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Review Article

Lactose Intolerance in Sub-Saharan Africa

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Summary: Lactose is a disaccharide mainly found in dairy and dairy-containing products which yields D-galactose and D-glucose on hydrolysis. Lactose intolerance (LI) is characterized by abdominal pain, bloating, flatulence, nausea and/or diarrhoea following ingestion of dairy or lactose-containing meals. LI affects about 75% of the world's population though the condition is poorly recognized despite being of great public health significance in sub-Saharan Africa (ssA). The aim of the review is to highlight the epidemiology, types, pathophysiology, genetics, diagnosis, management and prevention of LI. Literature search was performed using Pubmed, Crossref and Google Scholar data bases for the terms lactose, lactose consumption + lactose intolerance, sub-saharan Africa. The high prevalence of LI in most countries of ssA is a major cause for concern with malnutrition as an independent entity serving as a key contributor especially among children. Differential diagnosis for LI poses a huge challenge due to disparity in presentation of symptoms among individuals and unavailability of testing in most routine laboratories in ssA. Though wide variation in prevalence of LI exists between countries and regions within ssA, recognizing regional patterns of LI is important to guide prevention, diagnosis and management of the condition. There is also need for increased laboratory vigilance and preparedness to tackle the silent epidemic especially in ssA.

Keywords*: Lactose Intolerance, Epidemiology, Pathogenesis, Diagnosis, sub-Saharan Africa.*

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INTRODUCTION

Lactase is an enzyme produced by cells situated in the microvilli of the small intestine which hydrolyses dietary lactose into galactose and glucose for transport across the cell membrane. In the presence of osmotic pressure and deficiency or absence of lactase, unabsorbed lactose causes an influx of fluid into the bowel lumen, and as a result, unabsorbed lactose then enters the colon and is used as a substrate by intestinal bacteria, producing short-chain fatty acids and gas via fermentation. Since the fatty acids cannot be absorbed by the colonic mucosa, more fluid is drawn into the bowel. A proportion of the lactose can be absorbed, but the overall result of ingestion is a substantial rise of gas and fluid in the bowel, causing the symptoms of lactose intolerance (LI) (Misselwitz *et al*., 2019). Although lactase expression is not up-regulated by lactose ingestion, tolerance could be induced by adaptation of the intestinal flora (Deng *et al*., 2015).

Symptoms of LI usually occur between 30 minutes and a few hours after the ingestion of lactose though severity of symptoms can be influenced by the amount of lactose consumed, degree of lactase deficiency, and the form of food substance in which the lactose is ingested; typically, the more lactose consumed, the more frequent or severe the symptoms (Jansson-Knodell *et al*., 2020). LI denotes the emergence of gastrointestinal symptoms predominantly, abdominal cramps, nausea, vomiting, bloating and/or diarrhoea, after the consumption of lactose-rich food items (Shafi and Hussain, 2022). Some individuals may experience dyspepsia, flatulence, borborygmi or abdominal distension post consumption (Misselwitz *et al*., 2019). Less commonly it may present with a range of systemic symptoms like urinary difficulties, loss of concentration, headaches, muscle and joint pain, fatigue and mouth ulcers though it is unclear whether these atypical symptoms are related to the presence of functional diseases or directly due to lactose ingestion (Deng *et al*., 2015). In the general population, symptoms are often non-specific, mild and vary between individuals (Bridges, 2018; Misselwitz *et al*., 2019).

The prevalence of LI varies with ethnicity and is related to the use of dairy products in the diet which subsequently results in genetic selection of individuals with the ability to digest lactose. Globally, the estimated prevalence of lactose intolerance exceeds 65% (Catanzaro *et al*., 2021) with about

70% of the world's population having primary lactase deficiency (Heyman, 2006) and approximately 75% losing the ability to digest lactose at some point, while others digest lactose into adulthood (Sambasivarao *et al*., 2022). The prevalence of LI in ssA countries is between 34-100% (figure 1). Despite the high prevalence worldwide, adopting a standard diagnostic procedure remains a major challenge. Differences in diagnostic criteria and methodology have obscured the global adoption of a "gold standard" in the diagnosis of LI. The review aims to highlight the epidemiology, types, pathophysiology, genetics, prevention, management and guide laboratory diagnosis of LI in ssA.

