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Lactose Intolerance and Emerging Dairy Allergies as Public Health Perspective

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INTRODUCTION

Milk is a complete diet having a biggest source of lactose that provides energy to the consumers. Lactose is digested by the enzyme named as lactase (Vandenplas 2015). Some people are deficient with the normal level of lactase that leads to the lactose malabsorption. These individuals simply suffer with lactose intolerance (Martínez Vázquez et al. 2020). Severity of lactose intolerance depends on the amount of lactase present in the intestinal flora and gastrointestinal tract for absorption of lactose (Catanzaro et al. 2021). Globally, 57% of the people suffer from lactose intolerance just because of lacking lactase enzyme (Catanzaro et al. 2021). Keeping in view the prevalence record of lactose intolerance, Africa is on the top with 100% rate of affected people (Lember 2012). In Asia 70% people are prone to the lactose intolerance and dairy allergies from the milk (Lember 2012). Considering the data from American region it was just 15% among the whites and the rate was higher in African-Americans as 80% (Lember 2012; Storhaug et al. 2017).

Milk and dairy products always remain valuable sources of nutrients for young as well as adult mammals (Corgneau et al. 2017). Milk contains carbohydrates (carbohydrates and other oligosaccharides) in addition to proteins, fats, vitamins and minerals to enhance the growth of probiotic bacteria in children's intestine, mainly *bifidobacteria*, protecting infant's gut from infections. Milk lacks only a few vitamins and iron, so, it is also a perfect food for adults (Franzè and Bertelè 2010). But, in adult age, everyone cannot digest this food, resulting in intolerance (Matthews et al. 2005; Harrington and Mayberry 2008). Lactose intolerance results in pain, distended abdomen, diarrhea and flatulence (because of mal-absorbed lactose), that needs to be differentiated from other subclinical conditions, like lactose maldigestion and lactose malabsorption (Matthews et al. 2005). Lactose is only present in milk and milk derived products of mammals. It is formed by lactose synthetase system in mammary glands, that binds D-galactose to D-glucose by β-1,4 glycosidic bond. Lactase (a β-galactosidase) is required for digestion of lactose. It is found on the upper surface of microvilli's in small intestine, and more expressed in mid jejunum, where less fermentation occurs due to low bacterial population. It hydrolyses lactose to glucose and galactose, that upon digestion, get absorbed quickly by intestine and utilized as energy source and as a component of glycolipids and glycoproteins, respectively (Franzè and Bertelè 2010).

After weaning, lactase expression is down regulated in the enteric cells. It results in Lactase Non-Persistence (LNP), which bears least severity and is encountered the most (Wilt et al. 2010). When lactase deficiency is faced, lactose maldigestion occurs leading to lactose malabsorption, and it refers to a clinical condition exhibiting gastro-intestinal symptoms (Matthews et al. 2005; Misselwitz et al. 2013). The symptoms may be gastro-intestinal or extra-intestinal (Matthews et al. 2005). Lactose Malabsorption almost always result from lactase deficiency (Flatz 1987; Wilt et al. 2010). The symptoms that are consistently seen in lactose-intolerant individuals include diarrhea, bloat, nausea and abdominal pain (Deng et al. 2015). The amount of mal-absorbed lactose decides the clinical picture of lactose

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malabsorption. The clinical symptoms are ignored by a number of patients suffering from Lactose malabsorption and Lactose non-persistence if small quantity of lactose is taken (Wilt et al. 2010). The lactase expression varies over time in life; it is present throughout the intestinal mucous membranes during 8th week of pregnancy; increases up to 34th week, and at birth, it goes to its highest concentration (Deng et al. 2015). Few months after birth, enzyme activity starts to reduce, until it ends up (Franzè and Bertelè 2010). Considerable amount of lactase is synthesized during first year of life. Later, lactase synthesis is genetically reduced in LNP patients. Lactose-intolerance (LI) begins somewhere between 2 to 3 years and completes by 5 to 10 years of age, with exceptions reported in some cases(Swallow 2003). A significant part of human population possesses enzyme functionality throughout the life, but other mammals show unusual lactase maintenance (Deng et al. 2015). The incidence of LNP is greatly associated with ethnicity (Welsh et al. 1978). Generally, 70% to 100% of maldigesters originate mostly from conventional non-milk consuming regions. Whereas those from milk consuming regions possess less prevalence of LM (Caballero 2005). Functionally, it should be highlighted that 50% of normal enzyme activity is sufficient for lactose digestion (Franzè and Bertelè 2010).

