

# Analysis of lactose intolerance in students with suggestive symptoms of irritable bowel syndrome

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**ABSTRACT – Background** – Irritable bowel syndrome is a clinical condition presenting pain, distension and abdominal fullness, diarrhea, constipation, and other symptoms. It generates significant impacts on the quality of life of those affected. The pathophysiology is uncertain, but the role of various food types has been established in bowel sensitivity and its clinical manifestations. Carbohydrate intolerance, particularly to lactose, generates similar and sometimes indistinguishable symptoms from irritable bowel syndrome, and in clinical practice is both a frequent and underdiagnosed condition. Carbohydrate intolerance is related to enzymatic deficiencies, alterations of intestinal microbiota and even genetic change. The principal test for a diagnosis of lactose intolerance is the breath test, which measures hydrogen emission (produced only by bacteria), after ingestion of the corresponding substrate. **Objective** – The present work aims to verify the prevalence of lactose intolerance in university students, presenting gastrointestinal symptoms suggestive of irritable bowel syndrome. **Methods** – In a transversal study, to screen for those with suggestive symptoms, 124 medicine students participated by responding to a form. Those with abdominal pain were referred for anti-parasite treatment in order to exclude intestinal parasites as a secondary cause. Subsequently, using the hydrogen breath test, bacterial overgrowth was investigated, and if negative, lactose intolerance testing would be performed. Patients presenting high hydrogen concentrations of  $\geq 20$  ppm above the basal level were considered lactose intolerant. **Results** – Of the total of students researched (n=124), 7 were excluded because they did not completing all study phases. From those 117 individuals effectively included in the survey; 8 (6.8%) were diagnosed with lactose intolerance and 2 (1.7%) with bacterial overgrowth. Intolerance was more frequent in; female individuals (75%), age range 18 to 25 years (62.5%), being colored (50%), and in their 5th semester of studies (37.5%). The presence of at least one gastrointestinal symptom among those presenting intolerance (100%), and those not presenting intolerance (42.2%) was found ( $P=0.002$ ). In addition to abdominal pain (100%) ( $P<0.001$ ), the most recurrent gastrointestinal symptom in the lactose intolerant students was the distension/flatulence (62.5%) ( $P=0.026$ ). In relation to life habits and food patterns, there was no statistical difference between lactose tolerant and intolerant individuals, or for symptom frequencies. The more advanced students, completing more periods towards graduation, demonstrated more occurrences of gastrointestinal symptoms, yet without presenting significant statistical discrepancies. **Conclusion** – In view of the test sample quantity (n=21), a high prevalence of lactose intolerance (6.8%) in the academic environment, with epidemiological characteristics compatible to those found the literature is demonstrated, generating knowledge with understanding to prevent, diagnose, alleviate and treat lactose intolerant university students, and generate positive impacts towards well-being, improving the quality of life of these individuals.

**HEADINGS** – Irritable bowel syndrome. Lactose intolerance. Breath tests. Hydrogen, analysis. Abdominal pain.

## INTRODUCTION

Irritable bowel syndrome (IBS) constitutes a recurring functional disorder whose diagnosis is made from the Rome IV criteria based on the frequency and duration of manifestations of symptoms in the absence of detectable organic causes<sup>(1-3)</sup>. The presence, mainly of abdominal pain, alterations of intestinal habits (diarrhea and/or constipation), distension, and swelling make up the symptomatic frame, however, it is not specific to IBS<sup>(4)</sup>. The pathophysiology of IBS is complex and multifactorial, involving acute intestinal motor response, immunological mechanisms, visceral hypersensitivity, psychological stress, and changes in enteric nervous system/central nervous system interactions<sup>(5)</sup>.

There is also an important association between IBS and adverse reactions to certain foods; studies have shown that food intolerance

is more prevalent in patients with IBS than in controls. However, a causal relationship for this association has not yet been proved<sup>(6,7)</sup>. It is worth pointing out however that individuals with IBS present changes in intestinal motility and visceral sensibility, and the repercussions of poor digestion of certain foods are possibly more intense in patients with this syndrome<sup>(6)</sup>.

