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Research Article

**STUDYING THE INTOLERANCE AND MALABSORPTION OF
LACTOSE FOCUSING ON TREATMENT ALONG WITH
FUTURE ASPECTS**¹Dr Humaira Ilyas,²Dr Saira Sundus,³Dr Mamuna Ayub,^{1,2}MBBS, Services Institute of Medical Sciences, Lahore.³MBBS, Nawaz Sharif Medical College, Gujrat.**Article Received:** October 2020 **Accepted:** November 2020 **Published:** December 2020**Abstract:**

Milk is a vital part of the diet of every mammal but this leads 70% of the World's population to suffer lactose intolerance. In lactose intolerance LPH (Lactase-phlorizin hydrolase) level is low in the intestine which is not sufficient to break lactose into a simpler form, β -galactosidase which is present on the upper surface of microvilli of the small intestine is also responsible for the hydrolysis of lactose. Lactose is a disaccharide that needs to be hydrolyzed in the presence of lactase enzyme otherwise it may lead to severe clinical conditions categorized by flatulence, abdominal distension, Crohn's, ulcerative diseases, and diarrhea. It is due to recessive autosomal gene and varies from population-to-population Lactose intolerance has four types; primary, secondary, developmental, and cognitive lactose intolerance. Lactose malabsorption leads to lactose intolerance as the undigested lactose present in the gastrointestinal tract cause severity. Lactose intolerance can be diagnosed by testing but among all of them, genetic tests and human blood tests are consistent and economical. For lactose intolerance patients therapeutically interventions and probiotic foods articulating β -galactosidase were recommended because it hydrolyzed the indigestible lactose to digestible lactic acid. Additionally, supplemented plant-based milk can be used as a substitute of milk which can fulfill the daily recommended allowance of calcium and vitamins. This article aims to provide coherent knowledge on lactose intolerance, lactose malabsorption, and to articulate the supplementary diet for lactose-intolerance patients from the latent use of probiotic strains.

Corresponding author:**Dr. Humaira Ilyas,**

MBBS, Services Institute of Medical Sciences, Lahore.

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INTRODUCTION:

Dairy products and milk is the necessary constituent of the human diet. According to the report of the World Health Organization, milk and its derivatives consumed widely in the developed countries about six billion people consider them as the center of their diet¹. Milk is a rich source of protein, essential minerals, vitamins, fats, and many micronutrients. Milk is a rich source of vitamin A, D, and calcium. The proteins including whey and casein are present abundantly in milk. For mammals, milk is considered crucial as they fed on their mother's milk which has all healthy macronutrients required for nourishment. It lacks only a few vitamins and iron otherwise it is a complete diet for growing adults along with food. Milk contains carbohydrates composed of lactose. Lactose is an oligosaccharide formed from the combination of glucose-galactose. Oligosaccharide supports the growth of probiotic bacteria like Bifidobacterium also known as gut bacteria necessary for normal gut functioning especially in the intestine of infants^{2, 3}. Lactose facilitates the absorption of manganese, magnesium, calcium, and phosphate by developing gram-positive intestinal bacteria. Lactose intolerance issue has been discovered since, the age of Hippocrates. Lactose is a disaccharide sugar that needs to be hydrolyzed by the lactase enzyme before absorption otherwise it may cause many diseases like gastrointestinal infections and diarrhoea⁴. Lactase enzyme hydrolyses the lactose sugar into a simpler form of glucose and galactose⁵. Lactose intolerant patients were reported in South Africa suffering diarrhea, nausea, and flatulence⁶. Recent studies have defined lactose intolerance as a syndrome that is mainly categorized by the pain in the gastro intestine while lactose malabsorption and maldigestion both are the subclinical conditions