Figure 1:
Estimated Prevalence of Lactose Intolerance in ssA

EPIDEMIOLOGY

LI is the commonest form of food intolerance that does not involve immunological mechanisms and reported to allegedly affect more than two-thirds of the world's population (Queiroz *et al*., 2019). Most individuals are born with the ability to digest lactose which is the main source of nutrition until weaning and can ingest up to 20g of lactose or 12oz of milk daily without symptoms (Sambasivarao *et al*., 2022). Depending on the ethnic group, the enzyme activity gradually decreases from 2-5 years (Shafi and Hussain, 2022) or during the first 10 years of life except among those with a highly conserved mutation in the promoter region of the lactase gene (Storhaug *et al*., 2017). Variations in prevalence have been reported not only within countries but also between countries (Storhaug *et al*., 2017). The prevalence of LI varies according to ethnic characteristics and age with most causes being genetically determined (Queiroz *et al*., 2019; Shafi and Husain, 2022). Epidemiological studies report highest rates of LI among populations that historically consumed agricultural products as the main source of food since their early stages of survival (Wortmann *et al*., 2013). High prevalence of LI in certain populations is explained by two hypotheses. The first hypothesis upholds that alleles for lactase enzyme persistence were rare until the beginning of the consumption of dairy products, and unfermented milk and as a result, natural selection increased those allele frequencies. The second hypothesis advocates that alleles of LCT gene for a persistent phenotype which favored the acquisition of the habit of consuming milk and its derivatives were already present from the outset (Burger *et al*., 2007; Itan *et al*., 2009; Krüttli *et al*., 2014).

TYPES

There are various forms of lactase deficiency that can result in lactose intolerance; developmental lactase deficiency, congenital lactase deficiency, primary lactase deficiency and secondary lactase deficiency.

a. **Developmental Lactase Deficiency;** This is a type of lactase deficiency that occurs in pre-term/premature infants of less than 34 weeks of gestation due to underdevelopment of the infant intestines resulting in inability to hydrolyze lactose (Talia and Kiran, 2023). It largely arises from congenital deficiency of lactase and other disaccharidases, typically temporary and rapidly improves as the intestinal mucosa matures (Coutis, 2013).
b. **Congenital Lactase Deficiency;** It is otherwise known as alactasia and occurs due to the inheritance of the two defective alleles of the lactase (LCT) gene and the condition worsens due to the loss of nutritional components, and often leads to delay in growth, dehydration, and alkalosis (Shafi and Husain, 2022). It is a life-long genetic condition involving the complete deficiency of lactase expression from birth, despite having an otherwise normal intestinal mucosa. Congenital lactase deficiency is an extremely rare disorder with an unknown incidence reported in only a few infants (Heyman, 2006). Fewer than 50 cases have been reported globally with a higher frequency in Finland, where about 1 in 60,000 newborns are affected by this disorder (Shafi and Husain, 2022). Affected newborn infants present with intractable diarrhoea as soon as human milk or lactose-containing formula is introduced and if not recognized and treated quickly, the condition becomes life-threatening due to dehydration and electrolyte loss risk. Treatment is simply removal and substitution of lactose from the diet with a commercial lactose-free formula (Heyman 2006).

c. **Primary Lactase Deficiency:** Primary lactase deficiency (PLD) is regarded as the commonest "genetic disease" and predominant cause of LI caused by the non-persistence of β-galactosidase (Bayless *et al*., 2017). About 70% of the world's population have PLD resulting from genetically programmed decrease in lactase synthesis after weaning (Heine *et al*., 2017; Misselwitz *et al*., 2019), with global estimates reporting a prevalence of about 80% in the Black population (Cantazaro *et al*., 2021). The age of onset of PLD differs among populations due to decrease in lactase enzyme activity with increase in age (Heyman,

2006). The enzyme activity usually begins to decrease during childhood and symptoms manifest in adolescence or early adulthood (Talia and Kiran, 2023) though acute development is also possible.

