Vol.67: e24230928, 2024
https://doi.org/10.1590/1678-4324-2024230928
ISSN 1678-4324 Online Edition

BABT
Brazilian Archives of Biology and Technology

Review - Human and Animal Health

Food Introduction and Its Implications on the Development of Celiac Disease in Childhood

Giovanna Tardem Oliveira[1]
https://orcid.org/0009-0005-5154-5224

Jéssica Brandão Reolon[1]
https://orcid.org/0000-0001-7388-8256

Odonis Rocha Júnior[2]
https://orcid.org/0000-0002-6754-2141

Juliana Sartori Bonini[2]
https://orcid.org/0000-0001-5144-2253

Luana Mota Ferreira[3]
https://orcid.org/0000-0001-9951-587X

Marcel Henrique Marcondes Sari[2*]
https://orcid.org/0000-0002-9913-9306

[1]Universidade Estadual do Centro-Oeste, Departamento de Medicina, Guarapuava, Paraná, Brasil; [2]Universidade Estadual do Centro-Oeste, Departamento de Farmácia, Guarapuava, Paraná, Brasil; [3]Universidade Federal do Paraná (UFPR), Departamento de Farmácia, Curitiba, Paraná, Brasil.

Editor-in-Chief: Paulo Vitor Farago
Associate Editor: Paulo Vitor Farago

Received: 04-Sep-2023; Accepted: 25-Jan-2024

*Correspondence: marcesarih@hotmail.com; Tel.: +55-55-98416-9884 (M.H.M.S.).

HIGHLIGHTS

- Early gluten exposure does not impact the celiac disease development in children.
- There is an indirect link between breastfeeding, gluten exposure and celiac disease.
- Gastrointestinal infections have an effect on the disease.
- The protective effect of late gluten introduction is still a hypothesis.

Abstract: This study investigated the relationship between food introduction and celiac disease development. This bibliographic review was conducted from May to June 2023 and covered publications from 2013 to 2023. The Virtual Health Library (VHL) and PubMed databases were used, with the following search terms: “Celiac Disease,” “Gluten enteropathy” (with the Boolean operator “OR”), “Infant,” “Preschooler” (also using the Boolean operator “OR”) and “Food Introduction.” A total of 28 articles were found and, after careful analysis, only 6 met the inclusion and exclusion criteria. These articles addressed topics such as the relationship between dietary patterns and the risk of celiac disease, the prevalence of the disease in children born before and after the epidemic in Sweden, the feasibility of introducing allergens and their relationship with breastfeeding, and the implications of introducing gluten into the diet and early weaning in celiac disease. The results of the study highlight the importance of further research into this topic to develop possible methods of prevention and intervention in the manifestation process of celiac disease. From the bibliographic review, it was possible to identify the variables that imply the development of celiac disease and refute the hypotheses of the direct influence of the early introduction of gluten in the diet on the manifestation of the disease.

Keywords: gluten enteropathy; malabsorption syndrome; gastrointestinal disease; infant; preschool.

INTRODUCTION

Introducing food to a baby is a significant step in their development. It marks the beginning of their transition from solely consuming breast milk or formula to gradually incorporating solid foods. The World Health Organization (WHO) recommends introducing solid foods around the age of 6 months, according to their guidelines published in 2023 [1]. However, the ideal age for this transition is not the only important factor to consider. Exposing the child to a variety of flavors, textures, and nutrients during this process promotes a healthy acceptance of new foods [2]. Moreover, the early and gradual introduction of allergenic foods into the baby's diet has been studied extensively as a way to prevent allergies [3] and other immunological reactions, such as those experienced by celiac patients.

Celiac disease is a chronic autoimmune disorder that affects the mucosa of the small intestine. This condition is triggered by the consumption of gluten, a type of protein found in wheat, barley, and rye grains. Only individuals with a genetic predisposition are affected by this condition [4]. The key genetic determinants are the HLA II genes DQA and DQB, which are highly variable and located in the major histocompatibility complex on chromosome 6.