Carbohydrate intolerance, in particular lactose, affects approximately 80% of the world's population; it is quite prevalent in the Brazilian population<sup>(8)</sup>. Affected individuals present many complaints, including abdominal pain, diarrhea, nausea, increased peristalsis, meteorism, flatulence and abdominal distension. The presentation of symptoms is similar, sometimes being unspecific, or indistinguishable from IBS, which makes it either difficult to diagnose, under diagnosed, or diagnosed late<sup>(9)</sup>. It is noteworthy that an unbalanced diet, and life habits with too much consump-

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tion of lactose-rich products, associated with changes in intestinal microbiota, accentuates intolerance causing grievances to the life quality of individuals. In certain situations, enzyme decreases occur and the non-digestion of food generates the symptomatology. The un-metabolized food portion reaches the large intestine where the bacteria produce hydrogen<sup>(7,10)</sup>.

The detection of increased values of exhaled hydrogen, through the breath test, is a non-invasive first-choice method for diagnosis of lactose intolerance (LI)<sup>(11)</sup>. Although it is an indirect method, it presents good correlation with intestinal lactate levels and has both significant sensitivity (80% to 92.3%) and specificity (69% to 100%)<sup>(12)</sup>. It is worth pointing out that the reliability of the examination may be affected by factors that interfere with elimination of hydrogen in the exhaled air, generating false-positive or false-negative results. Such factors include recent use of antimicrobials, absence of non-fermenter bacterial microbiota, bacterial overgrowth in the small intestine, excessive methane production, alterations of intestinal motility, and high-fiber intake prior to examination<sup>(13)</sup>.

Extrinsic factors related to LI include carbohydrate intake dosage, anxiety, stress and the presence of functional gastrointestinal disease<sup>(14)</sup>. These aggravating elements are often present in the daily life of university students. University study, although an exciting milestone in the lives of young people can be stressful for some. This stems from the demands that each course requires, the need to obtain good results, personal expectations, and that often the student is distant from the family home<sup>(15)</sup>. Thus, university student stress levels and eating habits are important aggravating factors for gastrointestinal disorders, including carbohydrate intolerance<sup>(14)</sup>.

The signs and symptoms of carbohydrate intolerance can be avoided or mitigated with early diagnosis. Screening by means of a questionnaire, and subsequent realization of the hydrogen breath test by medical students presenting gastrointestinal symptoms suggestive of IBS, might lead to a more satisfactory prognosis. As a result, the present work aimed to verify the prevalence of LI in students that already present gastrointestinal symptoms suggestive of IBS, differentiating and enabling therapeutic intervention for a potential improvement in the quality of life for these academics.

## METHODS

### Number of participants

The research obtained the participation of 117 student volunteers from the medical school of the São Francisco Valley Federal University at the Paulo Afonso Campus /BA, aged between 18 to 45 years.

### Type of study

A cross-analytical study was carried out during the period of March to August of 2018.

### Inclusion criteria and screening forms

The students were informed about the proposals of the project and signed a free and informed consent term (IC), confirming participation in the research according to the standards established by the Ethics Committee on Research (CEP). It is also emphasized that the study was only initiated after CEP approval under the registration number CAAE 70321417.2.0000.5196.

With the intention of screening those with suggestive abdominal symptoms for IBS, the university students who agreed to participate in the survey responded to a form concerning LI. The variables

contained in the form were of demographic nature (age, gender, ethnicity and graduation period); related to lifestyle (smoking and alcohol use); predominant food consumption (fibers, meats, pasta and vegetables); consumption of processed foods; intestinal habits; feces consistency; history of food intolerance; and presence of gastrointestinal symptoms (abdominal pain, changes in shape and/or consistency of feces, frequency of evacuations, flatulence/abdominal distension and nausea); and as to whether crises were associated with emotional problems and/or often resulted in missing class.

In addition, the form was theoretically based on the Rome IV criteria, containing the following questions:

Whether the respondent presented recurring abdominal pain, at least once a week during the last three months, with a first occurrence at least six months ago? If the answer was yes, three other questions were asked:

1. Is this pain related to defecation (whether worsening or improving)?
2. Is this pain associated with change in the frequency of evacuations?
3. Is this pain associated with a change in the aspect of the feces?

The students who cited abdominal pain were referred to anti-parasite treatment with nitazoxanide and subsequent breath test performance.

### Exclusion criteria for false positives

In order to avoid false positive results related to the abdominal symptoms, treatment with anti-parasitic medicine was performed to exclude intestinal parasitoses, which can generate symptoms similar to lactose intolerance. The use of antibiotics from four weeks prior to the examination also constituted a criterion of exclusion, since it consists of bacterial overgrowth therapy, and could mask differential diagnosis of LI. Further, students who did not participate in all the stages of the study were excluded from the research.

