Lactase Enzyme Deficiency in Pediatric GI Disorders

Reviewed by:

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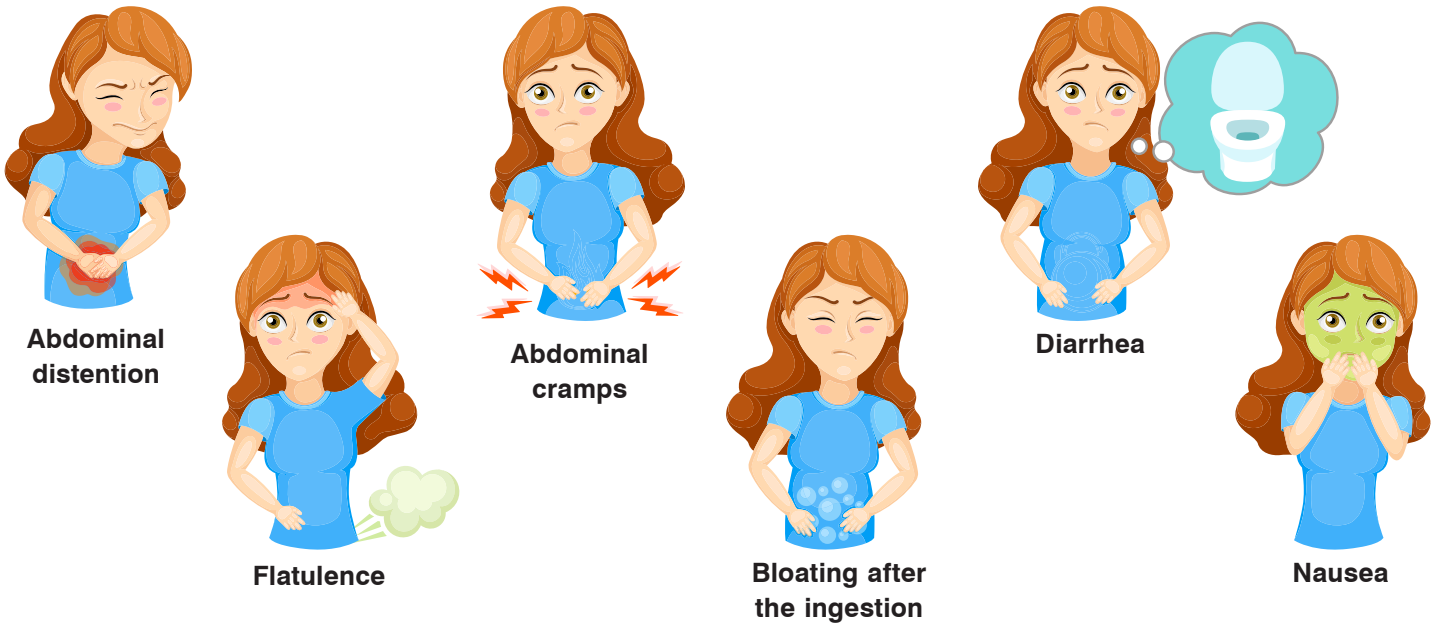
Introduction[1]

- Lactase enzyme deficiency is commonly correlated with intestinal lactase deficiency and dietary lactose malabsorption.
- It is identified by lactose intolerance, the inability to digest lactose resulting in one or more GI symptoms after the lactose ingestion.
- Patients must be counselled and reassured that ingestion of lactose does not cause permanent damage and there is no need for a totally lactose-free or severely restricted diet.
- Dairy products should not be completely eliminated since they provide key nutrients.
- Other necessary counselling must be done to avoid foods that contain lactose as fillers and to distinguish certain foods that are hidden sources of lactose.