This genetic disorder is considered to be the most common, with a prevalence of 0.5% to 1% in many populations [5]. Its diagnosis can be complicated due to the variety of symptoms that patients may experience. These symptoms are not only associated with gastrointestinal issues, such as chronic diarrhea, constipation, abdominal pain, and malabsorption of nutrients, but can also occur outside of the intestine, such as headaches, fatigue, osteoporosis, growth retardation, infertility, and even depression [6]. To manage symptoms and potential complications, the only effective approach post-diagnosis is complete avoidance of gluten in the patient's diet [7]. Additionally, as exposure to gluten can trigger the disease in those genetically predisposed, there are ongoing studies looking at the role of food introduction in this process.

In light of these factors, the purpose of this review is to examine research on the introduction of food and its guidance in relation to the development of celiac disease in infants.

MATERIAL AND METHODS

This study is categorized as a narrative literature review, which involves a process of selecting, synthesizing, summarizing, and interpreting the literature that has been published across various platforms, such as electronic journals and books. It is important to note that this process may be subject to the author's subjectivity. This type of study aids in consolidating a particular area of knowledge and provides fresh perspectives on the subject, both theoretically and contextually [8].

Between May and June 2023, data was collected from the Virtual Health Library (BVS) and PubMed databases. The search terms used were "Celiac Disease" and "Gluten Enteropathy" using the "OR" operator, as well as "Infant" and "Preschool" also using the "OR" operator, and "Food Introduction". Inclusion criteria included articles published in English from 2013 to 2023, of the types of clinical trials, randomized controlled, and cohort studies. Literature reviews were excluded.

After selecting articles that met the criteria, the stages of exploratory and selective reading were followed, with an emphasis on materials that fit the objectives of the study. Analysis of selected texts involved interpretive reading and writing.

For individual publication analysis, a script was developed that considered the authors, year of publication, objective, design, methods, results and conclusions.

RESULTS

After conducting searches, 28 articles were found. The inclusion and exclusion criteria were applied, resulting in the selection of 6 articles for data analysis (Figure 1). The selected articles include prospective cohort studies, randomized clinical trials, observational cohort studies, cross-sectional screening, and population-based randomized controlled trials covering different topics related to food introduction instructions and the development of celiac disease. One of the articles evaluates the effect of gluten consumption on celiac disease development in children aged 11 to 36 months. Two articles investigate the effect of early gluten introduction on the disease's development, with one analyzing the relationship between childhood dietary patterns and celiac disease risk. One article looks at the prevalence of celiac disease in children born at different times in Sweden and the relationship with infant feeding. Another article examines the feasibility of introducing allergenic foods to breastfed children compared to those who received exclusive breastfeeding for up to 6 months. Finally, one article studied the relationship between infant feeding, hospitalization, HLA allele, rotavirus vaccination status, and celiac disease autoimmunity, as shown in Chart 1.

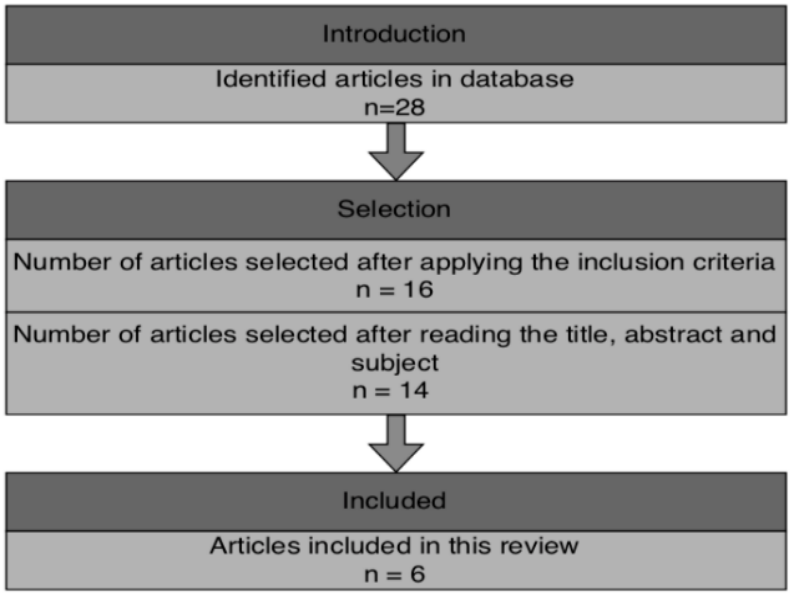

Figure 1. Flowchart of the steps taken to select articles.