### Hydrogen breath test

In order to detect lactose intolerance in the students with suggestive abdominal symptoms, the hydrogen breath test was performed. Guidelines were provided to the students in preparation for the exam in order to ensure reliable results. The recommendations consisted in not using oral or injectable antibiotics as well as probiotics for the four weeks prior to the test; to not ingest milk, or milk derivatives, alcohol beverages, fruit juices, laxatives or high-fiber foods for 24 hours before the test; to begin fasting 12 hours before the test; and to neither smoke or perform physical activity on the day of the exam<sup>(12)</sup>.

In the beginning, while still in fasting, the students blew into a portable (Gastro + Gastrolyzer<sup>®</sup>) device to obtain exact hydrogen measurements in parts per million (ppm), from the breath expired. Possible presence of bacterial overgrowth must be excluded before carrying out the lactose breath test. Therefore, after in-fast collection was carried out, an intake of 75 g of glucose diluted in 250 mL of water was administered and collections of breath hydrogen concentrations were recorded in intervals of 15, 30, 45, 60, 90 and 120 minutes, (totaling 2 hours). An increase in hydrogen of  $\geq 20$  ppm above the basal value after 90 minutes was considered positive for bacterial overgrowth<sup>(12)</sup>.

Once bacterial overgrowth is excluded, the hydrogen test using lactose as its substrate is performed. After collection during fasting, setting the basal value; ingestion of 25 g of lactose diluted in

250 mL of water permits hydrogen concentration measurements in intervals of 15, 30, 45, 60, 90, 120, 150 and 180 minutes, totaling three hours of duration. Poor lactose absorption is defined as an elevation in hydrogen concentration of at least 20 ppm above the basal level<sup>(12,16)</sup>. According to the examination results the students were classified as either: lactose tolerant or lactose intolerant. Registration notes are made of any complaints, as well as the presence of symptoms throughout the day.

It is valid to consider an important limitation of the applied hydrogen test, in which it consists of possible false negative results for LI in individuals with excessive production of methane<sup>(12)</sup>. It is known that the methanogenic bacteria of the intestinal microbiota use four molecules of hydrogen to produce a single methane. Thus, the interpretation of the breathing test can be affected, since the increased production of methane is associated with a significant reduction of the hydrogen levels<sup>(17)</sup>. In general, given the importance of association with gastrointestinal symptoms (constipation and slowing of gastrointestinal transit) and interaction with hydrogen production, measurement of methane should be performed in all respiratory tests<sup>(12)</sup>. However, it is worth mentioning that this measurement increases costs of the test, since portable gas chromatographs do not measure methane, limiting our study in this aspect.

### Statistical analysis

The software Stata version 12.0 (Stata Corporation, College Station, USA) was used for processing and analysis of the data. Absolute and relative frequencies were calculated for sample characterization and other variables of interest. Fisher's exact test was used to assess associations for the presence of lactose intolerance and gastrointestinal symptoms with descriptive variables, adopting a statistical significance level of 5%.

## RESULTS

A total of 124 students (of which 7 were excluded because they did not complete all of the study steps) were evaluated through the screening form. From the application of the Rome IV criteria and the evaluation of symptomatic individuals, with emphasis on those with abdominal pain, it was found that although manifesting suggestive symptomatology, none of the students researched fitted rigorously within a classical diagnosis of IBS.

Of the 117 individuals effectively included in the survey, it was found that 8 (6.8%) were diagnosed with LI and 2 (1.7%) with bacterial overgrowth. From the total sample, 66 (56.4%) were female, and 51 (43.6%) of male. Among the lactose intolerant, women represented 75% of the cases, while men represented 25% of the cases. Ages between 18 and 25 years were the most frequent in the study population (83.8%), and in the LI group (62.5%). In relation to ethnicity, mixed-race (54.7%) and whites (34.2%) prevailed, being that among the lactose intolerant; mixed-race were in the majority (50%), followed by whites (25%) and blacks (25%). As for the semester of study, most of the students researched were in their third semester (29.1%). However, fifth semester individuals prevailed by presenting positive breath tests (37.5%). There was however no statistically significant difference between gender, age, ethnicity, or semester of study in either group evaluated (lactose tolerant or intolerant). The characteristics of the study population are present in TABLE 1.