Abdominal distension caused by lactose fermentation by the microflora in the gut and the osmotic effect that occurs due to the presence of lactose molecules in GIT are the pathogenic mechanisms resulting in above mentioned symptoms. In a few of LI patients, it has also been reported that some strains of micro-organisms reduce carbon-dioxide to methane that can lead to constipation (Misselwitz et al. 2013). Headache, asthenia, joint/muscle pain, skin lesions, loss of concentration and mouth ulcers are the most common extra-intestinal symptoms that have been reported in many cases (Matthews et al. 2005). 2.6 L carbon-dioxide and 4 L of hydrogen gas are released by the degradation of 12.5 g of lactose (Wolin 1981). Whereas, the normal amount of gas excreted is lower than 1 L of gas per day (Tomlin et al. 1991). Yet, the presence of systemic syndrome by lactose-intolerance is in debate, and the mechanism of pathogenesis has also not been distinctly explained. As the systemic and gastro-intestinal symptoms appear many hours post consumption of lactose containing food and there are a wide variety of even non-dairy products containing lactose, which are used as additives in food, the patient is not always believed to develop these symptoms after consuming lactose (Dainese et al. 2014). There are various factors that decide the threshold level of lactose in different individuals that includes amount of lactose ingested, lactase activity level, food matrix (taken with other diet components), time of stay in gut, and intestinal micro-floral composition (Deng et al. 2015).

Although, ingestion of lactose does not enhance the expression of lactase, it has been reported that tolerance may get improved by regularly taking small quantities of lactose. This way, the intestinal microflora become adapted to lactose (Shaukat et al. 2010). So, administering the increasing amounts of lactose can regularly address the symptoms in patients of lactose intolerance (Hertzler and Savaiano 1996; Briet et al. 1997). Modulating the enteric micro-environment by enhancing the colonization of β-galactosidase activity harboring strains, could be an efficient treatment strategy for lactose intolerant subjects (Fassio et al. 2018). The symptoms relieving strategies include intake of lactose-free food components or the products having surplus amounts of probiotic bacteria, as well as the usage of exogenic enzyme formulations (Corgneau et al. 2017). The difference of lactose digestion in normal individual and lactose intolerant individual has been shown in Fig. 1.

Calcium Intake and Diet Competence

It is a well-known fact that calcium is enormously beneficial and a consolidative element of body, the skeleton alone comprising 99% of body's calcium (Emkey and Emkey 2012). The calcium homeostasis in plasma is necessary for sustaining activities of life, like maintaining skeleton, hormonal regulation, nerve impulse conduction and vascular functions (Del Valle et al. 2011; Brini et al. 2013). Calcium in diet gets absorbed in small intestine, and most of it accumulates in bones via circulation. The unabsorbed calcium excretes out of body in feces and urine (Del Valle et al. 2011).

Dairy has been a significant mean of calcium in diet and hence studied widely. 120 mg/ 100 ml Ca is present in bovine milk. In North America and Europe, dairy products account 75% of dietary calcium, vegetables and fruits 15%, mineral water 5% and other foods account rest of amount (Guéguen and Pointillart 2000; Fishbein 2004). Under normal conditions, 40% of Ca is absorbed from dairy products, so the bioavailable is the amount which is absorbed by small intestine and help in mineralizing bones (Melse-Boonstra 2020). Physiological factors (growth, pregnancy and lactation related) determine Ca storage in bones, and several hormones (PTH, calcitonin, calcitriol and estrogens) regulate it.