Types of Lactase Deficiency

1. **Primary Lactase Deficiency[1]:** It is the most common form of lactose malabsorption, distinguished by the relative or absolute absence of lactase which develops over time, usually after age 2 when the body produces less lactase.
2. **Secondary Lactase Deficiency[1]:** This deficiency is observed due to injury to small bowel mucosa. The causative factors comprise any GI illness that significantly damages the brush borders of the small intestines or significantly increases bowel transit time. It occurs due to damage to the intestinal lining from GI disorders such as:
   - **Celiac Disease[1]:** It is a clinical condition of absorption related to an immunologic reaction to gluten or other proteins in the diet found mainly in wheat products. Etiology includes genetic predisposition, toxic effects of gluten/gliaden, an immune reaction to gluten, and exposure to adenovirus type 12.
   - **Inflammatory Bowel Disease (IBD)[2]:** It is described as a chronic inflammatory condition of the GI tract. It is an idiopathic disease distinguished by swings between intestinal inflammation and remission. It is characterized by abdominal pain and cramps, weight loss, diarrhea, cachexia, disrupted digestion, rectal bleeding and a substantial personal burden. IBD is divided into 2 major conditions such as Ulcerative Colitis (UC) and Crohn's Disease (CD).
   - **Gastroenteritis[3]:** It is a syndrome of diarrhea or vomiting resulting from a non-inflammatory infection in the upper small bowel or inflammatory infection in the colon. This can be due to bacteria, viruses or parasites, but in many cases, no pathogen is recognized.
   - **Crohn's Disease[4]:** It is a relapsing systemic inflammatory clinical condition affecting the GI tract with extraintestinal manifestations and associated immune disorders. It is characterized by abdominal pain, fever, and clinical signs of bowel obstruction or diarrhoea with passage of blood or mucus, or both. It can result from an impaired interaction of the intestinal commensal microbiota that is normally in a state of symbiotic mutualism with the human host (immune system).
3. **Congenital Lactase Deficiency[5]:** A decrease or absence of lactase enzyme activity since birth due to autosomal recessive inheritance is observed.[5] It is a severe autosomal recessive genetic condition that impacts the functional capacity of the intestinal protein "lactase-phlorizin hydrolase" (LPH). It is diagnosed during the first few days of the newborn's life because of the inability to digest lactose. The symptoms are similar to other carbohydrate malabsorption disorders like congenital sucrase-isomaltase deficiency and severe osmotic watery diarrhea.[6]
4. **Developmental Lactase Deficiency[5]:** It is observed in premature infants born at 28 to 37 weeks of gestation wherein the infant's intestine is underdeveloped, resulting in an inability to hydrolyze lactose. This condition can be improved with increasing age because of the maturation of the intestine, which results in adequate lactase activity.

Symptoms in Pediatric Patients[7]



Diagnosis[1]

Diagnosis involves clinical history and dietary manipulation. During a diagnostic lactose-free diet, all sources of lactose must be eliminated which comprises reading food labels to identify hidden sources of lactose such as:

- Bread and other baked products
- Processed breakfast cereals and milk powder
- Instant soups, and breakfast drinks, milk, curds, whey, milk by-products, and milk solids
- Potato chips and other processed snacks
- Processed meats
- Protein powders and bars

The lactose breath hydrogen test might be used in diagnosis. An increase (>20 ppm) in expired hydrogen after 60 minutes is diagnostic of lactose intolerance. The lactose breath hydrogen test is positive in 90% of patients with lactose malabsorption. False-negative results are reported in cases of absence of bacterial flora, recent use of oral antibiotics, or recent high colonic enema wherein the false-positive results are distinguished by increased breath hydrogen secretion unrelated to lactose might be obtained during sleep or exercise or with previous use of aspirin and with smoking. Differential diagnoses of lactose malabsorption comprise any of the malabsorption syndromes and might include IBS, IBD, infectious diarrhea, celiac disease, diverticulitis, and parasitic infection which may be ruled out by stool testing for parasites or pH, blood testing for celiac disease or IgA deficiency, or biopsy as required.