Of the total (n=117), 54 (46.1%) reported gastrointestinal symptoms and 21 (17.9%) reported abdominal pain. Considering

TABLE 1. Characteristics of the study population. Paulo Afonso, BA, 2018.

Variables	All (n=117)		Tolerants (n=109)		Intolerants (n=8)		P-value*
	n	%	n	%	n	%	
Gender							
Female	66	56.4	60	55.1	6	75.0	0.463
Male	51	43.6	49	45.0	2	25.0	
Age							
18-25	98	83.8	93	85.3	5	62.5	0.083
26-30	13	11.1	11	10.1	2	25.0	
31-35	4	3.4	4	3.7	0	0.0	
36-42	2	1.7	1	0.9	1	12.5	
Ethnicity							
White	40	34.2	38	34.9	2	25.0	0.384
Mixed race	64	54.7	60	55.1	4	50.0	
Black	12	10.3	10	9.2	2	25.0	
Indigenous	1	0.9	1	0.9	0	0.0	
Academic profile							
1° semester	32	27.4	30	27.5	2	25.0	0.827
3° semester	34	29.1	32	29.4	2	25.0	
5° semester	27	23.1	24	22.0	3	37.5	
7° semester	24	20.5	23	21.1	1	12.5	

n: absolute frequency; % = relative frequency. \*P-value <0.05. Fisher exact test.

abdominal pain as an inclusion criterion for the realization of the hydrogen test, it was found that the presence of at least one gastrointestinal symptom in the lactose intolerant (100%), and the lactose tolerant (42.2%) was statistically significant ( $P=0.002$ ). It was observed in the students with LI, that in addition to abdominal pain itself ( $P<0.001$ ), the most frequent complaints were the flatulence and abdominal distension (62.5%), in which significance was noted between the lactose intolerant and lactose tolerant groups ( $P=0.026$ ). The frequency of gastrointestinal symptoms in the university students is presented in TABLE 2.

TABLE 2. Symptoms of gastrointestinal tract in lactose tolerant and intolerant university students. Paulo Afonso, BA, 2018.

Presence of gastrointestinal symptoms	Tolerants (n=109)		Intolerants (n=8)		P-value*
	n	%	n	%	
At least one of the symptoms below	46	42.2	8	100.0	0.002
Abdominal pain	13	11.9	8	100.0	<0.001
Stool shape changed	17	15.6	3	37.5	0.136
Altered bowel frequency	26	23.9	3	37.5	0.407
Consistency of feces altered	23	21.1	3	37.5	0.374
Abdominal distension / flatulence	25	22.9	5	62.5	0.026
Nausea	5	4.6	2	25.0	0.073

n: absolute frequency; % = relative frequency. \*P-value. Fisher exact test.

As for intestinal transit, 50% of the LI individuals referred to daily evacuations. Moreover, most of the lactose intolerant sampling (75%) reported feces consistency as normal; 25% reported hardened feces. In lactose tolerant students there was higher normality prevalence (91.7%), and less (2.8%) hardened stools, yet without presenting statistical significance. Of the total sample (n=117), 29.9% mentioned having a positive family history of food intolerance. The prevalence of the family history was greater in those with LI (50%), than in the lactose tolerant (28.4%) students, however, there was no statistical association between these variables. The intestinal habits and food intolerance history of the sample surveyed are presented in TABLE 3.

**TABLE 3.** Intestinal habit and history of food intolerance in lactose tolerant and intolerant university students. Paulo Afonso, BA, 2018.

Variables	Tolerants (n=109)		Intolerants (n=8)		P-value*
	n	%	n	%	
Habitual intestinal transit					
Evacuate every day	71	67.0	4	50.0	0.228
Evacuate more than once a day	11	10.1	0	0.0	
Evacuate every other day	21	19.3	3	37.5	
Evacuates less than 3 times / week	4	3.7	1	12.5	
Habitual stool consistency					
Normal	100	91.7	6	75.0	0.052
Pasty	6	5.5	0	0.0	
Hardened	3	2.8	2	25.0	
History of food intolerance					
Family	31	28.4	4	50.0	0.237
Personal	20	18.4	2	25.0	0.644

n: absolute frequency; % = relative frequency. \*P-value. Fisher exact test.