Calcium is mainly absorbed by intestine via passive diffusion, whereas at low and modest calcium intake, active transport occurs under Vit-D regulation (Guéguen and Pointillart 2000). Vit-D fortified milk has been shown to improve Ca absorption (Kaushik et al. 2014). Many of the components in dairy sources help in Ca and other substances' absorption by passive diffusion such as casein, phospho-peptides, lactose, phosphorous and whey proteins. Many dairy components inhibit the Ca uptake as well (Table 1). Lactose acts as a prebiotic, as it increases the production of *bifido-bacteria* that trigger Ca absorption in cecum and colon and maintain low pH (Shi et al. 2001; Szilagyi 2002; Whisner et al. 2013). Ca absorption from vegetables depends upon the phytate and oxalate content (being higher in spinach, cabbage, beetroot, broccoli, sprouts) in these. These bind with cations ($Ca^{2+,}$ Mg^{2+}, Zn^{2+}, and Fe^{2+}) and form indigestible and insoluble complexes, restricting their

Table 1: Different Components of dairy food sources affecting Ca Absorption

Sr. No.	Food Element	Effect on Ca Bioavailability	Reference
1	Vit-D	Enhances active Ca absorption at its low and modest level	(Guéguen and Pointillart 2000)
2	Phospho-peptides and Casein	Enhance passive diffusion, they bind with Ca resulting in its slower release into solution in chyme	(Mykkänen and Wasserman 1980, Lee et al. 1983; Li et al. 1989)
3	Proteins (α-lactalbumins and β-lactoglobulins)	Same effect as Phospho-peptides and Casein	(Guéguen and Pointillart 2000)
4	Amino Acids (L-Arginine and L-lysine)	Same effect as Phospho-peptides and Casein	(Lee et al. 1983)
5	Lactose	Enhances passive diffusion due to broadened paracellular spaces in intestinal cell lining*	(Bronner 1992)
6	Phosphorous	Decreases absorption-it binds Ca to undigestible food complexes. In distal part of nephron, re-absorption increases. Increases uptake of absorbed Ca into bones.	(Guéguen and Pointillart 2000)
7	Sulphonated Proteins	Negative Ca balance due to hypercalciuria induction	(Guéguen and Pointillart 2000)
8	Fat	No effect on Ca absorption. It forms insoluble soaps with Ca that dissociate at acidic gastric pH	(Allen 1982)

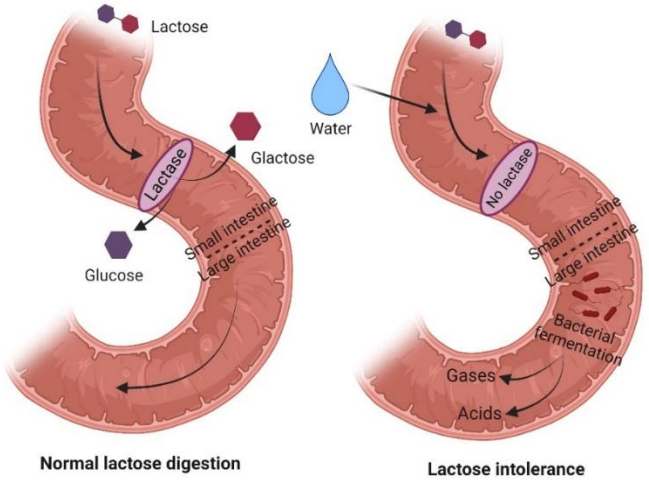

Fig. 1: Difference of Normal Lactose Digestion and lactose Intolerance in Intestine (Created on Bio render)–Created by Biorender

bioavailability (Melse-Boonstra 2020). Adults face negative Ca balance after they achieve peak bone mass (~35y) and ~10 mg Ca is lost every-day. In post-menopausal women, this loss may reach 40 mg /day or more (Avioli 1984; Arasi et al. 2022).

According to studies, it happens at higher lactose concentrations.(Pansu et al. 1981; Cochet et al. 1983; Krebs et al. 2015), the amounts present in milk and dairy products are less likely to promote much absorption (Tremaine et al. 1986; Griessen et al. 1989).

