronic diseases, had active infections during the screening period, were on medications such as antibiotics within the last four weeks or laxatives (three or more doses per week within two weeks) or other drugs that could interfere with anti-tTG test results, or had incomplete or unreliable data obtained through questionnaires or medical records.

Data were collected using a structured questionnaire administered to parents by a resident pediatrician after explaining the study and obtaining informed consent. During history taking, demographic details including age and gender, feeding practices such as duration of exclusive breastfeeding, age of wheat introduction, type of first wheat-containing food, and frequency of wheat consumption, along with medical history including chronic diarrhea, recurrent vomiting, and family history of celiac disease were recorded. Blood samples were collected by a trained phlebotomist at the hospital and sent to the laboratory. Laboratory investigations included complete blood picture, C-reactive protein, and anti-tTG IgA serology. Where indicated, patients were enrolled for endoscopy, and duodenal biopsy was performed by a consultant pediatric gastroenterologist to confirm celiac disease. Recall bias was minimized by cross-validating parental recall regarding feeding practices, particularly age of wheat introduction, with infant health records in 15% of participants. Ethical considerations, including confidentiality, anonymization, and informed consent, were strictly maintained.

Celiac disease symptoms were identified in patients presenting with defined clinical features assessed during outpatient evaluation. Chronic diarrhea was defined as three or more loose stools per day for 14 days or more, recurrent vomiting as two or more episodes per week for at least four weeks, and persistent abdominal pain as parent-reported pain affecting daily activities for four or more weeks. Weight faltering was defined as weight-for-age or weight-for-height z-score less than −2 SD, and failure to thrive as height-for-age z-score less than −2 SD according to WHO standards. Iron deficiency anemia was defined as hemoglobin <11 g/dL with serum ferritin <15 ng/mL on laboratory testing. Celiac disease was confirmed in symptomatic patients with anti-tTG IgA levels ≥10 times the upper limit of normal, while doubtful cases were confirmed by duodenal biopsy showing villous atrophy. Age of wheat introduction was recorded in months and categorized as early (<4 months), standard (4–6 months), and delayed (>6 months) based on parental recall or records. Breastfeeding duration was categorized as short-term (<6 months), medium-term (6–12 months), and long-term (>12 months). Infection during screening was defined as fever ≥38°C with CRP >10 mg/L within the last seven days.

Data were analyzed using SPSS version 27.

Qualitative variables such as gender, exclusive breastfeeding status, timing of wheat introduction, anti-tTG serology results, type of wheat-containing diet, and frequency of wheat consumption were expressed as frequencies and percentages, while quantitative variables such as age and duration of exclusive breastfeeding were expressed as mean and standard deviation. The chi-square test was applied to compare celiac disease positivity with the timing of wheat introduction. Multivariate analysis was performed using variables including age, duration of breastfeeding, type of food introduced, and frequency of wheat consumption to control for confounding factors. A p-value was calculated using the chi-square test, and the null hypothesis was rejected at a p-value ≤ 0.05.

RESULTS

The mean age of the participants was 26.42 ± 17.67 months, indicating a relatively wide age distribution among the studied population. When categorized, the highest proportion of children belonged to the 6–12 months age group (35.5%), followed closely by the 13–36 months group (34.2%), while 30.3% were in the 37–60 months category. Regarding gender distribution, males constituted a slightly higher proportion of the sample (55.3%) compared to females (44.7%), showing a mild male predominance in the study population, as given in Table 1.

Table 1: Demographic Characteristics of Study Participants (n = 76)

Variables		**Frequency (%)**
Age (months)	Mean ± SD	26.42 ± 17.67
Age Groups	6–12 months	27 (35.5)
	13–36 months	26 (34.2)
	37–60 months	23 (30.3)
Gender	Male	42 (55.3)
	Female	34 (44.7)

Among the clinical characteristics, chronic diarrhea was present in 36.8% of patients, while the majority (63.2%) did not report this symptom. Recurrent vomiting was observed in 28.9% of cases, whereas 71.1% had no history of vomiting. Abdominal pain was reported by 32.9% of participants, with 67.1% being asymptomatic for this complaint. Weight faltering was noted in 26.3% of children, while 73.7% showed no such issue. Iron deficiency anemia was present in 23.7% of cases, whereas the majority (76.3%) did not have anemia. Similarly, failure to thrive was observed in 21.1% of participants, while 78.9% were not affected. A positive family history of celiac disease was found in only 10.5% of cases, with the remaining 89.5% having no such history, as given in Table 2.