In relation to lifestyle, among those diagnosed with LI, 62.5% reported consuming alcohol. The prevalence of alcoholism was discreetly lower (55.6%) in tolerant individuals, so there was no statistical significance between the use of ethanol and higher LI prevalence (TABLE 4). In the context of the predominant foods consumed, 62.5% of the lactose intolerant students consumed pasta regularly with no predominance in vegetable intake. On the other hand, in the lactose tolerant group, consumption of vegetables was greater (21.1%), yet consumption of pasta was similar to those presenting LI (62.4%). There was no relevant statistical difference. Further, consumption of processed foods more than once per week was more prevalent in the lactose tolerant students (60.6%) than in the lactose intolerant (50%), again, not presenting significant discrepancies between these variables.

As for the frequency of gastrointestinal symptoms according to specific variables amongst lactose intolerant students, it was observed that the female individuals (compared to males) presented greater frequencies for all of the symptoms cited. In addition, the university students, from 26 to 30 years of age, black in color, and studying in the seventh semester demonstrated greater frequencies

involving gastrointestinal symptoms. Although these associations were well evidenced, there was no significant statistical difference. The consumption of alcohol and processed foods, as well as the predominance of meat and pasta in the food presented varying frequencies as to the symptoms evidenced, without presenting a well-defined pattern. However, those whose consumption presented high-fiber intake also presented a greater manifestation of symptoms as compared to the others, but without statistical significance.

## DISCUSSION

Through breath test analyses carried out in the university students of both sexes in the age range of from 18 to 45 years, it was demonstrated that the prevalence of lactose intolerance was 6.8%. By sex, women were more lactose intolerant than men. According to Frye and collaborators<sup>(18)</sup>, LI is not related to the sexual chromosomes but the autosomal and recessive genetic character is determinant. Thus, no significant difference in the results between male and female individuals was expected, and in the present study, the data confirmed no significant differences between them, corroborating the results reported in the literature<sup>(19,20)</sup>.

Our study found that the lactose intolerant women presented a greater frequency for gastrointestinal symptoms than men. Similar results were evidenced in a Dutch study<sup>(21)</sup>, in which from a sample consisting of 16.758 individuals, 26% reported having gastrointestinal symptoms with a high prevalence of females (66%), and also in a Brazilian study by Del' Arco and collaborators<sup>(22)</sup>. Differences between the sexes in intestinal motility and visceral sensibility have already been suggested in the literature as factors associated with the higher frequency of functional gastrointestinal disease in women, including IBS and intestinal constipation<sup>(23,24)</sup>. Hormonal changes intrinsic to the female sex, such as estrogen increases in certain phases of the menstrual cycle are directly associated with decreased intestinal transit<sup>(25)</sup>. Other more frequent factors for women, such as stories of sexual, physical and emotional abuse may also be involved in manifestations of gastrointestinal disorder<sup>(26)</sup>.

**TABLE 4.** Lifestyle and eating pattern among college students tolerant and intolerant to lactose. Paulo Afonso, BA, 2018.

Variables	Tolerants (n=109)		Intolerants (n=8)		P-value*
	n	%	n	%	
Lifestyle					
History of smoking	4	3.7	0	0.0	1.000
History of alcoholism	60	55.6	5	62.5	1.000
Predominant food pattern					
Fibers	24	22.0	2	25.0	1.000
Beef	48	44.0	3	37.5	1.000
Pastas	68	62.4	5	62.5	1.000
Vegetables	23	21.1	0	0.0	0.353
Consumption of processed foods					
Daily	17	15.6	1	12.5	0.770
More than one day per week	66	60.6	4	50.0	
One day a week or less	26	23.9	3	37.5	

n: absolute frequency; % = relative frequency. \*P-value. Fisher exact test.



According to Sevá-Pereira and collaborators<sup>(27)</sup>, LI occurs in 58 million Brazilian's over the age of 15. Little or no lactate enzyme activity often occurs during childhood. However, since enzyme production suffers autonomic recessive genetic influence, the exact age varies between populations. According to Moreira<sup>(28)</sup>, after weaning, the activity of lactate is reduced and with age, the decline increases, reaching only 5% to 10% of the levels presented at birth, setting the stage for hypolactasia. The most prevalent age group among the LI patients studied was 18 to 25 years (62.5%) followed by 26 to 30 year olds (25%). In previous studies a high prevalence of adults with LI, has been reported, but in more advanced age ranges of around 30 to 40 years old<sup>(20,29,30)</sup>. This result is plausible, since university students between 18 to 25 years of age, make up the majority of the student body, and consequently the total sample of this study (83.8%).