d. Secondary Lactase Deficiency; The deficiency arises due to medical conditions mainly influencing the intestinal tract hence infections that affect the microvilli result in the loss of enzyme synthesis since the enzyme is secreted from the edge of the duodenum (Shafi and Husain, 2022). The ephemeral nature of SLD is caused by modification of the intestinal mucosa which leads to lactase expression reduction and lactase deficiency with resultant lactose malabsorption which may resolve after one to two months but may be permanent if caused by a long-term underlying condition (Heyman, 2006)

Medical conditions that may cause secondary hypolactasia include Crohn disease, enteropathies, bacterial, actinic or viral enteritis, celiac disease, severe malnutrition, inflammatory bowel diseases, certain medications that can cause villous atrophy such as chemotherapeutic drugs, antibiotics like neomycin, aminoglycosides, kanamycin, tetracycline and polymycin (Fassio *et al*., 2018; Asfari *et al*., 2020).

BIOCHEMICAL AND GENETIC PERSPECTIVES

a. The Unique Nature of Lactose Sugar; Lactose is the major disaccharide carbohydrate in milk occurring as β-D-Galactopyranosyl-(1→4)-D-glucose. Hydrolysis of lactose in the intestinal tract produces galactose and glucose that are absorbed into the enterocytes as sources of energy and structural elements. It has variable concentration depending on the species but exclusively found in milk of mammals. Human milk contains about 7g of lactose while other mammals such as cow and sheep contain 4.8g each and goat has 4.1g per 100 mL of milk respectively (Rossi *et al*., 1997).

b. The Lactase-Phlorizin Hydrolase (LPH) Enzyme: Lactose hydrolysis is catalyzed by lactase-phlorizin hydrolase (LPH) (EC 3.2.1.108–EC 3.2.1.62), located in the brush border membrane of small-intestinal enterocytes. LPH is expressed only in the small intestine and restricted to absorptive villi enterocytes. The site restriction control of LPH in the enterocytes is revealed by a tightly controlled pattern along the proximal-distal axis in all mammals with high levels in mid-jejunum and low levels in the duodenum and distal ileum (Naim, 2001). The enzyme is a trans-membrane glycoprotein with molecular weight of 160 kDa, having a C-terminus (26 amino acid) intra-cellularly and an N-terminus at the luminal surface of the lipid bilayer of the microvillus membrane of enterocytes. The trans-membrane-spanning region constitutes of 19 hydrophobic amino acids short sequence. It is a multifunctional specific enzyme catalyzing primarily lactose and other substrates such as phlorizin, cellobiose, lactosylceramide, cellotriose, and flavonoid glucosides. The enzyme has a four-fold internal homology designated as I, II, III and IV domains assumed to be due to two independent duplication events during evolution (Boll *et al*., 1991; Montgomery *et al*., 2007). Domains I and II are not glycosylated and observed to regulate protein folding in the endoplasmic reticulum having no enzymatic activity while III and IV are deeply glycosylated containing a glutamate residue in each nucleophile at the two active sites. The amino acid sequence around the active site glutamic acid (E) in domain III is PIYITENG while that of domain IV is PIYVTENG. First, embryonic LPH (195 kDa) is synthesized in the endoplasmic reticulum and undergoes co-translational, dolichol-dependent, high-mannose glycosylation, yielding a molecular mass of 215 kDa. In the golgi, complex glycosylation of domains III and IV occur, yielding a structure of 220kDa (N-glycosylations in asparagine and O-glycosylations in threonines and serines). The glycosylation plays a role in the enzymatic activity as well as folding and ease of intracellular transport (Naim and Lentz, 1992). The subsequent cleavage of a small N-terminal pro-enzyme and of domains I and II protect the remaining molecule, which is inserted into the microvillus membrane. The final extracellular cleavage by pancreatic proteases re-orients the pro-enzyme producing the mature LPH enzyme (Segurel and Bon, 2017).

c. Biochemical Variability of Lactose in Milk: Milk contains the primary carbohydrate, lactose, synthesized by epithelial cells of mammary glands in mammals essentially for the development and nutrition of infants. The onset of lactose synthesis and its composition in milk varies between species and throughout lactation. Little is documented about the precursors, genes, proteins and ions that regulate lactose synthesis (Mattar *et al*., 2012). Human infants receive about 40% of their caloric requirements from the approximately 70 g/d of lactose they consume in the first six months of life (Segurel and Bon, 2017).