Lactose Malabsorption

Milk acquires a great importance in the human diet and is an essential part of diet since thousands of years due to its high nutritive value and the variety of nutrients incorporated in it (Harrington and Mayberry 2008). One of the important nutrients in milk is lactose which is commonly called as “milk sugar” and is found in various dairy products. Except for walruses and sea lions, lactose is the major source of carbohydrate in milk of majority of the mammals including humans (Reich and Arnould 2007). The significance of lactose lies in the fact that it is a major precursor of many important biological metabolites which are vital for the human life. For instance, lactose is essential for the formation of glucocerebrosides; the molecules which are considered the vital components of nerve cells being the part of plasma membranes of nerve cells (Luna and Gallardo 2007). Lactose (β-galactosyl-1,4 glucose) is basically a disaccharide which is further made of galactose and glucose found in milk and is absorbed and digested in the small intestines of humans. Prior to its absorption, lactose needs to be hydrolyzed in the gastrointestinal tract of humans into two components with the action of an enzyme known as lactase. The enzyme lactase-phlorizin hydrolase (lactase) is mainly expressed in the brush border of the intestinal villi where it resides on the membrane of enterocytes (Misselwitz et al. 2019; Usai-Satta et al. 2022). Two identical polypeptide chains of size 160 kDa are combined with the intra cytoplasmic part to make up this enzyme and it shows the optimum activity at a pH between 6 and 8 in the small intestine. Lactose malabsorption occurs when the activity of lactase is reduced or declined which may be the result of deficiency of this enzyme in the intestinal cells; commonly referred as lactase deficiency. Any damage to the mucosal wall of intestine may cause lactase deficiency or even lead to failure of this enzyme to express and hydrolyze the lactose into absorbable components (Misselwitz et al. 2019). In a study, the results showed that Japan, Vietnam, and Uganda had the highest prevalence of lactose malabsorption (100%), while it was the lowest (14%) in the Central Italy (Ingram et al. 2009; Swallow 2003).

The metabolism of lactose is highly dependent on the expression and activity of lactase enzyme. Malabsorption of lactose is mainly subjected to the lactase deficiency which can be further classified in to 3 categories viz, congenital, primary and secondary (Bouchoucha et al. 2021). The other name used for lactase deficiency is hypolactasia. The most frequently occurring condition is primary hypolactasia in

which the the activity of lactase at the brush border of intestine decreases progressively and is wholly due to the autosomal recessive condition. C/T-13910 is a single nucleotide polymorphism that may have important role in developing lactose malabsorption in specific populations around the world (Schirru et al. 2007). Another type of hypolactasia is the congenital which occurs due to an autosomal recessive condition and is very rare to be found in most of the populations (Anguita-Ruiz et al. 2020).

Lactose Intolerance

There is a common misunderstanding among the people regarding the term's lactose malabsorption and lactose intolerance and in fact, the latter is not synonymous with lactose malabsorption. Lactose intolerance is a manifestation of symptoms which occur due to the malabsorption of lactose from the small intestine. Lactose intolerance is a condition that is characterized by the occurrence of abdominal signs including diarrhea, abdominal pain, bloating, and borborygmi (Zhao et al. 2010). It must be noted that the development of abdominal signs is not compulsory to every patient of lactose malabsorption because many patients show no signs of intolerance after ingesting lactose in their diets. However, the presence of lactose malabsorption is a pre-requisite or necessary condition in order to initiate the onset of intolerance or abdominal signs. The severity of lactose intolerance or more specifically the occurrence of abdominal signs is dependent on various intrinsic and extrinsic factors including the amount of lactose intake in the diet, the intake of other food items along with lactose diet which can influence the bowl transit time, the rate at which the undigested lactose is transferred to large intestine, and most significantly the expression and activity of lactase enzyme in the brush border of the small intestine (He et al. 2008; Windey et al. 2015). Regarding the threshold levels of lactose for causing lactose intolerance in patients, a study revealed that half pint or 8 oz of milk was enough to cause cramps or develop bloating in almost 54% participants in the study (Bayless et al. 2017; Mitchell et al. 1975). Several diagnostic tests are available for the detection of the lactose malabsorption and lactose intolerance in different populations.