Mechanism of Lactose Malabsorption

Lactose is the constituent of rare plant species. The metabolism of lactose involves some particular individuality. Biochemically lactose synthetases subunit A (human galactosyltransferase) is not enough efficient to synthesize lactose in the human body so, for the efficient synthesis of lactose glucose need subunit B because in the female the lactose synthesis needs hormonal adjustment which includes a decreased proportion of progesterone and increased rate of prolactin⁷. Lactose absorption is directly interconnected with the lactase enzyme. Lactase is β -galactosidase by nature which is present on the upper surface of microvilli's enterocytes in the small intestine and multiplies to medium jejunum. The bacterial meditation is low in the medium jejunum so therefore less fermentation arises over there⁸. Lactase hydrolyses the oligosaccharide to two

monosaccharides which is a simpler form of galactose and glucose absorbed by the enterocytes that are present on the upper surface of microvilli. Glucose is utilized in the form of energy that is required for the normal functioning of the human body while galactose is utilized in the form of conjugated glycolipids and glycoproteins. Lactose intolerance, lactose malabsorption, and maldigestion are three different terms so they should not be mingled with each other. Lactose maldigestion occurs when disaccharide is not assimilated appropriately as lactase is deficient while lactose malabsorption is when the undigested form of disaccharide cannot be absorbed by the body. During the period between conception to delivery, lactase concentration is changing timely. When eight weeks of gestation is ongoing the lactase is present all over the small intestine's mucous membrane of the baby and as the time passes it increases till about 34th week of gestation, then lactase concentration attained its peak at the time of birth⁹. After birth, within a few weeks of life, the concentration of lactase started to decline or even vanished. The lactase concentrations vary from person to person in human's adulthood similarly in all mammals the concentration of lactase varies from normal range to completely decline. To normalize this condition two main aspects have made this conceivable which include the perseverance from dairy culture by a mutation in lactase and the other one includes lactic acid bacteria (LAB) association that make it digestible by hydrolyzing indigestible lactose into simpler lactic acid which is easily absorbed by organism¹⁰. In the Northern European population lactose intolerance issue is exceedingly reported so, to overcome this issue mutation of lactase in adults by perseverance from dairy culture is preferred as from a biological aspect, 50-52% lactase action is enough for normal digestion of lactose².

Genetic Morphology and History

The mammals have a distinctive feature that makes them exceptional for all others that is milk production. The mammary glands present in them are responsible for the production of milk to feed their young ones¹¹. Breastfeeding is a protective, healthier, and nourished way for the normal growth and development of infants. About 1928 amino acids combined to form lactase-phlorizin hydrolase which is the lactase enzyme of the small intestine. On the small strand of chromosome 2 LCT genes is present which encoded this enzyme. This enzyme performs two purposes of which one is phlorizin hydrolase function and the other is lactase hydrolase function. Phlorizin hydrolase function is to break hydrophobic alkyl chains so that from them beta-glycosides can be separated while lactase split substrates of cellotetrose,

cellulose, cellotrioses, and cellubiose¹². The lactase diligence or non-diligence is profoundly related to SNP (single nucleotide polymorphism) in the Caucasian population. This can be used as a tool to predict the mutation in the genotypes as it is reported by Caucasians that some genes like TT.CT and CC show some mutations which ultimately resulted in the cause of lactose malabsorption, maldigestion, intolerance, and hypolactasia. The CT genotype is responsible for the intermediary level of lactase countenance which is considered normal for the absorption of lactase but in lactase malabsorption, this heterozygous genotype results negative. The CC genotype is considered as the prognosticator of hypolactasia as it is associated with a diminishing level of lactase in the intestine¹³. The studies have declared that only one allele is responsible for lactase persistent activity which is present on the lactase mRNA of heterozygous genotype. According to Finnish population cases, they declared that LCT (lactase gene) shows polymorphism in G/A-22018 genotype while in Saudi Arabia it is G-13915 that displays polymorphism with lactase perseverance, and in African tribes, it is considered G-13907, G-14010, and G-13915¹⁴. The overall result indicates that lactase activity is independent as it varied from population to population⁹.

Mechanism of Lactose Intolerance

Primary lactase deficiency leads two-third of the World's population to suffer from lactose intolerance as the lactase synthesis is decreased¹⁵. About 40 cases of infant's primary and secondary lactase deficiency have been reported in Finland¹⁶. Adult-type Hypolactasia or primary lactase deficiency is caused when the lactase enzyme started declining in adults of age 2-5 years due to non-perseverance of lactase while Secondary hypolactasia is forfeiture of lactase enzyme causing Crohn's, ulcerative diseases (inflammatory bowel diseases), acute malnutrition, bacterial or viral enteritis, celiac disease, short bowel syndrome, stagnant loop syndrome and use of chemotherapeutic drugs (polymycin, kanamycin, and tetracycline, etc.) due to clinical conditions^{17,18,19}. Lactose malabsorption leads to lactose intolerance as the undigested lactose present in the gastrointestinal tract cause severity. In lactose intolerance firstly intestinal water content increases due to osmotic pressure which leads to acute diseases.