Chart 1. Articles that were identified in the Virtual Health Library (VHL) and Pubmed databases, according to their authors, year of publication, objective, design, method, results and conclusions.

Author/Publication year - Crespo-Escobar et al. (2017) [9] **Objectives -** The aim is to test whether consuming high doses of gluten during childhood increases the likelihood of developing celiac disease. The data used for this evaluation comes from the PreventCD trial study. **Design and methods -** A study involving 715 children from 5 European countries with celiac-related genes examined their gluten intake from 11 to 36 months. Infants were given 100 mg gluten/day or a placebo from 4 to 6 months, gradually increasing until 10 months, then unrestricted. The aim was to assess the impact of post-10-month gluten consumption **Results -** At 10 months, children from different countries showed significant variations in gluten consumption ($P < 0.001$). However, within the same country, there was no difference in gluten intake between those who developed celiac disease and those who didn't ($P > 0.05$). Factors like country, gender, intervention group, and gluten consumption pattern didn't influence celiac disease risk. Interaction between HLA risk group and gluten pattern was mostly insignificant, except for DQ2.2/DQ7 haplotype which had higher risk (HR: 5.81; 95% CI: 1.18, 28.74; $P = 0.031$). **Conclusion -** Most children with genetic risk from various European countries do not develop Celiac Disease due to gluten consumption patterns and the amount of gluten consumed between 11-36 months of age, regardless of their HLA genotypes.
Author/Publication year - Ivarsson et al., (2013) [10] **Objectives -** To investigate and compare the total prevalence of celiac disease in two 12-year birth cohorts and relate the results to infant feeding observed in each cohort. **Design and methods -** The ETICS screening study occurred in two phases with 13,279 children from distinct birth cohorts: 1993 epidemic-born and 1997-born. Previously reported and confirmed cases were taken into account. Blood samples were collected and tested for serological markers, with positive results leading to referrals for small bowel biopsies. Adolescent feeding practices were examined for both cohorts. Prevalence comparisons were presented as prevalence ratios. **Results -** Out of every 1000 people, 29 in 1993 and 22 in 1997 had celiac disease. Those born in 1997 had a lower risk of having celiac disease than those born in 1993 (prevalence ratio: 0.75; 95% confidence interval: 0.60-0.93; $P = 0.01$). The cohorts had different infant feeding practices, particularly in the amount of dietary gluten introduced to infants during ongoing breastfeeding. **Conclusion -** The decreased prevalence of celiac disease among 12-year-olds suggests a potential strategy for preventing the disease. Medical research supports the gradual introduction of gluten-containing foods starting at 4 months of age, ideally while continuing to breastfeed.

Author/Publication year - Vriezinga et al., (2014) [11]

Objectives - To investigate the hypothesis that the introduction of gluten in the diet of children aged 4 to 6 months would reduce the risk of celiac disease.

Design and methods - A randomized, double-blind, placebo-controlled dietary intervention study involved 944 HLA-DQ2 or HLA-DQ8 positive children with a celiac-related first-degree relative. In the study, 475 participants received 100 mg of active gluten daily from 16 to 24 weeks of age, while 469 received a placebo. They measured anti-transglutaminase type 2 and antigliadin effects. The study's objective was to ascertain the occurrence of biopsy-confirmed celiac disease by age 3.

Results - The analysis focused on 80 children, median age 2.8 years, with 59% girls. Among them, 77 were biopsy-confirmed for celiac disease, and 3 were diagnosed based on 2012 diagnostic criteria to avoid underestimation. Celiac disease incidence at age 3 was 5.2%, similar in gluten and placebo groups. Rates of antibodies were alike in both groups. Celiac development wasn't notably affected by breastfeeding (exclusive or continued during gluten introduction) or the intervention's impact.