Lactase Non-Persistence in Humans

Except humans, all other adult mammals show considerable decline in the production of intestinal lactase and is considered to occur just after the weaning (Romero-Velarde et al. 2019). However, in some individuals, the levels of lactase remain high even after the weaning is complete leading to condition known as lactase persistence. In contrast to the previous condition, lactase non-persistence (LNP) is characterized by the comparatively low levels of intestinal lactase or decreased expression and activity of this enzyme known as hypolactasia. In case of humas, the most prevalent phenotype is LNP with a prevalence rate of 65-70% in most of the populations (Ingram et al. 2009). In LNP, there is downregulation of the lactase gene; MCM6 which is situated on chromosome 2 having a size of 50 kb. A study showed the impact of C/T-13910 and G/A-22018 variants of DNA in downregulating the expression of intestinal lactase (Enattah et al. 2002). The homozygotes are T/T 13910 and C/C 13910 responsible for lactose persistence and LNP respectively, while the heterozygote responsible for reducing the activity of lactase to half is C/T 13910 (Bayless et al. 2017). The genetic variance and the downregulation of MCM6 gene is shown in Table 2.

The prevalence of lactase non-persistence has been calculated in various studies involving various ethnic groups in order to find out the epidemiological variations in the occurrence of LNP. According to studies, the highest prevalence of LNP was found in China (100%), while in Iraqi Jews it was 93%, and was lowest in the Swedish population which was merely 10% (Bayless et al. 2017; Corgneau et al. 2017; Raz et al. 2013).

Common Cow Milk Allergies

Cow milk (CM) is nutritious biological fluid introduced into infant's diet and cow milk allergy (CMA) is most common food allergy. CMA is immune mediated response to cow's milk protein that occurs consistently with ingestion. CMA is a complex food allergy and often misconception disorder among the general public health due to confession between CMA and milk intolerance. Both of these terms for distinct disorders and require separate technique for diagnosis and strategies for management and cure. In CMA, the immune system is involved in adverse reaction to harmless milk proteins. Allergy symptoms damage tissues due to immune system aberrant inflammatory response. CMA is not a single disease because it involves a spectrum of immunological mechanisms generally classified into IgE mediated and non-IgE mediated allergy. CMA incidence varies with age. IgE mediated CMA is most frequently observed food allergen and more dominant food allergy in children's (2-6%) and decrease into adulthood (0.1-0.5%) (Ross et al. 2005; Sicherer and Sampson 2018; Arasi et al. 2022). After consuming dairy milk or items containing dairy milk, the symptoms of IgE-mediated CMA frequently start to manifest within few minutes. These symptoms may include vomiting, diarrhea, skin rash, breathing difficulty, and anaphylaxis, which can be fatal (Walsh et al. 2016). The reported cases of patients show the 5-90% skin manifestation, 60% gastrointestinal symptoms and 0.8-9% anaphylaxis (Connor et al. 2022). Various diagnostic techniques are employed for identification but available diagnostic methods have constraints that impede our capacity to understand the underlying epidemiology (Sicherer and Sampson 2018). The best technique for identification is double blind placebo controlled oral food

Table 2: The genetic variance and the downregulation of MCM6 gene

Genetic variance (Polymorphism)	Allelic Variant	Lactase Activity	Prevalence
Lactase Non-persistent (LNP)	C/C 13910	Inactive	65-70%
Heterozygotes	C/T 13910	Activity is partial	Variable
Lactose persistent	T/T 13910	10 times more activity than hypolactasia	Almost 30%