Pretto and collaborators<sup>(31)</sup>, in Rio Grande do Sul, evaluated the prevalence of LI through the breath test, finding a prevalence of 8.4% in a sample of 225 individuals. Among those presenting intolerance, 5.2% were white, contrasting with 15.5% non-whites. Our study demonstrated three-fold lactose intolerance rates in non-white (black, mixed race, and indigenous) individuals as compared to whites, corroborating data from Pretto and collaborators<sup>(31)</sup>. In Brazil, there are other studies that present similar findings in relation to ethnicity, while using different diagnostic methods<sup>(27,32)</sup>.

From these tendencies, theories have been discussed in the literature in order to explain the differences found in the prevalence of LI in different populations in accordance with historical, environmental and behavioral data<sup>(33,34)</sup>. It is suggested that the persistence of lactate activity in certain population groups occurred due to selective pressure on those who depended on dairy products as a source of food. This was due to increasing dependence on pastoral activities in relation to agriculture, as occurred, about 7000 to 9000 years ago, in populations of Northern and Central Europe<sup>(35,36)</sup>. It is believed that this feeding pattern may have favored the emergence and propagation of dominant genes, arising from mutation, granting persistence to the production and activity of lactate, and constituting an advantage from an evolutionary point of view<sup>(36)</sup>.

In our study, the presence of abdominal pain was used as an inclusion criterion for realization of the hydrogen breath test. The symptom is part of the definition of IBS, according to the criteria of Rome IV<sup>(1-3)</sup>. In addition, the most frequent gastrointestinal symptoms in the lactose intolerant students were flatulence/abdominal distension (62.5%) ( $P=0.026$ ), followed by changes in the form (37.5%), or consistency of the feces (37.5%), in the frequency of evacuations (37.5%), and nausea (25%). Similar data were found by Ponte<sup>(20)</sup>, at the Walter Cantídio University Hospital (HUWC) in Fortaleza/CE. In Germany, Schiffneret<sup>(37)</sup> conducted a survey, in which the most common complaints among individuals with LI were abdominal pain (34.5%), vomiting (14%), and abdominal distension (10.4%), presenting a strongly significant correlation between diagnoses of LI and IBS. Unlike the work of Schiffneret<sup>(37)</sup>, the present study did not reflect any relation to IBS, since none of the surveyed students fell within the diagnostic criterion, although they manifested suggestive symptoms.

The variability of the symptoms presented in individuals with LI is influenced by several factors including osmolality, fat content contained in the dairy product, gastric emptying time, bowel movements, and sensitivity of the intestine to distension caused by non-hydrolyzed lactose<sup>(38)</sup>. These factors are much more evident in those that have IBS, since such characteristics in these individuals; visceral hypersensitivity, intestinal transit reduction and excessive colonic fermentation promote a sense of stuffiness and abdominal distension much more intensely than in healthy individuals<sup>(39)</sup>. Thus,

Monsbakken and collaborators<sup>(40)</sup> when evaluating 84 patients with diagnosed IBS verified that in 70% of the cases, food intolerance was associated. Milk, as a symptom exacerbate, was considered the food most referred to (42%). In addition, a Chinese study investigating the frequency of LI in 109 patients with IBS against 50 healthy control individuals reported a significantly elevated prevalence of LI ( $P=0.002$ ) in those suffering from IBS (45%) as compared to the group control (17%)<sup>(41)</sup>.

In this perspective, the clinical distinction between IBS and LI is very difficult, since the symptoms of these entities are similar, being easily confused. Thus, it is essential to exclude LI, which is easily treatable, before diagnosing IBS<sup>(42)</sup>. Several authors suggest the suspension of foods with lactose for one to two weeks in cases of suspected intolerance. In the absence of improvement of symptoms it is possible empirically to exclude LI, however, IBS and lactose malabsorption may coexist in the same individual<sup>(43,44)</sup>. In addition, Celiac Disease and other disorders related to gluten also present clinical manifestations that mimic IBS, and make up the spectrum of food intolerances associated with the syndrome. Gluten is considered a trigger for symptoms in 20% to 45% of individuals who have IBS. Although not yet accepted globally, serological tests for the diagnosis of celiac disease in patients with IBS are warranted<sup>(45,46)</sup>. Thus, understanding about the role of dietary components in inducing gastrointestinal symptoms in IBS is complex and not fully elucidated, which contributes to the challenge in diagnosing the syndrome, which is sometimes delayed or lost<sup>(43)</sup>.

