Original Article

# DIETARY PATTERNS IN INFANCY MODIFY THE RISK OF CELIAC DISEASE

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**ABSTRACT:**

**OBJECTIVES**

To determine the association of various feeding and weaning patterns in infancy with celiac disease.

**METHODS:**

This was a case control study conducted at the department of Pediatrics, Madina Teaching Hospital, University Medical & Dental College, Faisalabad during 6 months period starting from January to June 2013. Data was collected from cases and controls meeting the inclusion criteria during period of six months. Relevant information was recorded on the predesigned questionnaire and analyzed by SPSS 19. P value <0.05 was considered significant. Odds ratio was calculated to find the association of breastfeeding and weaning with celiac disease.

**RESULTS:**

Duration of breastfeeding, age of weaning and amount of wheat introduction had statistically significant difference between cases and controls. (p. <0.001) the odds ratio for weaning earlier than 6 months was (OR 5.05, 95% CI, 2.23-11.43, p< 0.001)**.** The odds of having celiac disease was more if wheat started in diet earlier than 6 months of age (OR 13.7, 95% CI: 3.79-50.20, p=0.0001), delaying the wheat introduction between 6-12 months resulted in OR 10.54( 95% CI 3.63-30 p <0.0001). Duration of breastfeeding was significantly associated with anemia (p 0.016) Timing of gluten introduction was not associated significantly with the clinical spectrum of diseases.

**CONCLUSION:**

Clinical spectrum and incidence of celiac disease is affected by various feeding and weaning patterns in infancy. We need more studies to generate our own data regarding the association of our cultural foods with celiac disease. It will help us to build up our dietary and weaning recommendations during infancy.

**KEY WORDS**: dietary patterns, weaning, celiac disease, breastfeeding

## INTRODUCTION:

Celiac disease is an immune-mediated disorder; characterized by chronic inflammation of the small intestine leading to malabsorption and it is precipitated by the ingestion of gluten in genetically susceptible persons.[1]The incidence of celiac disease is increasing all over the world. The disease is being rapidly recognized throughout the world including Middle East, Asia, South America and North Africa.[2,3,4,5,6] Celiac disease is multifactorial in origin. Genetic, immunological and environmental factors contribute towards its complex pathogenesis.

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The triggering agent is gluten peptides that initiate the immune response resulting in activation of CD 4 and CD 8 lymphocytes.[7]The genetic predisposition has been identified in the major histocompatibility complex region on chromosome 6p21 with 90% of CD patients expressing HLA DQ2 and remaining DQ 8.[8]

Environmental factors in the form of exposure to various weaning diets, lack of breastfeeding, and timing of introduction of gluten in diet may contribute towards altering the immunological processes and subsequent development of celiac disease. Various studies in the past have been conducted to evaluate the etiological role of various patterns of infant feeding in celiac disease.[9,10,11] A larger consumption of wheat gluten in healthy infants was reported to be associated with higher occurrence of celiac disease in Sweden and Italy than in infants in Finland, Denmark, and Estonia.[12,13] Protective role of breastfeeding against development of celiac disease has also been documented previously showing a negative association of breastfeeding with celiac disease.[14,15] Talking about the clinical presentation, prolonged breastfeeding may influence the incidence of symptomatic disease but the role of timing of gluten introduction is still unclear.[1]

The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee recommended avoidance of both early (< 4 mo) and late (> 7 mo) introduction of gluten and introduction of small amounts of gluten gradually while the child is still being breastfed.[16] AAP Committee on Nutrition supports the introduction of complementary food between 4 and 6 months of age, while the AAP section on breastfeeding recommended exclusive breastfeeding until 6 months of age.[17,18] Hence, there is a difference in recommendation of different organizations depending upon their own data and experience. Furthermore the timing of introduction of solid foods and cereal grains may be associated with risk of food allergy including wheat allergy.[19]