challenge (DBPCFC). Apart from this unblinded oral food challenge (OFC) is less efficient and not always appropriate in clinical practices but well validated particularly among young infants (Bøgh and Larsen 2021). The serum specific IgE measurement and skin prick tests (SPT) predict the response possibility but in isolation it's not sufficient. The atopy patch test is also most often used for the diagnosis of atopic dermatitis that measures the milk allergen induced T cell activation. The Patients approximately 70% with IgE mediated CMA would react to whole milk products but patients can tolerate the treated products (alters in milk proteins) (Leonard 2015; Flom and Sichere 2019). There is currently no cure for CMA. Finding new therapeutic techniques in a clinical trial environment is difficult. Obstacles to the diagnosis and effective care of CMA in clinical practice include delayed diagnosis and inadequate understanding of the underlying pathophysiology (Gore and Custovic 2004). The only effective management strategy is to avoid cow's milk throughout the course of the disease. CMA patients often have allergies to various foods. Because an infant's immune system is not fully developed at birth, and the gastrointestinal tract is still immature, the intestinal lining leakage may occur if large amounts of intact cow's milk are fed. Intervention techniques in CMA aim at three levels: 1) primary prevention (breast feeding, partially hydrolyzed formulas, probiotics) of early sensitization; 2) secondary prevention (making cow milk less allergic) of triggering allergic reactions, and 3) induction of tolerance in already sensitized patients (Pessler and Nejat 2004; Restani et al. 2002; Lund and Ahmad 2021). The use of immune modulatory food adjuvants such as probiotics is a promising new method for primary prevention. The only effective therapeutic method for CMA sufferers is to eliminate diet milk proteins. It will remain to be a focus of fundamental food allergy investigation in the future years (Ross et al. 2005; Pessler and Nejat 2004). The composition of cow milk containing major proteins and allergens has been enlisted in Table 3.

Cow milk allergy (CMA) represents first from of allergy that can induce severe and life threating reaction. There is need of safe diagnostic techniques, best therapeutic treatment and preventions. The various forms of adverse reaction to dairy milk have been shown in Fig. 2.

Benefits of Calcium and Dairy Products

Calcium is the most plentiful mineral present in human body. It is fundamental not only for bone health, but also contributes to heartbeat, muscle contractions and other metabolic activities (Jaiswal 2001). Several nutrients are needed for development of bones in early years and their preservation to lessen the occurrence of osteoporosis and fracture in adult age (Rizzoli 2014). It has been deduced that protein and the minerals (Ca, P, Mg, Mn, Zn, Vit-D and Vit-K) are vital for the maintenance of strong bones (European Commission regulation 2012). Milk and dairy products contain considerable amounts of all these nutrients except Vit-D (Thorning et al. 2016). These minerals affect bone physiology and structure. For example, protein and calcium help in mineralization of bone by forming collagen and hydroxyapatite crystals, respectively (Heaney 2009).

The current data propose that the consumption of milk and dairy products is linked to lower probability of obesity in children, and in adults. It is associated with better body composition and weight loss during restricted energy provision. Additionally, milk and dairy products' consumption also reduces risk of type-II Diabetes Mellitus and cardiovascular diseases, such as stroke (Thorning et al. 2016). The relationship among consumption of milk in infancy and boosted growth and mineralization of bones has been postulated extensively since 1920's (Mann 1926). Consumption of dairy products enhance the release of type-I Insulin-like growth factor, that helps in developing skeletal muscles (Caroli et al. 2011). The lactose, casein phospho-peptides or Vit-D in dairy products help in enhanced calcium absorption from products and explain their positive effects on bones (Camara-Martos and Amaro-López 2002).

A high intake of calcium and Vit-D through dairy products can lower the circulating Parathyroid Hormone (PTH), improve bone mass, and can lower bone turnover (Heaney 2009). When blood calcium level falls, PTH concentration increases, that causes bones to release calcium, that results in bone resorption and ultimately reduced Bone Mineral Density (BMD)(Renner et al. 1998). There are some likely mechanisms through which dairy products can have positive impacts considering composition and size of body. Firstly, interaction of Ca and Vit-D may affect lipogenesis and lipolysis of adipocytes and fat oxidation(Shi et al. 2001; Zemel 2002; Zemel 2003). Secondly, Ca may help in lowering absorption and enhancing excretion of fat (Christensen et al. 2009). Thirdly, Ca may help in regulating hunger and intake of food-fat (Tordoff 2001). Fourth mechanism may be associated with the positive impacts of nutritious elements in dairy products like branched chain amino acids (BCCAAs) (Zemel 2005) and medium-chain triglycerides (Marten et al. 2006; Kouvelioti et al. 2017). In developed countries, the recommended amount of dairy products by children under the age of 9 y is ≈ 500 ml and for adults is >600ml dairy/day (Dror and Allen 2014).