In our study, it was observed that most of the lactose intolerant students (75%) reported feces consistency as normal; 25% presented hardened consistencies ( $P=0.052$ ). Typical for individuals with LI would be softened and diarrheic stools, as has been cited in previous works<sup>(47,48)</sup>. Since non-hydrolyzed lactose reaches the colon without being absorbed, its osmotic effects draw water towards the colonic lumen, with a consequent decrease in fecal consistency and increased intestinal transit<sup>(11)</sup>. However, it is worth pointing out that manifestation of symptoms depends on the amount of lactose ingested, as well as the lactate reserve present. A good part of individuals with LI support ingestion of up to 6–12g of lactose without developing symptoms<sup>(49)</sup>, and according to the literature, complaints related to flatulence, distension, and abdominal pain are more frequent than diarrhea<sup>(50)</sup>.

Multiple factors interfere in the manifestation of gastrointestinal symptoms, and lifestyle plays a prominent role in the process. Eating habits and stress have an important influence since they are responsible for potential modifications in the composition of the intestinal microbiota<sup>(51)</sup>. In this study, individuals with LI whose consumption presented high-fiber intake presented greater manifestation of symptoms than those who do not predominantly consume fibers, yet without statistical significance. In a classic review carried out by Hammonds and Whorwell<sup>(52)</sup>, evaluating 13 studies with high fiber diet patients with functional gastrointestinal disorders, it was evidenced that positive effects occurred only in patients with constipation. It is worth mentioning that an excess of soluble fibers in some individuals may exacerbate abdominal pain by causing increased colonic distension through augmented gas production, a consequence of bacterial fermentation<sup>(39,53)</sup>.

There are several aspects of medical school that are important sources of stress, such as curriculum overload, the competitive environment, the pace of evaluations, little time for social activities, and certain responsibilities inherent to the profession<sup>(54,55)</sup>. Emotions have an intimate relationship with intestinal function, and serotonin, a hormone related to wellness is produced, stored, and released in the intestines. Exposure to stress may be responsible for disturbing bi-directional interactions between the enteric nervous system

and the central nervous system; serotonergic changes promote deregulation of gastrointestinal motility, visceral sensitivity, and immune function<sup>(56,57)</sup>. Although there was no relevant statistical difference, in our study it was observed that the students presenting crises in association with emotional problems also presented more frequent modifications of their intestinal habit, corroborating the data found in the literature.

Further, the students who were closer to graduation demonstrated gastrointestinal symptoms more frequently, yet without relevant statistical difference. Similar results have been observed in other studies, in which the presence of gastrointestinal disorders occurred more frequently in students who are closer to completing their course as compared to those who are just beginning their studies<sup>(58,59)</sup>. It is thus inferred that academic training over the years may alter the quality of student life, with the disease being more pronounced in those that are exposed to stress for longer periods of time<sup>(60,61)</sup>.

## CONCLUSION

In summary, the data obtained in our study are consistent with the most recent literature on this topic. In view of the quantity of the sample that realized the test (n=21), the high prevalence of LI (6.8%) in the academic environment can be demonstrated; with epidemiological characteristics similar to those found in previous studies. Further, it could be inferred that prolonged exposure to the stressful factors inherent in studying medicine can influence and accentuate gastrointestinal discomforts.

Although there have been studies performed worldwide<sup>(18,62)</sup>, there are few Brazilian publications on the prevalence of LI in young adults using the hydrogen breath test, (most studies are performed in children). Comparison of our results is thus hampered

by the shortage of similar Brazilian based studies. However, the results of this research may serve as a basis for future research in medical students, including other variables and larger sample size, including follow-up of IBS research in students according to the Rome IV Criteria and future evaluation of levels of hydrogen and methane, simultaneously, through the respiratory test.