Conclusion – A study conducted on high-risk children showed that introducing gluten to them between 16 to 24 weeks of age did not increase the risk of developing Celiac Disease by the age of 3.

Author/Publication year - Perkin et al., (2016) [12]

Objectives - To determine the feasibility of early introduction of multiallergenic foods for exclusively breastfed infants from 3 months of age and the effect on breastfeeding performance.

Design and methods - A randomized controlled trial was conducted on a population basis. The group that followed the early introduction guidelines (EIG) maintained breastfeeding while gradually introducing six allergenic foods: cow's milk, peanuts, boiled egg, egg yolk, sesame, white fish (cod), and wheat. The standard introduction group, on the other hand, adhered to British infant feeding recommendations by exclusively breastfeeding for approximately six months and not introducing any foods before the age of six months.

Results - A total of 1303 infants were included in the study. The early introduction group (EIG) consumed each of the 6 foods 2 to 3 times per week at 5 months of age, while the standard introduction group did not consume any of them ($P < 0.001$ for all comparisons). By 6 months of age, less than 5% of EIG infants had not been introduced to allergenic foods. However, achieving the strict intake target established by the protocol was challenging for 42% of EIG participants. Both groups had higher breastfeeding rates than what is typically seen among matched mothers in the UK government data ($P < 0.001$ at 6 and 9 months of age).

Conclusion - Introducing certain types of allergenic foods before a baby is 6 months old appears to be possible without impacting breastfeeding. This has significant implications for developing strategies to prevent food allergies.

Author/Publication year - Lionetti et al., (2014) [13]

Objectives - To investigate the relationship between the risk of developing celiac disease, the age at which gluten is introduced into a child's diet, and the child's early eating pattern.

Design and methods - The study involved 832 newborns with a first-degree relative having celiac disease. Randomly divided into two groups, Group A introduced gluten at 6 months, while Group B did so at 12 months. HLA genotype was determined at 15 months, and celiac disease was screened at various intervals up to 10 years, including intestinal biopsies for positive cases. The study's goal was to establish celiac autoimmunity and overt celiac disease prevalence among 5-year-old children.

Results - Among the 707 participants remaining in the study for 36 months, 553 with standard or high-risk HLA genotypes completed it. At age 2, a higher percentage of children in group A had celiac autoimmunity and overt celiac disease compared to group B, with significant differences (16% vs. 7%, P=0.002) for autoimmunity and (12% vs. 5%, P=0.01) for overt disease. However, by age 5, the differences between the groups became insignificant for both autoimmunity (21% in group A and 20% in group B, P=0.59) and overt disease (16% and 16%, P=0.78). At age 10, children with high-risk HLA faced a notably higher risk of celiac autoimmunity (38% vs. 19%, P=0.001) and overt celiac disease (26% vs. 16%, P=0.05) compared to standard-risk HLA. Other factors like breastfeeding didn't show associations with celiac disease development.

Conclusion - Delaying the introduction of gluten and breastfeeding did not affect the likelihood of developing celiac disease in at-risk individuals, but it was linked to a later onset of the disease. The presence of a high-risk HLA genotype was a significant indicator of the disease.

Author/Publication year - Kemppainen et al., (2017) [14]

Objectives - To investigate temporal associations between caregiving and the development of celiac disease autoimmunity, and to examine the effects of HLA alleles, rotavirus vaccination status, and infant feeding.

Design and methods - A study monitored 6,327 at-risk children aged 1 to 4 in the US and Europe for HLA celiac disease. They were tested for tissue transglutaminase until March 31, 2015. Parents reported on their child's health every three months since birth. The study analyzed factors like complications, rotavirus vaccination, gluten introduction timing, breastfeeding, and celiac disease autoimmunity risk using proportional hazards models.