Lactose variability has become an interesting aspect in milk production and constitutes over 80% of total carbohydrate of most placental mammal comprising of glucose and galactose. There is a negative relationship between the content of lactose and fat in milk, this variability ensures the offspring receive a steady source of calories accordingly (Buller and Grand, 1990).

d. Genetic Basis of Enzymatic Defect in LI: It is believed that humans have the ability to digest milk lactose because they possess the β-galactosidase enzyme, lactase-phlorizin hydrolase (LPH). In majority of humans after weaning, the levels of the enzyme declines and the condition is referred to as lactase non-persistence (LNP) while few individuals that sustain high levels of LPH can digest milk into adult hood and the condition is called lactase persistence (LP) (Priehodova *et al*., 2017). LP alleles have spread through migration and show strong signals of selection (Gerbault, 2013). Though LNP is a familial condition for humans, domestication of animals for diary purposes contributed to LP alleles spread among early populations (Wiley, 2020). However, populations who consume dairy products with reduced lactose content have lower incidences being reported.

The LPH enzyme, with highest levels of activity during the lactation period, is encrypted by the lactase (LCT) gene, located on chromosome 2q21 mainly expressed in the apical part of microvilli within the brush border membrane of enterocytes (Montgomery *et al*., 1991). LP can be independently caused by single nucleotide polymorphisms (SNPs) ranging from 5 to 18 or more in a regulatory region

called minichromosome maintenance complex component 6 (MCM6), which is located upstream of the LCT gene (Troelsen *et al*., 2003; Fang *et al*., 2012). The percentage LP haplotype globally is approximately 35%, with the lowest frequencies present in ssA and southeast Asia (Hassan *et al*., 2016).

Migration events have played a role in the geographic distribution of LP-associated variants in Africa (Campbell and Ranciaro, 2021) with the LI phenotype polymorphism responsible for natural selection in many communities (Queiroz *et al*., 2019). LI though common in pastoralist populations from Africa (~50% in Fulani, ~90% in Tutsi), has an estimated prevalence between 5%–20% among West African agriculturalists (Deng *et al*., 2015). The major variants C/G-13907 and T/G-13915, among the Beja of East Africa, show remarkable frequencies in Sudanese populations, especially those of pastoralists, in line with the historical links and nomadic populations bidirectional migration between East Africa and Arabia. The C/T-13910 variant, commonly linked with European populations is also uniquely present among the Fulani (Hassan *et al*., 2016). The C14010 allele which is thought to have originated from eastern Africa is present in Bantu- and Khoisan speaking pastoralist groups in southern Africa (Campbell and Ranciaro, 2021).

e. Polymorphic Defect of LCT gene in LI: Located on chromosome 2q21 and comprising 17 exons, the human LCT gene encodes 1927 amino acids from the initiation to the stop codon and covers about 49kb with a resultant mRNA of more than 6kb thereby forming a complete translation product. Initially, several genetic variants were identified within the coding region and the 50-flanking region but observed to show no significance (Boll *et al*., 1991). Certain mammals including man, mouse, rat and pig are reported to have identical sequence of their first 100 bp of the proximal LCT promoter with similar regulatory pattern. The binding sites for GATA, hepatocyte nuclear factor 1-α (HNF1-α), caudal type homeobox 2 (Cdx-2) and transcription factors are positioned relative to the transcriptional start site (Boudreau *et al*., 2002; Anguita-Ruiz *et al*., 2020). Other transcription factors such as HOXC11 (homeobox C11), HNF-3, FREAC-2/3 (fork-head box F2) and C/EBP (CCAAT/enhancer binding protein) are reported to interact with the LCT 50-flanking sequence with some in the more distal loci (Mitchelmore *et al*., 2000; Anguita-Ruiz *et al*., 2020). Exon 17 of MCM6, function as a regulatory enhancer of LCT in the cell cycle ending 3.5 kb from the start site of the human LCT gene. The transcriptional start site of the MCM6 gene is located approximately 39 kb 5' of the LCT transcriptional start site (Harvey *et al*., 1996; Mattar *et al*., 2012).

