

Mini Review

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Why is there a High Prevalence of Lactose Intolerance in Brazil? - A Mini Review



Araújo Edilene Maria Queiroz^{1,2*}, Almeida Daniela Oliveira², Coutinho-Lima Claubert Radamés Oliveira², Santos Luama Araújo^{1,2}, Brandão Najara², Sacramento Joselita Moura³ and Vázquez Mírian Rocha⁴

¹Nucleus of Research and Extension in Nutritional Genomics and Metabolic Dysfunctions (GENUT), Life Sciences Department (DCV), University of the State of Bahia (UNEB), Brazil

²Interactive Process of Organs and Systems (PPGorgsystem), Health Sciences Institute, Federal University of Bahia, Brazil

³Nutritional Assistance Nucleus and Familial Hypercholesterolemia Research Center (NANPHF), Life Sciences Department (DCV), University of the State of Bahia (UNEB), Brazil

⁴Nucleus of Studies and Nutritional Orientation to the Athlete (NONA), Life Sciences Department (DCV), University of the State of Bahia (UNEB), Brazil

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***Corresponding author:** Edilene Araujo, Universidade do Estado da Bahia, Departamento de Ciências da Vida, prédio 1. Rua Silveira Martins, 2555, Postal code: 41000-150, Cabula, Salvador, Bahia, Brazil

Abstract

Lactose intolerance (LI) affects two-thirds of the population worldwide, and its prevalence varies according to ethnic characteristics. The aim of this mini review is to present and discuss the frequency of LI in Brazil, pointing out the importance to prevent the worst outcomes that LI may evoke. Our findings showed that there is high LI prevalence among Brazilians (>63%), and it is related to genetic programming inherited from different populations worldwide.

Keywords: Lactose intolerance; Adult-type hypolactasia; LCT gene; MCM6 gene; 13910C>T; Genetic programming; Small intestine; Enterocytes; Expiration; Abdominal pain; Flatulence; Diarrhea; Borborygmos; Gut bacteria

Abbreviations: ATH: Adult-Type Hypolactasia; LCT Gene: Lactase Gene; LE: Lactase Enzyme; LI: Lactose Intolerance; MCM6 Gene: Maintenance of Microsomal Type 6 Gene; OLTT: Oral Lactose Tolerance Test

Introduction

Lactose intolerance (LI) affects many people around the world, including in Brazil, and its prevalence varies according to ethnic characteristics [1]. One of the main causes of LI is the adult-type hypolactasia (ATH), which is characterized by a progressive reduction in the activity of the lactase enzyme (LE) from 2 years of age. By the time of adolescence, ATH individuals have only 5 to 10% of the activity levels found at birth [2]. ATH is genetically determined, non-transient and non-reversible, and has an autosomal recessive inheritance pattern [1,3].

When lactose is not properly hydrolyzed by small intestine enterocytes, it reaches the colon in its intact form. In the colon, fermentation of lactose by gut bacteria generates short-chain fatty acids and gases, such as methane, which may be eliminated as flatus or by expiration [4]. As consequence, there is an increase in intracolonic pressure as well as in intestinal transit, which leads to abdominal pain, flatulence, diarrhea, and borborygmos.

In some cases, LI individuals may experience constipation, probably due to the production of methane [4]. Besides the aforementioned symptoms that lead to great discomfort, ATH

may still be associated with diseases, such as colorectal cancer [5] and metabolic syndrome [6].

LI is the most common example of food intolerance that does not involve immunological mechanisms [7]. Although it allegedly affects more than two-thirds of the population worldwide, studies on its prevalence are scarce, mainly in Brazil [8]. Therefore, the aim of this mini review is to present and discuss the frequency of LI in Brazil, pointing out the importance to prevent the worst outcomes that may be evoked by this disturbance in a long term.

Methods

A focused search utilizing available articles at PubMed database was performed to examine information about LI

prevalence in different Brazilian ethnical groups as well as its history and epidemiology. It was only included ISSN numbered periodicals, or the ones that have a good impact factor.

Epidemiology and History of LI in Brazil

Epidemiological studies report that the highest rates of LI are among populations that historically consumed agricultural products as the main source of food since their early stages of survival [2]. Some of these populations are among the African countries, Latin America, southern Europe, Mediterranean region, southern Italy, Greece and also among Jews. In some Asian and in the Middle East countries, LI reaches almost 100% of prevalence [1]. In countries with great cattle farming activity and large dairy consumption, such as in Northern Europe, North America and Oceania, the frequency of LI is low among Caucasians, not exceeding 5% of prevalence [1,2].

There are two hypotheses to explain the high prevalence of LI in the world. The first advocates that alleles for LE persistence were rare until the beginning of the consumption of unfermented milk and dairy products, and, as time went by, natural selection increased those allele frequencies. In contrast, the other hypothesis affirms that alleles of LCT gene for a persistent phenotype were already present from the outset, and this fact favored the acquisition of the habit of consuming milks and derivatives [9-11].

Paleontological analysis of the DNA of the Neolithic and Mesolithic periods enabled some researchers to confirm the absence as well as a very low frequency of the LCT alleles

for persistent LE activity, which corroborates with the first hypothesis [9]. However, in a study that evaluated 794 chromosomes of people from several countries by performing an intra-allelic microsatellite variation, other authors suggested that the allele -13910T (persistent LE activity allele) of the MCM6 gene (maintenance of microsomal type 6 gene/LCT gene upstream region) was present before the Neolithic period [12]. The latter authors suggest that the allelic variants of LE persistence originated from different mutations that occurred independently in Europe and Africa. According to the authors, two populations has undergone a strong natural selection process to survive, due to the maintenance of milk consumption and its derivatives during adulthood [10,11,13]. Another recent hypothesis is that in regions where there was little sun exposure during the year (i.e. Northern Europe), there was a natural selection for LE persistence due to the requirement of vitamin D sources in the diet, and milk is known to be an important source of this vitamin [14].