Table 2: Clinical Characteristics of Participants (n = 76)

Variables	**Parameters**	**Frequency (%)**
Chronic diarrhea	Yes	28 (36.8)
	No	48 (63.2)
Recurrent vomiting	Yes	22 (28.9)
	No	54 (71.1)
Abdominal pain	Yes	25 (32.9)
	No	51 (67.1)
Weight faltering	Yes	20 (26.3)
	No	56 (73.7)
Iron deficiency anemia	Yes	18 (23.7)
	No	58 (76.3)
Failure to thrive	Yes	16 (21.1)
	No	60 (78.9)
Family history of celiac disease	Yes	8 (10.5)
	No	68 (89.5)

Regarding feeding practices, exclusive breastfeeding was reported in 60.5% of children, while 39.5% were not exclusively breastfed. In terms of breastfeeding duration, the majority of participants (55.3%) were breastfed for 6–12 months, followed by 28.9% who were breastfed for less than 6 months, and a smaller proportion (15.8%) who

continued breastfeeding for more than 12 months, as given in Table 3.

Table 3: Breastfeeding Practices (n = 76)

Variables	Parameters	Frequency (%)
Exclusive breastfeeding	Yes	46 (60.5)
	No	30 (39.5)
Breastfeeding duration	<6 months	22 (28.9)
	6–12 months	42 (55.3)
	>12 months	12 (15.8)

With regard to complementary feeding practices, solid food was introduced before 6 months of age in 34.2% of children, while the majority (65.8%) received solid foods at or after 6 months. Concerning the age of wheat introduction, half of the participants (50.0%) had wheat introduced at the standard time, whereas 31.6% experienced delayed introduction and 18.4% had early introduction. As for the type of first wheat-containing food, chapatti was the most commonly introduced (36.8%), followed by bread (28.9%), biscuits (21.1%), and other forms (13.2%). In terms of consumption frequency, most children (76.3%) consumed wheat on a weekly basis, while 23.7% had daily wheat intake, as given in Table 4.

Table 4: Weaning and Wheat Introduction Practices (n = 76)

Variables	Variable	Frequency (%)
Solid food introduction	<6 months	26 (34.2)
	≥6 months	50 (65.8)
Age of wheat introduction	Early	14 (18.4)
	Standard	38 (50.0)
	Delayed	24 (31.6)
First wheat-containing food	Chapatti	28 (36.8)
	Bread	22 (28.9)
	Biscuits	16 (21.1)
	Others	10 (13.2)
Frequency of wheat consumption	Daily	18 (23.7)
	Weekly	58 (76.3)

Out of the total 76 participants, 23.7% were diagnosed as positive for celiac disease, while the majority (76.3%) were found to be negative, indicating that most children in the study did not have celiac disease, as given in Table 5.

Table 5: Laboratory Findings and Celiac Disease Status (n = 76)

Variable	Frequency (%)
Celiac disease status	
Positive	18 (23.7)
Negative	58 (76.3)

A statistically significant association was observed between the age of wheat introduction and the occurrence of celiac disease ($p = 0.005$). Among children with early wheat introduction (<4 months), a higher proportion were diagnosed with celiac disease (57.1%) compared to those without the disease (42.9%). In contrast, children with standard (4–6 months) and delayed (>6 months) wheat introduction had considerably lower frequencies of celiac disease, with only 15.8% and 16.7% testing positive, respectively, while the majority in these groups remained negative (84.2% and 83.3%). Overall, these findings indicate that early introduction of wheat is associated with a higher likelihood of developing celiac disease, as given in Table 6.

Table 6: Association of Celiac Disease with Age of Wheat Introduction (n = 76)

Age of Wheat Introduction	Negative n (%)	Positive n (%)	Total n (%)	p-value
Early (<4 months)	6 (42.9)	8 (57.1)	14 (100.0)	**0.005**
Standard (4–6 months)	32 (84.2)	6 (15.8)	38 (100.0)	
Delayed (>6 months)	20 (83.3)	4 (16.7)	24 (100.0)	
Total	58 (76.3)	18 (23.7)	76 (100.0)	

Multivariate logistic regression analysis demonstrated that early wheat introduction (<4 months) was a significant independent predictor of celiac disease, with children having 4.21 times higher odds of developing the disease (AOR = 4.21, 95% CI: 1.52–11.68, p = 0.006). Similarly, breastfeeding for less than 6 months was also significantly associated with increased risk, showing 3.18 times higher odds of celiac disease (AOR = 3.18, 95% CI: 1.12–9.04, p = 0.030). Although daily wheat consumption showed an increased risk (AOR = 2.75), it did not reach statistical significance (p = 0.054). Age of the child was not significantly associated with celiac disease (AOR = 1.02, 95% CI: 0.98–1.06, p = 0.210), as given in Table 7.