Management Strategies

Treatment should only be started in the presence of symptoms of intolerance. The intensity of symptoms varies in different people and it is recommended that individuals tailor their intake to the threshold at which symptoms occur.[1]

1. Dietary Modifications

- Avoid high-lactose foods like whole milk, cheese, and ice cream.[1]
- Include lactose-free products and plant-based alternatives (e.g., almond or soy milk).[8]

2. Lactase Supplements

- **Available as tablets or drops**
  - * Exogenous lactase as pills has been used to manage lactose intolerance in children, and adolescents.[9]
  - * Enzymatic supplementation might be an intermediate step between dairy restriction and the use of diets with low levels of FODMAPS.[9]
  - * Oral lactase supplementation relieves symptoms in children and lactase drops when added to milk formula or given prior to breastfeeding significantly reduce crying in infants with colic.[10]

Alleviation of Infant Colic Symptoms by Reducing Lactose Intake with Lactase[11]

- Lactase pretreatment of feeds was correlated with markedly and statistically significant lower breath hydrogen and lower cry time when compared with placebo pretreatment.
- Pre-incubation of feed with lactase was correlated with a significant active/placebo difference in both cry time and breath hydrogen in those who used lactase as recommended.

Role of Lactase in Infant Colic Management[12]

- Transient lactose intolerance might have a role in the etiology of infant colic.
- Lactase drops added to milk formula 24 hours before the feeding resulted in a significant reduction in crying time in babies with infant colic. Lactase drops might need prior incubation with milk to be effective in infant colic.

Use of Oral Lactase for Infantile Colic Management[13]

Transient lactose intolerance is considered an instant source of infantile colic. The only diet for infants below 6 months is milk, lactase enzyme supplementation with milk might result in colic symptoms.

A randomized, double-blind, placebo-controlled study (n-162) was conducted to examine the efficacy and safety of oral lactase enzyme in the treatment of infantile colic with the primary outcome of comparing crying or fussing duration and number of colic days, and the secondary outcome of comparing the parent satisfaction and adverse effects in children receiving lactase or placebo.

- Infants (age <5 months) fulfilling the Rome IV diagnostic criteria for infantile colic with no evidence of acute/chronic illness were included.
- The mean daily duration of crying or fussing demonstrated a progressive decline from the first to fourth week in both the groups but was significantly lesser in infants receiving lactase at the end of every week of assessment.
- After 4 weeks, better parental satisfaction in terms of perception of their child's mood, alertness, activity and oral intake was observed in infants receiving lactase.
- Also, there was a lesser number of days with colic, and better parental satisfaction in terms of positive change in the child's mood, alertness, activity, and oral intake.
- Treatment with lactase was well tolerated by all the infants and no adverse effects were reported during the treatment.

Lactase drops when added to milk formula or breastfeed before feeding resulted in a significant reduction in crying in infant with colic.

They may provide significant symptomatic relief in infantile colic in terms of reducing the crying or fussing duration and number of colic days.

A short course of oral lactase drops may be offered to infants with colic who fit the Rome IV diagnostic criteria.

Role of Oral Lactase Enzyme on Infantile Colic in the First 4 Months of Life[14]

Infantile colic is a self-limited process in which a healthy infant experiences continuous crying and it is diagnosed as the "rule of three" wherein crying is more than three hours per day, more than three days per week, for longer than three weeks.

Babies have immature digestive systems and their gut does not produce a sufficient quantity of lactase enzyme required for lactose digestion. The undigested lactose enters the colon where bacteria ferment it and produce lactic acid and hydrogen gas resulting in lactose intolerance which is distinguished by abdominal pain, distention, bloating, diarrhea and flatulence.

A study (n-200) was conducted to investigate the role of lactase enzyme supplements in infant colic in the first 4 months of life.

- Infants of 0-4 months of age with abdominal colic lasting for 3 hours or more for 3 days or more and without improvement with usual treatment with free abdominal ultrasound were included.
- Infants were divided into 2 groups: Group A (n-100)—Infants were treated with lactase enzyme supplement as 5 oral drops before maternal milk or 2 oral drops for

every 20 cm of milk formula twice daily and Group B (n-100)— Infants were managed with abdominal massage and anti-colic (e.g., Simethicone, Dimethicone).

All infants in group A and group B had normal abdominal ultrasound.

At X-ray in erect position, at group (A), 83% infants had gaseous distension, and 17% of them had marked gaseous distension. Wherein group (B), 88% infants had gaseous distension, and 12% of them had marked gaseous distension.

There was no statistical difference between the two groups.

Oral lactase drops might provide significant symptomatic relief in infantile colic by reducing the crying and number of colic days.