Symptoms of Lactose Intolerance

In lactose intolerance, the indigestible lactose has generated osmotic pressure due to which it energies fluid into the lumen of the gut which ultimately leads to osmotic diarrhea. Volatile fatty acids and gases including carbon dioxide, hydrogen and methane

were produced by gut microbiota lead to clinical symptoms. About 25% of the population reported symptoms other than clinical are vertigo, headache, lethargy, and memory impairment due to carbohydrate intolerance^{20, 21}. Lactose test outcomes in combination with other foods do not reflect the actual daily consumption of lactose. In Asian countries, cases were reported in which the dairy protein 'casein' is considered as the cause of lactose intolerance due to the variety of casein protein as there are many cow's varieties and so have different gene type. This difference leads to different casein production A1 and A2 (Asian cow's casein). It is reported that the A1 casein is responsible to induce motility and disturb the gastrointestinal tract causing abdominal pain as it interacts with the μ receptor of the intestine. The role of casein vary from population to population^{22,23}.

Diagnosis

Lactose breathing test and Anamnesis is considered as the core diagnosis of adult-type lactose intolerance²⁴. The test involves the measurement of hydrogen exhaled from the breath; it is a non-intrusive rapid test. In children, 1g/kg dose of lactose is managed. After half day of fasting about 500mg of milk (25g) is recommended and considered as a normal range of usage²⁵. For non-alveolar erosion of exhaled air, the concentration of carbon dioxide and oxygen should be measured accurately in all inhalation tests. To check the accuracy of the test the concentration of methane should be considered because for the researcher it gives a precise estimation about hydrogen concentration. After all, if the concentration of methane is greater than ten parts per million then the hydrogen test resulted in positive. The most efficient and reliable test is LTT (lactose tolerance test). The susceptible patient with lactose intolerance has given 50g of dissolved lactose and then the plasma glucose concentration test is performed from time to time. When the plasma-glucose level is 1.4mol/L then the lactose intolerance test is positive this test is not so much reliable because the glucose level of blood keeps fluctuating²⁶.

Future Aspects

Probiotics or Gut microbes are defined by the World Health Organization as microorganisms that benefit the gut health and express beta-galactosidase activity which helped in the absorption of lactose²⁷. A lactose perseverance person confronted dairy food as well as lactose encounter while lactose non-perseverance person needs to eradicate dairy foods from his diet. In this contemporary era, advances have been made and paved the path towards dairy food substitutes²⁸. In

western countries dairy is considered to be a rich source of calcium that is essential for bone development so for them the innovative products that are the substitute them introduced in the market²⁹. Fermented foods are considered healthier and suggested for lactose intolerant patients because these are a rich source of gut microbiota which hydrolysis lactose e.g. yogurt, tofu, lassi, and fermented milk. Bifidobacterium and Lactobacillus are the most common probiotics in foods and this has paved a pathway for probiotic-foods because lactose intolerance issue is alleviating day by day such food supplement would help to enhance the lifestyle of patients. Prebiotic-foods will develop the strongest prospective for effective probiotics use^{30, 31, 32}.

CONCLUSION

In the contemporary era, lactose intolerance comprehends an intricate meaning than in past. People may confuse the terms lactose intolerance, lactose malabsorption, and lactose maldigestion all of them are interrelated to lactose intolerance but still is the difference and their role varied from population to population. Although the lactose tolerance issue is continued for ages still it is becoming an alleviating issue that needs further research and advanced diagnosis. Many tests were performed but all of the genetic tests and human blood tests are consistent and economical. For lactose intolerance patients therapeutically interventions and probiotic foods articulating β -galactosidase were recommended because it hydrolyzed the indigestible lactose to digestible lactic acid. The studies revealed that still the outcomes of probiotics on lactose intolerance are comprehensive so advance careful studies are required to reconnoiter potential of probiotics.

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