Table 7: Multivariate Analysis of Factors Associated with Celiac Disease (n = 76)

Variable	Adjusted Odds Ratio (AOR)	95% CI	p-value
Early wheat introduction (<4 months)	4.21	1.52–11.68	0.006
Breastfeeding <6 months	3.18	1.12–9.04	0.030
Daily wheat consumption	2.75	0.98–7.69	0.054
Age (months)	1.02	0.98–1.06	0.210

DISCUSSION

The timing of gluten introduction during infancy has been proposed as an important environmental factor influencing disease development. Early or inappropriate introduction of wheat-based foods may alter gut immunity and increase susceptibility to celiac disease. Breastfeeding practices and duration may also play a protective role by modulating immune responses and gut maturation. Therefore, understanding the relationship between infant feeding patterns and the risk of celiac disease is crucial for developing preventive strategies.

In the present study, celiac disease was identified in 23.7% of children, and a significant association was observed between early wheat introduction (<4 months) and disease occurrence, with 57.1% positivity in this group compared to 15.8% and 16.7% in the standard (4–6 months) and delayed (>6 months) groups (p = 0.005). Multivariate analysis further confirmed early wheat introduction as an independent predictor (AOR = 4.21; 95% CI: 1.52–11.68; p = 0.006), along with breastfeeding duration <6 months (AOR = 3.18; 95% CI: 1.12–9.04; p = 0.030), while daily wheat consumption showed a borderline association (AOR = 2.75; p = 0.054).

In contrast, Logan et al. (2020) in the EAT trial (n = 1004) reported that early gluten introduction at 4 months was associated with a reduced prevalence of celiac disease, indicating a protective effect when introduced at a controlled time and dose.[13] Similarly, Lebwohl et al. (2015) found no significant association between timing of gluten introduction and disease incidence (HR = 1.23; 95% CI: 0.79–1.91),[14] and Silano et al. (2016) also concluded that neither breastfeeding duration nor timing significantly influenced disease prevention.[15]

Regarding clinical characteristics, the findings of Javed et al. (2019) reported markedly higher frequencies of symptoms among celiac patients, including anemia (90.4%), failure to thrive (90.7%), chronic diarrhea (60.37%), vomiting (40.4%), and abdominal pain (35.9%), compared to lower proportions in the present study such as chronic diarrhea (36.8%), vomiting (28.9%), abdominal pain (32.9%), iron deficiency anemia (23.7%), and failure to thrive (21.1%). Family history was comparable, reported as 9% by Javed et al. versus 10.5% in the current study.[18]

Jamila et al. (2018) reported a celiac disease prevalence of 11.7% based on tissue transglutaminase IgA, with higher prevalence (53.0%) in individuals ≤15 years, which is lower than the 23.7% prevalence observed in the present study.[17] Nutritional and growth impairments were also highlighted by Ekşi et al. (2025), who demonstrated significantly lower BMI and nutrient intake in celiac patients (p < 0.05), while Fraz et al. (2026) showed that gluten-free dietary intervention significantly improved hemoglobin, ferritin, and inflammatory markers (p < 0.001).[20,21] Imran et al. (2016) reported excessive wheat (gluten) consumption across age groups,[16] while Iqra et al. (2023) emphasized the immunological mechanisms and inflammatory responses associated with gluten exposure, supporting the biological basis of disease development observed in the present study.[19] Overall, variations across studies may reflect differences in population characteristics, dietary patterns, and study designs, while maintaining consistent evidence of gluten exposure as a key factor in celiac disease.

Study Limitations:

This study was limited by a relatively small sample size, which may affect the generalizability of the findings. Being a cross-sectional design, causal relationships could not be firmly established. Additionally, recall bias regarding infant feeding practices may have influenced the accuracy of reported data.

CONCLUSION

Early introduction of wheat and shorter duration of breastfeeding were significantly associated with increased risk of celiac disease. Standard or delayed introduction of wheat appeared to be relatively protective. These findings highlight the importance of appropriate infant feeding practices in reducing the risk of celiac disease.

Acknowledgement: We sincerely acknowledge the support and guidance of our mentors, colleagues, and the staff of the participating hospital for their valuable assistance throughout this study.

Conflict of Interest: No

Funding Disclosure: None

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