f. Lactase Phenotypes and Epigenetics Alterations: The LI phenotype is a polymorphism naturally selected to promote survival of most populations globally (Queiroz *et al*., 2019). The LP mutation was first reported in 2002 with its alleles recording 14 kb upstream of the LCT gene and not within, or immediately upstream, of it. The reported variants in Middle East and Africa were i) -13910:C>T (rs4988235), ii) -13907:C>G (rs41525747), iii) -13915: T>G (rs41380347), iv) -14009: T>G (rs869051967) and v) -14010: G>C (rs145946881) with variable frequencies (Enattah *et al*., 2002; Ingram *et al*., 2007; Anguita-Ruiz *et al*., 2020). Additional eighteen genetic SNPs markers were also recorded that map the MCM6 and are also associated with LP.

Ingram *et al*., (2006) reported that neither the -13910*T allele nor the A haplotype (LCT core haplotype), upon which it resides, account for lactase persistence even after resequencing the 13.9 kb region. The association of the phenotype of LI with these genotypes has recently been confirmed for African populations (Ranciaro *et al*., 2014). Other mechanisms including epigenetic modifications in histone proteins and DNA may be responsible for LNP and LI in addition to gene mutations (Cantazaro *et al*., 2021).

PATHOPHYSIOLOGY AND DISEASE PRESENTATION

For several decades, detection, description, and diagnosis of lactose malabsorption has been multidirectional and non-specific which has resulted in confusion among physicians and patients. Evidently, it is not possible to make a definitive diagnosis based on clinical presentation of LI alone due to the poor association between self-reported lactose intolerance and the occurrence of symptoms even after ingestion of lactose in patients with lactase deficiency (Deng *et al*., 2015).

Lactose intolerance is the manifestation of a physiologic disorder known as lactose malabsorption which is due to a disequilibrium between quantity of ingested lactose and ability to hydrolyze the disaccharide by lactase (Heyman, 2006). Two physiological processes are involved; firstly, the increased osmotic load increases the intestinal water content. Secondly, lactose is readily fermented by the colonic microbiome leading to production of gas and short chain fatty acids primarily carbon dioxide (CO2), hydrogen (H2), and methane (CH4) though these biological processes are present also for other poorly-absorbed, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) that are found abundantly in diets. The unabsorbed lactose being present in the intestinal tract as a result of lactase deficiency has effects that can lead to symptoms of lactose intolerance such as osmotic or secretory diarrhoea and gas in susceptible individuals (Deng *et al*., 2015).

Although the link between infectious diarrhoea and secondary LI has been reported, the epidemiological data to validate this linkage is surprisingly rare (Harvey *et al*., 2018). A review of studies that clearly reported the global burden of secondary LI in relation to other diseases like childhood diarrhoea and pneumonia in children younger than five years showed the highest incidence and severity burden for these diseases were present in Africa and Asia though the studies were not performed in these regions (Walker *et al*., 2013).

SCREENING METHODS/DIAGNOSIS

There are numerous screening methods for diagnosing LI. Diagnostic investigations available include physiological challenges/tests, genetic and endoscopic investigations.

i. **Lactose Tolerance Test (LTT):** This is an indirect method based on the fact that lactose is broken down into

glucose and galactose by lactase (Law et. al., 2010). The method is therefore influenced by physiologic response to glucose (Sendino *et al*., 2020). Serial draws of blood samples are taken after ingestion of standard 50g lactose in adults. In children, 2g/Kg body weight is given, at a maximum of 25g (Scrimshaw and Murry, 1988). Blood glucose levels are checked at baseline, 60- and 120-minutes following ingestion of lactose. Blood glucose levels rising by less than 20mg/dL (<1.1mmol/L) compared to the baseline in addition to presentation of such symptoms as; bloating, diarrheoa and abdominal pain are diagnostic of LI (Alihashemi et. al., 2020).