Celiac disease is being recognized increasingly now in Southeast Asian countries where it was once considered a rare entity.[20,21] This changing epidemiology of the disease could be due to with increased use of cereal gains and variable weaning and feeding practices. To our knowledge very few studies have been conducted in Asian countries to evaluate the association of feeding and weaning patterns as risk factors of this overwhelming problem. In our setup various feeding and weaning patterns are observed, varying from exclusive breastfeeding, partial breastfeeding and top feeding at earlier age. Rusk and wheat bread and biscuits are usually the first to be introduced in lower socioeconomic status. Few children keep on taking milk and delaying the weaning beyond one year of age. These varying patterns of infant feeding not only influence the incidence of the celiac disease but also affect the clinical spectrum of disease and timing of disease presentation. In view of these varying observations, we conducted the study in our setup to find the association of feeding and weaning pattern with celiac disease and their effect on clinical spectrum of the disease.

## PATIENTS AND METHODS:

This was a case control study conducted at the department of Pediatrics, Madina Teaching Hospital, University Medical & Dental College, Faisalabad, during 6 months period starting from January to June 2013. Data was collected from fifty patients having celiac disease and sixty three referents not having celiac disease. Convenience sampling was done. All the patients diagnosed to have celiac disease (on the basis of clinical presentation, Tissue transglutaminase antibodies and/or histopathologically proven) and attending the pediatric department during the period of six months were included in the study. Controls were selected from patients coming to outpatient department or inpatient with illnesses other than celiac disease. Relevant information regarding breastfeeding, its duration, exclusive or partial, age of weaning, weaning diets and gluten introduction in diet, was recorded on the predesigned questionnaire. Data was analyzed by SPSS 19. Chi square test was applied to compare cases and controls in terms of their feeding and weaning patterns. P value <0.05 was considered significant.

Odds ratio was calculated to find the association of breastfeeding and weaning with celiac disease. Clinical spectrum of the disease was also compared among different feeding and weaning groups.

## RESULTS:

In our study, we included 50 cases of celiac disease and 63 age and sex matched controls. Their feeding patterns including breastfeeding, its duration, weaning age, and of gluten introduction in diet were compared (table I). Presence and lack of breastfeeding was not significantly different in both of the groups. (p 0.842) while duration of breastfeeding, age of weaning and amount of wheat introduction had statistically significant difference between cases and controls. (p. <0.001)

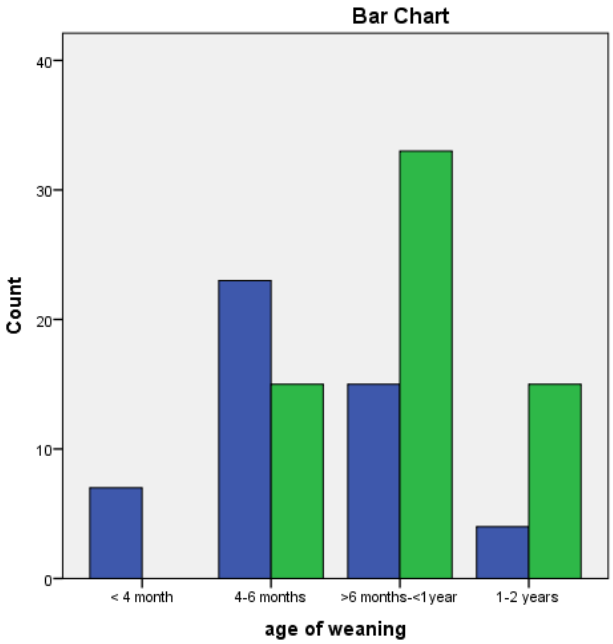
Odds ratio was calculated for duration of breastfeeding, considering quitting the breastfeeding below one year of age as risk factor. (OR 7.34, 95% CI 3.08-17.51,p <0.0001). The odds ratio for weaning earlier than 6 months was (OR 5.05, 95% CI, 2.23-11.43, p< 0.001). The risk of wheat introduction was more if wheat started in diet earlier than 6 months of age (OR 13.7, 95% CI: 3.79-50.20, p=0.0001), delaying the wheat introduction between 6-12 months resulted in OR 10.54(95% CI 3.63-30 p <0.0001).