Results - During the study, 13,881 gastrointestinal infections (GIE) and 79,816 respiratory infections were identified. Among 6,327 children, 11.6% (732) developed celiac disease autoimmunity. GIE increased the celiac disease autoimmunity risk by 33% over 3 months (hazard ratio [RR], 1.33; 95% confidence interval [CI], 1.11–1.59). Winter-born children introduced to gluten before 6 months faced a 2-fold risk (RR, 2.08; 95% CI, 1.46–2.98), while those without HLA-DQ2 alleles breastfed less than 4 months had a 10-fold risk (RR, 9.76; 95% CI, 3.87–24.8). However, rotavirus-vaccinated children introduced to gluten before 6 months showed a reduced risk (RR, 0.57; 95% CI, 0.36–0.88).

Conclusion - Children genetically prone to celiac disease face elevated celiac autoimmunity risk with gastrointestinal infections. Multiple factors like HLA genotype, childhood gluten intake, breastfeeding, and rotavirus vaccination influence this risk. This underscores the intricate interplay of infections, genetics, diet, and celiac disease causes in childhood

DISCUSSION

Celiac disease is a complex condition influenced by genetic, environmental, and immunological factors. Environmental triggers such as exposure to gluten, the age at which it's introduced, breastfeeding, intestinal microbiota, and gastrointestinal complications, particularly viral infections, can all contribute to its development. The age at which infants are introduced to gluten in their diet is becoming increasingly important to study as it may impact the development of the autoimmune condition in predisposed patients. We can better guide prevention and intervention strategies for at-risk infants and children by identifying an ideal age for gluten introduction and ingested amount. This need for research has arisen due to estimates that approximately 30% of the world's population carries human leukocyte antigen genes, mainly HLA-DQ2, yet only 1% of the population develops celiac disease. Environmental factors are believed to play a significant role in this difference [9].

Between 1984 and 1996, Sweden experienced a high rate of celiac disease. As a result, the country revised its recommendations for introducing gluten into infants' diets. In 1984, the consumption of gluten began at 6 months of age and almost doubled in quantity. However, in 1996, the protocol changed, and gluten was introduced for 4 months alongside breastfeeding. A study was carried out on children born during these two periods, and it was observed that children born in 1997 had lower rates of celiac disease than those born in 1993. This led to the conclusion that the early introduction of gluten and breastfeeding prevented the development of the disease in children up to 12 years old. This evidence was widely accepted and supported by several authors. [10]. However, the studies that supported this theory were later disproven due to unreliable data. This was due to the limitations of the continuous variables used and the lack of information regarding the amount of gluten consumed by different age groups [9].

There has been a long-standing belief that the early introduction of gluten in a child's diet is linked to celiac disease. However, a recent study of 715 children at high risk for celiac disease from 5 European countries (Germany, Hungary, Italy, Spain, and Holland) found no direct correlation between the amount of gluten consumed during the first months of life and the development of the disease. The study analyzed gluten intake between 11 and 36 months of age and the pattern of daily gluten intake (MDGI) in relation to the development of celiac disease up to the age of 6. Surprisingly, the countries with the highest MDGI rates did not have the highest number of celiac cases, nor did the countries with the lowest gluten consumption have the lowest number of cases. For example, Spain had the lowest daily gluten consumption for children up to two years yet did not have the lowest number of cases in the same age group. In contrast, Hungary had the highest consumption but a lower number of cases than Spain [9].

A similar discovery was made in another study involving 944 children who tested positive for HLA-DQ2 or HLA-DQ8 and had at least one first-degree relative with celiac disease. The children were divided into two

groups, one receiving a placebo and the other receiving 100mg of immunologically active gluten per day from the 4th to 6th month of life. The study analyzed the diagnosis of celiac disease in these children when they reached 3 years old, and the results showed that gluten intervention did not affect the frequency of disease development. The study also evaluated the idea that breastfeeding could protect against the development of celiac disease. It concluded that there was no correlation between the duration of breastfeeding and the onset of the condition, regardless of whether it was exclusive or not [11]. Additionally, the EAT study [12] refuted the belief held by some mothers that offering allergenic foods to infants would harm the reception of breast milk and lead to a shorter duration of breastfeeding.