ii. **Hydrogen Breath Test (HBT):** It is the commonest indirect approach for diagnosing LI. The intestinal flora ferments undigested lactose to methane, carbon dioxide and hydrogen gas which are eliminated via the lungs. HBT is based on the increase in expired hydrogen gas after lactose challenge. A standard dose of lactose, usually 20-50g is given orally to the patient (Misselwitz *et al*. 2019). Baseline respiratory/expired hydrogen gas is recorded followed by recording changes at 30 minutes interval (Bridges, 2018). Expired hydrogen gas levels greater than 20ppm (parts per million) compared to baseline within 3hrs of ingestion is diagnostic of lactose intolerance (Sendino *et al*., 2020 and Alihashemi *et al*., 2020). HBT has a sensitivity and specificity of 78% and 98% respectively (Gasbarrini *et al*., 2009). Thus, having the most diagnostic efficiency. HBT is not recommended for subjects with baseline hydrogen gas >20ppm. The method is greatly affected by colonic flora (Szilagyi *et al*., 2009) and as a result, bacterial overgrowth may lead to false positive results. On the other hand, intake of antimicrobials few days to the test procedure and subject's inability to produce hydrogen gas may result in false negative results and subjects must refrain from cigarette smoking and exercise 2hrs to the test in order to prevent hyperventilation and ensure accuracy of the results.

iii. **Endoscopic Biopsy:** The method involves assessment of lactase activity in a biopsy specimen of jejunum and duodenum (Bridges, 2018; Sendino *et al*., 2020) for the diagnosis of primary and secondary lactase deficiency (Matter *et al*., 2012; Deng *et al*., 2015; Bridges, 2018). The method has an estimated diagnostic sensitivity and specificity of 96% and 100% respectively (Kuokkanen *et al*., 2006 and Marton *et al*., 2012). Low lactase activity in the small bowel (jejuna/duodenal) biopsy is confirmatory for lactose intolerance (Scrimshaw and Murry, 1988).

The limitations of endoscopic biopsies are that no assessment of symptoms is made which impacts on the clinical relevance of these investigations because, only a proportion of subjects with lactase deficiency develop abdominal symptoms after ingesting glucose. The invasiveness of the test poses a huge limitation due to inhomogeneous expression of lactase across the epithelium (Deng *et al*., 2015) thereby making assay unavailable in many service laboratories (Harvey *et al*., 2018)

iv. **Genetic Testing:** Single nucleotide polymorphism cytosine (C)/thymine (T) upstream of the lactase gene is considered in the genetic testing for hereditary lactase persistence. The C/C genotype is lactose intolerant while the C/T or T/T genotypes are lactose tolerant. This method is costly compared to those described above. It involves the use of genotyping to assess lactase deficiency and often based on C/T-13910 polymorphism though other possible polymorphisms resulting in lactase deficiency can be found. The limitation of this method is it can only identify subjects with primary cause of gene under expression, but not hypolactasia caused by other conditions (Szilagyi *et al*., 2007; Bridges, 2018).

v. **Faecal pH Test:** This is a non-specific marker for lactose (or other carbohydrate) malabsorption. A pH of < 6.0 suggests lactose intolerance. The test is mostly recommended for infants below 2 years of age because of the high rate of false negative results.

vi. **Faecal Reducing Substances:** This is an indirect test for lactose (or other carbohydrate) malabsorption occasionally considered in the context of secondary lactose intolerance where a gastroscopy is being performed to determine an underlying cause (e.g., coeliac disease, Crohn's disease, protracted diarrhoea). Absence of the corresponding enzyme indicates a positive test. Nonetheless, if an individual has not ingested lactose recently a false negative report can be obtained. Inappropriate stool collection may make results of reducing substances inaccurate (Harvey *et al*., 2018).