Association of various feeding patterns with clinical presentation of celiac disease was also evaluated. In celiac disease patients, duration of breastfeeding was significantly associated with anemia (p 0.016) as more of the anemic patients among celiac disease group had breastfeeding of shorter duration. Short stature and rickets were significantly associated with age of weaning in celiac disease patients but chronic diarrhea, abdominal pain, distension and anemia were not. (table II). Timing of gluten introduction in weaning diet did not seem to be significantly affecting the clinical spectrum of diseases. (Table III).

**TABLE I: FEEDING AND DIETARY PATTERNS IN INFANCY IN CASES AND CONTROLS**

| FEEDING/DIETARY PATTERN | CASES | CONTROLS | P VALUE |
|---|---|---|---|
| Breastfeeding<br>Exclusive<br>Partial<br>No | <br>24<br>22<br>4 | <br>28<br>31<br>4 | 0.842 |
| Duration of breastfeeding<br>< 6 months<br>6-12 months<br><br>>1 to 2 years | <br>16<br>16<br>14 | <br>1<br>13<br>45 | < 0.001 |
| Age of weaning<br><4 months<br>4- 6 months<br>>6 months to 1 year<br>>1 year | <br>7<br>23<br>15<br>5 | <br>0<br>15<br>33<br>15 | <0.001 |
| Dietary wheat introduction<br><6 months<br>6- 12 months<br>>12 months | <br>20<br>23<br>7 | <br>16<br>3<br>44 | <0.001 |

**FIGURE I: COMPARISON OF AGE OF WEANING**




**AMONG CASES AND CONTROLS**

**TABLE II: CLINICAL SPECTRUM OF CELIAC DISEASE AMONG VARIOUS WEANING AGE GROUPS**

| CLINICAL FEATURES | WEANING AGE GROUPS | | | | P value |
|---|---|---|---|---|---|
| | < 4months | 4-6months | >6- <12 months | > 1- 2 years | |
| Chronic diarrhea | | | | | |
| Yes | 5 | 14 | 13 | 1 | 0.202 |
| No | 2 | 9 | 3 | 3 | |
| Abdominal distension | | | | | |
| Yes | 4 | 15 | 9 | 1 | 0.496 |
| No | 3 | 8 | 7 | 3 | |
| Short stature | | | | | |
| Yes | 7 | 19 | 13 | 0 | <0.0001 |
| No | 0 | 4 | 3 | 4 | |
| Rickets | | | | | |
| Yes | 7 | 19 | 11 | 1 | 0.002 |
| No | 0 | 4 | 4 | 4 | |
| Anemia | | | | | |
| Yes | 6 | 20 | 11 | 3 | 0.328 |
| No | 1 | 3 | 4 | 2 | |

**TABLE III: CLINICAL SPECTRUM OF CELIAC DISEASE ACCORDING TO TIMING OF WHEAT INTRODUCTION**

| CLINICAL FEATURES | DIEATARY GLUTEN INTRODUCTION | | | P VALUE |
|---|---|---|---|---|
| | < 6 months | >6 months-12 months | > 1year | |
| Chronic diarrhea | | | | |
| Yes | 13 | 17 | 2 | 0.177 |
| No | 7 | 16 | 4 | |
| Abdominal distension | | | | |
| Yes | 14 | 13 | 2 | 0.068 |
| No | 6 | 10 | 5 | |
| Short stature | | | | |
| Yes | 18 | 18 | 3 | 0.101 |
| No | 2 | 5 | 4 | |
| Rickets | | | | |
| Yes | 18 | 15 | 4 | 0.146 |
| No | 2 | 18 | 3 | |
| Anemia | | | | |
| Yes | 19 | 15 | 5 | 0.052 |
| No | 2 | 8 | 2 | |