Treating Underlying GI Disorders[15]

With the increasing recognition of the role of gut microbiota, various interventions targeting gut microbiota, such as probiotics, a low FODMAP diet, prebiotics, and antibiotics, are being utilized for managing GI disorders. Research reported that some patients with IBS have a sensitivity to carbohydrate malabsorption and a low FODMAP diet is commonly recommended for children with IBS. Low dietary fiber intake during childhood has been linked to the development of GI disorders. A randomized, double-blind controlled trial in children demonstrated that treatment with the soluble fiber significantly reduced the frequency of abdominal pain in children with IBS. In 5 RCTs investigating children with functional abdominal pain–not otherwise specified, the probiotic supplementation improved abdominal pain outcomes and reduced functional disability. In children with IBS, probiotics effectively reduced abdominal pain symptoms and reduced perceived abdominal distension.

Probiotic Use

Probiotics, known for their ability to survive and exert beneficial effects in the host, represent a promising therapeutic approach for functional GI disorders. They compete metabolically with pathogens, enhance the intestinal mucosal barrier, and modulate the intestinal inflammatory response.[16] Probiotics in fermented milk can help alleviate lactose intolerance by enhancing lactase enzyme activity in the small intestine, facilitating the digestion of the lactose. Studies reported that consuming milk supplemented with probiotics can serve as an alternative for individuals with lactose intolerance which allows them to consume dairy products freely, thereby meeting their nutritional needs.[17]

Lactase Deficiency in Specific Pediatric GI Disorders

- **Celiac Disease[18]:** In celiac disease symptoms of lactose intolerance are frequently observed in patients who do not respond well to a gluten-free diet, suggesting the need for targeted management with a lactose-restricted diet. In these cases, lactose intolerance may be due to secondary lactase deficiency or primary lactase deficiency especially in populations at high genetic risk for this condition. Avoiding milk products entirely may exacerbate nutritional deficiencies in celiac patients, worsening the challenges of their restrictive diet.
- **Post-Infectious Gastroenteritis[19]:** Secondary lactase deficiency arises from damage to the mucosal cells of the small intestine, which can occur in conditions like small bowel surgery, celiac disease, and Crohn's disease, as well as infections such as giardiasis and

- transient viral gastroenteritis. Additionally, prolonged inactivity of the GI tract can lead to secondary lactase deficiency. In most cases, this condition resolves once normal gut function is restored.
- **IBD[20]:** Risk factors for developing lactose intolerance include celiac disease, small intestinal bacterial overgrowth, drug-induced bowel inflammation, small intestine infections, and IBD. Studies reported that lactose intolerance affects 23.2% of children with UC and 22.6% of those with CD, with secondary lactose intolerance diagnosed in 6.7% of children with IBD. Another trial reported that approximately 30% of children with IBD experience lactose intolerance. Among IBD patients, about 40% of those with active disease and 33% in remission avoid lactose-containing products. Lactose intolerance occurs in roughly 10–20% of IBD patients.

Conclusion

Lactase enzyme deficiency, a common condition, arises from insufficient intestinal lactase levels and results in the malabsorption of dietary lactose. This deficiency results in lactose intolerance, characterized by the partial or complete inability to digest lactose—the primary sugar in milk and dairy products. Lactose intolerance typically presents with GI symptoms such as bloating, flatulence, nausea, abdominal pain, and diarrhea following the consumption of lactose-containing foods. Diagnosis often involves dietary elimination followed by reintroduction of lactose to observe symptom recurrence. Complete avoidance of milk and dairy products is not typically required, hence novel approaches such as lactose-free and partially digested dairy products can be used. When lactose-free diets are implemented, it is crucial to ensure adequate calcium intake through fortified foods or supplementation to meet daily recommendations. For patients with secondary lactose intolerance, further evaluation is needed to identify and address the underlying cause. Treating **the primary condition can alleviate symptoms and improve lactose tolerance. Gradual reintroduction of dairy products, tailored to an individual's tolerance level, can help maintain an adequate intake of essential nutrients while minimizing symptoms.**