vii. **Quick Lactose Intolerant Test (QLIT):** QLIT consists in execution of mucosal biopsies at the post-bulbar duodenum level and their subsequent incubation with lactose on a test plate. The incubation confirms the presence or absence of lactase activity. if there is a slight hypolactasia, there will be a light blue-coloured reaction; if lactase activity is present, a dark blue–coloured reaction occurs; if no staining develops, it is indicative of severe hypolactasia (Kuokkanen *et al*., 2006). The method, despite its high sensitivity, has some limitations, including high cost and invasiveness, and the size of biopsies which, if shorter or larger than 2 mm, may give false-positive or false-negative hypolactasia, due to patchy expression of lactase. Due to the bioptic nature, the method is conditioned by the patient's clinical conditions and coagulation (Mattar *et al*., 2013; Misselwitz *et al*., 2019).

Some quick test kits/point of care testing devices for diagnosis of LI are commercially available which support diagnosis by detecting activity of lactase from a biopsy specimen taken via gastroscopy from the upper small intestinal mucosa. The principle is based on a simple color change which is compared with a reference colour scale incorporated in the product package, lactase activity is detectable in 20 minutes. Severe and mild hypolactasia can easily be differentiated by this approach. The test uses a positive lactase control for daily verification of the performance of this test.

viii. **Gaxilose Test:** This non-invasive test consists of administration of a synthetic disaccharide that has a structure similar to lactose i.e. Gaxilose (4-O-β-D-galactopyranosyl-D-xylose). Similar to lactose, Gaxilose is also metabolized by lactase in the intestine and a molecule of galactose and one of xylose are derived, which are absorbed by enterocytes. Subsequently, measurement of xylose in the blood and urine, is carried out to quantify lactase activity (Hermida *et al*., 2006). The Gaxilose test is easy to use, non-invasive, well tolerated and does not cause discomfort to the subjects (Aragón *et al*., 2014; Monslave-Hernando *et al*., 2018).

If a dietary challenge proves inconclusive, alternative investigations and diagnoses should be considered, including stool examination if parasitic infestation is suspected and blood tests such as anti-tissue transglutaminase antibody, total immunoglobulin A concentration and quantitative immunoglobulins if coeliac disease or immunodeficiency is queried. These investigations along with others should be readily available in ssA to increase vigilance and preparedness of laboratories in the sub region.

Till date, no specific ideal diagnostic conditions or gold standard test has been independently singled out for LI region. Therefore, a combination of the above tests, though may be more costly and invasive, have been suggested to be most reliable. Despite the challenges, laboratory diagnosis for LI can still be performed with minimal resources. Hence the need for incorporating LI laboratory testing into clinical routine practice in the ssA sub region.

MANAGEMENT AND PREVENTION

Lactose intolerance (LI), although has a genetic basis, is also connected to culture and cultural dietary practices (Li *et al*, 2023) which is the basis of the expedience of examining the situation in ssA and the need for health care professionals to be vigilant. Inadequate indigenous population studies exist in most of SSA where dietary patterns vary from the rest of the world, especially from Caucasians leading to insufficient information that will inform epidemiological studies in ssA. Traditionally, low milk and milk products intake and high calorie intake is prevalent in most ssA. LI appears to parallel the increased consumption of milk and milk products with the embracing of Western Diet with some African regions consuming high calorie diet and low milk, presenting with low prevalence of LI (Redvers, 2019).

Although the medical basis of milk intake is essentially to ensure bone health and prevention of osteoporosis, calcium may be obtained from alternative sources to avoid LI. Understanding the above determinants are important for the management and prevention of LI and will involve understanding of population genetics, need for cultural balance and decreased frequent milk product consumption. Eliminating milk from modern ssA diet is not feasible, but a pragmatic approach including the reduction of the quantity of milk product consumed among others may be helpful. Indigenous food rich in calorie and micronutrient sources, and low in milk and milk products should be promoted. Importantly, as milk cannot be completely avoided, consumption should be proportionate to an individual's residual intestinal lactase activity. In addition to the laboratory medicine perspective, public health awareness must be raised. These will constitute the collective pragmatic approach to managing and preventing LI, although commercially produced enzymes are now available for individuals genetically deficient in lactase.

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