## DISCUSSION:

Celiac disease is a chronic enteropathy with a wide range of clinical manifestations. Various environmental and dietary factors including feeding and weaning age and diets may influence the risk of developing celiac disease and also affect the clinical spectrum of the disease including the age of onset of symptoms. In our study feeding patterns found to be different among cases and referents. Exclusive or partial breastfeeding among cases and controls was not statistically significant rather prolonged duration of breastfeeding had a more protective effect on celiac disease. Among controls majority were being breastfed for more than one year. Previously various studies have documented that protective effect of breastfeeding was more marked if it continued beyond the time when weaning diets were being introduced.[22] Breastfeeding may help by immune modulating factors resulting in maturation of gut flora, decreased chances of infections.[23,24] Whether prolonged breastfeeding modifies the risk of developing the disease or delays the onset of symptoms is still debatable.[16]

In our study, age of weaning was also significantly different in both the groups. Majority of the cases were being started weaning between 4-6 months of age. The concept of gluten tolerance window period was suggested by ESPGHAN (European Society of Gastroenterology, Hepatology and Nutrition) that recommended the slow introduction of gluten between 4 to 7 months of age while the child is still being breastfed in order to reduce the risk of celiac disease, type I diabetes mellitus and wheat allergy.[16] Gluten introduction below 4 months and after 6 months of age is associated with increased risk of developing autoimmunity. This concept was contradicted by the German study where genetically at risk children showed no association of increased risk of autoimmunity with various feeding and weaning patterns including formula milk, early gluten introduction.[25]similarly in our study most of the controls were exposed to wheat after one year of age. The hazard ratio of wheat introduction was reduced from (13.7, 95% CI: 3.79-50.20, p=0.0001) to HR 10.54(95% CI 3.63-30 p <0.0001) by delaying the wheat introduction in diet from < 6 months of age to > 6 months of age. We could not evaluate the association of amount of gluten ingested during weaning period with

celiac disease as most of the mothers could not appreciate the amount of gluten contain product intake by their children. This area needs to be explored further as a study conducted on the Swedish epidemic suggested that amount of gluten introduced during weaning might affect the symptoms of the disease but not the risk of developing silent disease.[25]

We also observed the effect of weaning age on disease presentation as well, as most of the patients weaned earlier than 6 months presented with short stature and rickets. Chronic diarrhea, anemia and distension had no significant difference among various weaning age groups in celiac disease patients. A study in US has shown that breastfed infants have a lesser chance of presentation with failure to thrive (69% vs. 88%, $p<0.05$) and short stature (37% vs. 62%, $p<0.05$), and had a higher rate of "atypical" symptoms ($p<0.01$).[26] Age of weaning might affect the clinical presentation as well as risk of occurrence of celiac disease, as it has been shown by previous studies that there is a difference in gut microflora of celiac disease patients and healthy controls. Weaning age and weaning diets in early infancy may affect the development of gut microflora in children.[27,28]

As celiac disease is multifactorial in origin clinical spectrum of the disease is dependent upon interplay of all these factors including feeding and dietary patterns in early infancy. Above all, genetic predisposition is very important. Atypical presentations of celiac disease or delayed presentation can be explained on the basis of theses varying dietary factors. The limitation of our study was its retrospective nature. This issue can be explored more closely by longitudinal studies with close follow up of the patients. Furthermore we could not eliminate the genetic predisposition as a risk factor among our cases and control groups. These various feeding and weaning practices may be affecting the individuals who are genetically predisposed in a different way than genetically normal population.

## CONCLUSION:

Clinical spectrum and incidence of celiac disease is affected by various feeding and weaning patterns in infancy. As Celiac disease is being recognized rapidly in our population both in its typical and atypical presenting forms, more studies are required to produce our own data to determine the effect of the dietary patterns in infancy which are common in our society, like breastfeeding, its duration, timing of weaning diet introduction and gluten introduction over celiac disease. This data will be helpful for us to build up our dietary and weaning recommendations during infancy taking into account our traditional and cultural diets and risk of food allergies.

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