References

1. Siddiqui Z, Osayande AS. Selected disorders of malabsorption. *Primary Care: Clinics in Office Practice.* 2011 Sep 1;38(3):395-414.
2. Kraneveld AD, Rijnierse A, Nijkamp FP, Garssen J. Neuro-immune interactions in inflammatory bowel disease and irritable bowel syndrome: future therapeutic targets. *European Journal of Pharmacology.* 2008 May 13;585(2-3):361-74.
3. Barrett J, Fhogartaigh CN. Bacterial gastroenteritis. *Medicine.* 2017 Nov 1;45(11):683-9.
4. Baumgart DC, Sandborn WJ. Crohn's disease. *The Lancet.* 2012 Nov 3;380(9853):1590-605.
5. Malik TF, Panuganti KK. Lactose intolerance. InStatPearls [Internet] 2023 Apr 17. StatPearls Publishing.
6. Wanes D, Husein DM, Naim HY. Congenital lactase deficiency: mutations, functional and biochemical implications, and future perspectives. *Nutrients.* 2019 Feb 22;11(2):461.
7. Heyman MB, Committee on Nutrition. Lactose intolerance in infants, children, and adolescents. *Pediatrics.* 2006 Sep 1;118(3):1279-86.
8. Dairy and alternatives in your diet. Available (Online) at URL: https://www.nhs.uk/live-well/eat-well/food-types/milk-and-dairy-nutrition/. Accessed on 14th January 2025
9. Francesconi CF, Machado MB, Steinwurz F, Nones RB, Quilici FA, Catapani *et al.* Oral administration of exogenous lactase in tablets for patients diagnosed with lactose intolerance due to primary hypolactasia. *Arquivos de Gastroenterologia.* 2016 Oct;53:228-34.
10. Yildirim ES, Aydin A, Ince T, Varol Z, Ünal B, Demir A. Simethicone Medication Should Be Avoided in Infants Receiving Oral Lactase Treatment. *Children.* 2024 Aug 17;11(8): 1009.
11. Kanabar D, Randhawa M, Clayton P. Improvement of symptoms in infant colic following reduction of lactose load with lactase. *Journal of Human Nutrition and Dietetics.* 2001 Oct;14(5):359-63.
12. Kearney, Malone, Hayes, Hyland. A trial of lactase in the management of infant colic. *Journal of Human Nutrition and Dietetics.* 1998 Aug;11(4):281-5.
13. Narang M, Shah D. Oral lactase for infantile colic: a randomized double-blind placebo-controlled trial. *BMC Pediatrics.* 2022 Aug 3;22(1):468
14. Ahmed AM, Bayomi AE, Syed Younis MM. The Effect of Oral Lactase Enzyme on Infantile Colic in The First 4 Months of Life: A Prospective Case-Control Study. *Annals of Neonatology.* 2024 Jan 1;6(1):93-112.
15. Thapar N, Benninga MA, Crowell MD, Di Lorenzo C, Mack I, Nurko *et al.* Paediatric functional abdominal pain disorders. *Nature Reviews Disease Primers.* 2020 Nov 5;6(1):89.
16. Whitfield KL, Shulman RJ. Treatment options for functional gastrointestinal disorders: from empiric to complementary approaches. *Pediatric Annals.* 2009 May;38(5):288.
17. Arifin Z, Boediarso AD, Tambunan T. Probiotic treatment in children with lactose intolerance "An open labeled the one group pre-test post-test experimental study." *Paediatrica Indonesiana.* 2006;46(3):139-43.
18. Basso MS, Luciano R, Ferretti F, Muraca M, Panetta F, Bracci *et al.* Association between celiac disease and primary lactase deficiency. *European Journal of Clinical Nutrition.* 2012 Dec;66(12):1364-5.
19. Williams SE, Seidner DL. Metabolic bone disease in gastrointestinal illness. *Gastroenterology Clinics of North America.* 2007 Mar 1;36(1):161-90.
20. Ratajczak AE, Rychter AM, Zawada A, Dobrowolska A, Krela-Kaźmierczak I. Lactose intolerance in patients with inflammatory bowel diseases and dietary management in prevention of osteoporosis. *Nutrition.* 2021 Feb 1; 82:111043.