According to studies conducted by Crespo-Escobar and coauthors (2017) [9] and Vriezinga and coauthors (2014) [11], there is no direct link between early gluten exposure and the development of celiac disease. However, they have discovered interesting facts that reveal a specific genotype's susceptibility to the condition. Those who are positive for HLA DQ2.2/DQ7 are at a higher risk of developing celiac disease when exposed to high levels of gluten. This genotype is more susceptible to external factors, as per Crespo-Escobar and coauthors (2017) [9]. Vriezinga and coauthors (2014) [11] have also identified that the influence of early introduction of gluten in the development of celiac disease in girls was related to a higher prevalence of homozygous HLA-DQ2 genotypes among them, which makes them more vulnerable to environmental factors. Both studies have concluded that there is a difference in celiac disease occurrence between males and females, with female children having a higher frequency.

A different study contradicted the belief that introducing gluten early on leads to celiac disease. Instead, it suggested delaying gluten intake to potentially prevent the onset of the disease. This approach aims to maintain the baby's health during a critical period of development. The study was conducted by Lionetti and coauthors in 2014 [13] and relates to the review by Pinto-Sánchez and coauthors (2016) [15], which determines the impossibility of making recommendations regarding the consumption of gluten when introducing food to infant, as the available data are not robust enough. This work points out the lack of evidence to consider that early exposure to gluten increases the risk of developing the disease, but discusses the hypothesis that late introduction has this role, concluding that more studies are needed to elucidate the confounding factors.

Kemppainen and coauthors (2017) [14] explored the relationship between breastfeeding and the introduction of gluten in an infant's diet in the development of celiac disease. These two factors play a role in the link between gastrointestinal infections and the onset of the celiac condition. In the TEDDY study, it was found that gastrointestinal infections occurring 3 months before seroconversion can induce celiac disease in individuals who are predisposed to it, especially those who are local carriers of non-HLA-DQ2 and breastfed for less than 4 months. Breastfeeding helps modulate this bond due to the passive immunization function of the child. Immunoglobulins A coat the intestinal mucosa and neutralize infectious agents, reducing the chance of contracting compatibility, especially viral infections, which can lead to celiac autoimmunity. Furthermore, early weaning increases the risk of gastrointestinal disorders and celiac disease. The interruption of breastfeeding is closely linked to the early introduction of gluten, and both factors cause modulating effects on gastrointestinal disorders. Additionally, the interval between exposure to gluten and gastrointestinal infection by rotavirus, considered the main trigger for celiac disease, influences the development of this autoimmune condition.

After conducting a thorough review, it has been discovered that recent studies on the topic at hand are lacking. Despite diligent searches for scientific literature and careful examination of the material found, there are still many unanswered questions. For instance, Szajewska and coauthors (2016) [16] have noted that there is insufficient data to determine the best recommendations for introducing gluten into infants' diets, as well as whether breastfeeding can aid in preventing celiac disease. Additionally, it is unclear whether there is any difference in the risk of developing the disease between children who were exclusively breastfed and those who were given formula. This is an important area for further research, as colostrum's role in the formation of intestinal microbiota [17] is closely related to celiac disease's pathogenesis [7].

CONCLUSION

After conducting a bibliographic review, it has been determined that the early introduction of gluten does not impact the development of celiac disease in predisposed children. The idea that a late introduction of gluten may offer some protection is still unproven, as has the hypothesis that late exposure may increase the risk of developing the disease. Additionally, simultaneous breastfeeding and gluten introduction do not delay or decrease the risk of developing autoimmunity, as previously believed.

However, there is an indirect connection between breastfeeding, gluten introduction, and celiac disease manifestation during the food introduction stage. This link is due to the effect that the gastrointestinal infections have on the disease, which has not yet been fully understood.

It is essential to conduct new studies on this topic to clarify the relationship between gluten introduction delay and celiac disease and to explain the connection with gastrointestinal infections. By advancing knowledge on this topic, it may be possible to provide forms of prevention and intervention in the process of developing celiac disease.