Despite some methodological limitations, our study greatly assists the academic community by generating knowledge and understanding towards prevention, diagnosis, alleviation, and treatment of university students with LI and bacterial overgrowth, generating positive impacts for their wellbeing, and improving their quality of life.

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## Authors' contribution

Silva CJ: data collection, implementation of the exam and writing of the text. Leite IDS: data collection and implementation of the examination. Rodrigues JW, Almeida SP, Nóbrega BP: implementation of the examination. Sampaio Filho JDR: research guidance.

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Silva CJ, Leite IDS, Rodrigues JW, Almeida SP, Nóbrega BP, Sampaio Filho JDR. Análise da intolerância à lactose em alunos com sintomas sugestivos da síndrome do intestino irritável. *Arq Gastroenterol.* 2019;56(3):304-11.

**RESUMO – Contexto** – A síndrome do intestino irritável é uma condição clínica que cursa com dor, distensão e plenitude abdominal, diarreia, constipação, entre outros sintomas. Gera impacto significativo na qualidade de vida das pessoas acometidas. Sua fisiopatologia é incerta, mas o papel de vários tipos de alimentos está estabelecido na sensibilização intestinal e nas manifestações clínicas. A intolerância aos carboidratos, particularmente a lactose, gera sintomas similares e por vezes indistinguíveis da síndrome do intestino irritável e é uma condição frequente e subdiagnosticada na prática clínica. Está relacionada a deficiências enzimáticas, alterações da microbiota intestinal e mesmo alterações genéticas. O principal exame para o diagnóstico da intolerância à lactose é o teste respiratório, que mede a emissão de hidrogênio produzido apenas por bactérias, após a ingestão do substrato correspondente. **Objetivo** – O presente trabalho tem como objetivo verificar a prevalência de intolerância à lactose em universitários que apresentem sintomas gastrointestinais sugestivos da síndrome do intestino irritável. **Métodos** – O estudo, caracterizado como do tipo transversal, teve a participação de 124 discentes de medicina que responderam um formulário, a fim de realizar a triagem daqueles com sintomatologia sugestiva. Aqueles com dor abdominal foram encaminhados para o tratamento antiparasitário, a fim de excluir parasitose intestinal como causa secundária. Posteriormente, através do teste respiratório com hidrogênio expirado, foi feito primeiro a pesquisa de supercrescimento bacteriano e caso fosse negativo seria realizado o da intolerância à lactose. Foram considerados com intolerância aqueles que obtiveram uma elevação na concentração de hidrogênio  $\geq 20$  ppm acima do nível basal. **Resultados** – Do total de alunos pesquisados (n=124), 7 foram excluídos por não cumprirem todas as etapas do estudo. A partir dos 117 indivíduos efetivamente incluídos na pesquisa, verificou-se que 8 (6,8%) foram diagnosticados com intolerância a lactose e 2 (1,7%) com supercrescimento bacteriano. A intolerância foi mais frequente nos indivíduos do sexo feminino (75%), faixa etária de 18 a 25 anos (62,5%), cor parda (50%) e do 5º semestre (37,5%). Verificou-se que a presença de pelo menos um sintoma gastrointestinal entre aqueles que possuem intolerância (100%) e os que não possuem (42,2%) foi estatisticamente significativa ( $P=0,002$ ). Além da própria dor abdominal (100%) ( $P<0,001$ ), o sintoma gastrointestinal mais recorrente nos discentes intolerantes foi a distensão/flatulência (62,5%) ( $P=0,026$ ). Em relação aos hábitos de vida e padrão alimentar, não houve diferença estatística entre os indivíduos intolerantes e tolerantes, bem como na frequência de sintomas. Os discentes dos períodos mais avançados da graduação se destacaram por manifestarem com maior constância os sintomas gastrointestinais, porém sem apresentar discrepâncias estatísticas significativas. **Conclusão** – Tendo em vista a quantidade da amostra que realizou o teste (n=21), pode-se provar a alta prevalência da intolerância à lactose (6,8%) no meio acadêmico, com as características epidemiológicas compatíveis com a literatura. Assim, foi possível gerar conhecimento para entender, prevenir, diagnosticar, aliviar e tratar os universitários intolerantes, gerando impactos positivos para o bem-estar, melhorando a qualidade de vida desses indivíduos.

**DESCRITORES** – Síndrome do intestino irritável. Intolerância à lactose. Testes respiratórios. Hidrogênio, análise. Dor abdominal.

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