Although there is an important African ancestry in Brazil, a study with mitochondrial DNA shows that the Africans immigrants came from continental regions where the 13910T allele in MCM6 gene is prevalent [15] and not from the African Funali (people with high prevalence of LI) during slavery in Brazil [1]. However, this allele (13910T) was present in only 20% of Brazilian black population, suggesting that there was miscegenation with Europeans (with high lactose intolerance prevalence). Indeed, due to high miscegenation with populations from several countries, the LI prevalence is different, considering the Brazilian region and the ethnic group, as shown in Table 1.

Table 1: Description of the lactosntolerance prevalence studies in Brazil.

Author/Year Reference	Diagnostic Method	Prevalence (%)	Ethnicity	N	Age (Years)	Country's Region
Sevá-Pereira [16]	OLTT	45.0	Caucasians	80	20-52	Southeast
		85.0	African descendants			
		100.0	Asians			
Sparvoli [17]	OLTT	75.5	Trihybrids (Caucasians African-descendants Asians)	37	18-52	Northeast
Sparvoli [18]	OLTT	46.0	Caucasians	70	19-59	South
		73.0	African-descendants			
Pretto et al. [19]	Hydrogen breath test	5.2	Caucasians	225	8-18	South
		15.5	Non-Caucasians			
Alves et al. [20]	Hydrogen breath test	89.3	Terenas Indigenous people	251	0-10	Midwest
Escoboza et al. [22]	Intestinal biopsies immunohistochemistry	53.2	Caucasians	115	5-60	Southeast
		91.3	Non-Caucasians			
Pereira-Filho & Furlan [21]	OLTT	44.1	Not mentioned	1.088	0 a >60 (upper limit not reported)	South
Bernardes-Silva et al. [23]	Genetic test (-13910 C>T and -22018 G>A)	37.0	Caucasians Mulatto African-descendants	75 Irritable bowel syndromes	Adults	Not mentioned

Mattar et al. [24]	Genetic test (-13910 C>T)	57.0	Caucasians Mulatto African-descendants Japanese-descendants	567	Mean age: 42.1 (16.8) Minimum and maximum limits not reported	Southeast
		57.0				
		80.0				
		100.0				
Mattar & Mazo [1]	Genetic test (-22018 G>A)	94.6	Brazilians (Japanese-descendants)	56	Adults	Not mentioned
Friedrich et al. [6]	Genetic test (-13910 C>T)	68.1	Brazilians (African-descendants and European-descendants)	981	Adults and teenagers	South Southeast North
		48.6				

Adapted from Wortmann et al., 2013; OLTT: Oral Lactose Tolerance Test; Average: 63,27%

According to Table 1, in a Southeastern study with 80 healthy subjects, lactose malabsorption was detected in 71% of the sample, by oral lactose tolerance test (OLTT). In this study, there were differences among ethnic groups: LI was present in 45% of Caucasian individuals, 85% of Afro-descendants and 100% of Asian-descendants individuals [16]. In Rio Grande do Sul, a state located in far south of Brazil, a study using OLTT to assess LI prevalence found that 75.5% of residents that came from Northeastern regions of the country had LI [17]. Later, the same author observed that there were different results when the ethnic factor was taken into account: the prevalence of LI was 46% and 73% among Caucasian and Afro-descendant individuals, respectively [18]. Another study held in Rio Grande do Sul, but now with typical Southerners residents, the prevalence of LI in a sample of 225 schoolchildren between 8 and 18 years old was 8.4%; however, when considering their ethnicity, the prevalence was 5.2% among Caucasians and 15.5% among non-Caucasians subjects [19]. Among the indigenous children of Terenas people from the state of Mato Grosso do Sul, LI prevalence was 89.3% [20].

Another study that evaluated 1088 people in the south region of the country found 44.1% of LI prevalence using OLTT methodology [21]. In Southeast region, Escoboza & cols [22] demonstrated that 60.8% of 115 people had ATH, using immunohistochemistry of intestinal endoscopic biopsies [23]. When stratified by ethnicity, the authors found out 53.2% of ATH prevalence among Caucasians and 91.3% among non-Caucasians. In 2009, Mattar et al. [24] evaluated the allele frequency of 13910C of the MCM6 gene in 567 asymptomatic and dyspeptic Brazilian subjects. The sample was stratified according to ethnicity into white, mulatto, black and Japanese descendant groups, and the frequency of the studied allele was 57%, 57%, 80% and 100%, respectively.

In 2010, 56 Brazilian adults, descendants of Japanese immigrants, had their MCM6 gene evaluated and the allele -22018G was a better predictor of LI phenotype than the allele -13910C in the same gene [1]. However, among Brazilian African-descendants, the 13910C- allele was the best predictor of LI phenotype, and the LI prevalence was 68.1% [6]. In our recent published article we showed that 254 patients with metabolic

syndrome, 87% were positive for OLTT and the -13910C genetic test and 85.8% were also positive for OLTT and -22018G [24].

Conclusion

This brief review demonstrated that there is a high prevalence of LI in Brazil (>63%), especially in African-Brazilians and Japanese descendants. The cause of the high frequency of this condition among Brazilians is related to a genetic programming inherited from some populations worldwide. The lactose tolerance phenotype may be an adaptation (polymorphism) naturally selected to promote survival of most communities throughout the world.

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