Funding: This research received no external funding.
Acknowledgments: The authors are grateful to Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Fundação Araucária – PR (TED 27/23) for the financial support.
Conflicts of Interest: The authors declare no conflict of interest.

REFERENCES

1. World Health Organization. Guideline for complementary feeding of infants and young children 6–23 months of age. Geneva: World Health Organization; 2023.
2. Nicklaus S. The role of food experiences during early childhood in food pleasure learning. Appetite. 2016 Sep 1;104:3-9.
3. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker Jr JR, Beck LA, *et al.* Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. J. Allergy Clin. Immunol. 2017 Jan 1;139(1):29-44.
4. Hill P, Holmes GK, Asquith P, Holmes, G. British Society of Gastroenterology guidelines on the diagnosis and management of coeliac disease. Gut. 2015 Apr;64(4):691-2.
5. Geha R, Notarangelo L. Case Studies in Immunology: A Clinical Companion. 6th ed. New York: Garland Science, Taylor & Francis Group; 2012.
6. Therrien A, Kelly CP, Silvester JA. Celiac Disease: Extraintestinal Manifestations and Associated Conditions. J. Clin. Gastroenterol. 2020 Jan;54(1):8-21.
7. Caio G, Volta U, Sapone A, Leffler DA, Giorgio R, Catassi C, et al. Celiac disease: a comprehensive current review. BMC Med. 2019 Jul 23;17(1):23.
8. Elias CSR, Figueiredo RM, Rocha RA. [When does the end come? A narrative review on the end of the school period for mentally disabled students]. SMAD Rev. Eletrônica Saúde Ment. Álcool Drog. 2012;8(1):48-53.
9. Crespo-Escobar P, Mearin ML, Hervás D, Auricchio R, Gemma C, Gyimesi J, et al. The role of gluten consumption at an early age in celiac disease development: a further analysis of the prospective PreventCD cohort study. Am. J. Clin. Nutr. 2017 Apr 1;105(4):890-6.
10. Ivarsson A, Myléus A, Norström F, Pals MVD, Rosén A, Högberg L, et al. Prevalence of childhood celiac disease and changes in infant feeding. Pediatrics. 2013 Mar;131(3).
11. Vriezinga SL, Auricchio R, Bravi E, Castillejo MSG, Chmielewska A, Escobar PC, et al. Randomized Feeding Intervention in Infants at High Risk for Celiac Disease. N. Engl. J. Med. 2014 Oct 2;371(14):1304-15.
12. Perkin MR, Logan K, Marrs T, Radulovic S, Craven J, Flohr C, et al. Enquiring About Tolerance (EAT) study: Feasibility of an early allergenic food introduction regimen. J. Allergy Clin. Immunol. 2016 May 1;137(5):1477-86.e8.
13. Lionetti E, Castellaneta S, Francavilla R, Pulvirenti A, Tonutti E, Amarri S, et al. Introduction of Gluten, HLA Status, and the Risk of Celiac Disease in Children. N. Engl. J. Med. 2014 Oct 2;371(14):1295-303.
14. Kemppainen KM, Lynch KF, Liu E, Lönnrot M, Simell V, Briese T, et al. Factors That Increase Risk of Celiac Disease Autoimmunity After a Gastrointestinal Infection in Early Life. Clin. Gastroenterol. Hepatol. 2017 May 1;15(5):694-702.e5.
15. Pinto-Sánchez MI, Verdu EF, Liu E, Bercik P, Green PH, Murray JA, et al. Gluten Introduction to Infant Feeding and Risk of Celiac Disease: Systematic Review and Meta-Analysis. J. Pediatr. 2016 Apr;168:132-43.e3.
16. Szajewska H, Shamir R, Mearin ML, Ribes-Koninckx CR, Catassi C, Domellöf M, et al. Gluten Introduction and the Risk of Coeliac Disease: A Position Paper by the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J. Pediatr. Gastroenterol. Nutr. 2016 Mar;62(3):507-13.
17. Davis EC, Wang M, Donovan SM. Gut microbiome and breast-feeding: Implications for early immune development. J. Allergy Clin. Immunol. 2022 Sep;150(3):631-42.