Table 3: Cow milk compositions of major proteins and allergens characteristics (Restani et al. 2002; Ross et al. 2005; Bøgh and Larsen 2021)

Protein	Major Protein Composition (mg/ml)	Allergen	Size (kDa)	Disulphide (S-S) bridge in immunoglobulin's
α_s1-casein	11.6	Bos d 9 (Major)	23.6	0
α_s2-casein	3	Bos d 10 (Major)	25.2	0
β-casein	9.6	Bos d 11 (Major)	24	0
k-casein	3.6	Bos d 12 (Major)	19	1
α-lactalbumin	1.2	Bos d 4 (Major)	14.2	4
β-lactoglobulin	3	Bos d 5 (Major)	18.3	3
Serum albumin	0.4	Bos d 6 (Minor)	66.3	18
Immunoglobulins	0.6	Bos d 7 (Minor)	160	No. varies according to class and subclass
Lactoferrin	0.3	--- (Minor)	80	16

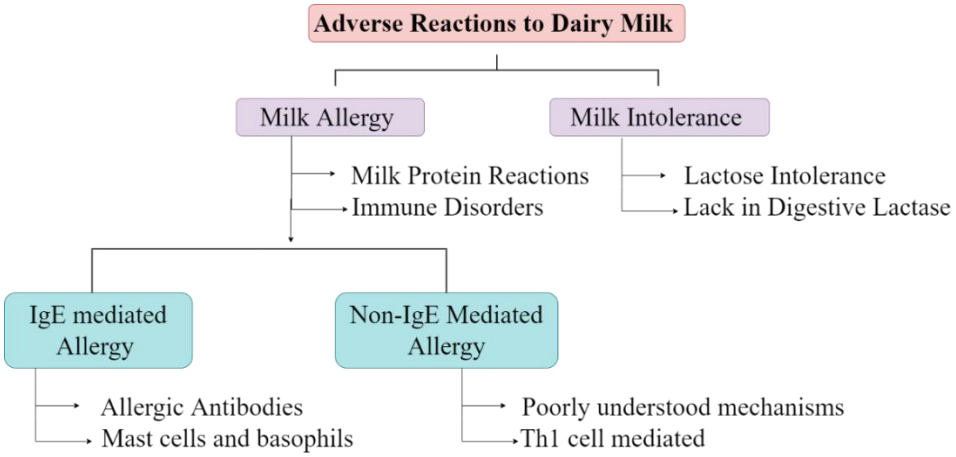

Fig. 2: Possible adverse reactions to dairy milk

Calcium in vascular smooth muscle cells regulates the blood pressure via vasoconstriction and varying vascular volume (Fardella and Rodriguez-Portales 1995; Yim and Yoo 2008). It has been reported by a systematic review of calcium supplementation and lipid metabolism that supplementing calcium reduces the low-density lipid (LDL) cholesterol and increases high-density lipids (HDL) cholesterol by suppressing the calciotropic hormones that lower the intracellular calcium in fat cells, initiating lipogenesis and fat storage (Chen et al. 2017). Furthermore, calcium in diet can also reduce the serum cholesterol level by preventing the absorption of saturated fatty acids and cholesterol (Vinarova et al. 2016). It has been found by randomized control trials (RCTs) that calcium dosage of 1200-2000 mg/day with 36-60 month treatment period can lessen the risk of recurring colo-rectal cancer (Bonovas et al. 2016). Moreover, calcium binds with bile acids in the intestinal lumen and prevents the multiplicative and carcinogenic effects of bile acids (Fardella and Rodriguez-Portales 1995; Newmark et al. 1984; Cormick and Belizán 2019).

Conclusion

Lactose intolerance (LI) and cow milk allergy (CMA) are two different terms that often used interchangeably. We should promote the appropriate use of CMA and LI terms. The prevalence of CMA is low in adults and high in infants (childhood disease). CMA is an immunological mediated reaction that affects the various body systems and can cause high mortality. LI is non-immunological reaction that's being high in dark skinned population with limited symptoms of gastrointestinal tract. LI and CMA incorporate more complex meaning than the past and their confusion leads to delay in diagnosis of CMA. LI can be managed by reducing the intake of lactose quantity but CMA can only be managed by avoiding the cow milk as strictly as possible.

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