

# Frequency of Primary and Secondary Lactose Intolerance in Dyspeptic Adult Population and Comparison Based on age of Onset, Duration and Sex

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## ABSTRACT

**Objectives:** The objectives of this study were to find out the frequency of primary and secondary lactose intolerance in adult population attending outpatient department and to compare them in terms of age of onset, duration and sex.

**Methods:** Hundred adults aged between 18-60 years of both sexes presented with diarrhea, abdominal distension or bloating, abdominal cramps, nausea or vomiting and altered bowel habits were included. Those with inadequate pretest fasting within 12 hours, smoked recently, used antibiotics within 2 weeks prior to hydrogen breath test and with lung disorders were excluded. Hydrogen breath test employing hydrogen breath analyzer (Bedfont Scientific Limited, UK) was used to determine the lactose intolerance. During this test hydrogen level in exhaled air was measured by using hydrogen breath analyzer after administration of 50 gm dose of lactose in 250 ml of water at 30 minutes interval for 2-3 hours.

**Results:** Intolerance of lactose was observed in 40% patients. Among those lactose intolerant patients, 80% were found to have primary lactose intolerance and 20% were found to have secondary lactose intolerance. The common causes of secondary lactose intolerance were celiac disease in 87.5% patients and bacterial overgrowth in 12.5% patient. The frequency of age of onset among primary lactose intolerance aged 15-30 years, 31-45 years and 46-59 years were 20%, 25% and 35%, whereas the corresponding figures for secondary lactose intolerance were 2.5%, 15% and 2.5% respectively. The duration of symptoms among primary lactose intolerance patients from 1-5 years, 6-10 years, 11-15 years and 16-20 years was 50%, 22.5%, 5% and 2.5% whereas the corresponding figures for secondary lactose intolerance were 10%, 5%, 2.5% and 2.5% respectively.

**Conclusion:** This study revealed that the frequency of primary lactose intolerance was significantly high among higher age groups  $p < 0.05$  and the commonest cause of secondary lactose intolerance was celiac disease.

**Keywords:** Lactose Intolerance, Dyspeptic, Breath test

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## INTRODUCTION

Lactose intolerance is the most common cause of carbohydrate malabsorption. Recognition of this prevalent condition is important, as it is easily managed by simple dietary adjustments. Accurate diagnosis of lactose intolerance can significantly relieve patient anxiety and avoid inappropriate investigation and treatment. People who have trouble digesting lactose can learn which dairy products and other foods they can eat without discomfort and which ones they should avoid.<sup>1</sup> Lactose intolerant adults can drink about 250 ml of milk per day and can take drugs containing low dose lactose without severe symptoms<sup>2</sup>.

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Lactose intolerance is the inability to digest significant amount of lactose, the predominant sugar of milk. This inability results from a shortage of the enzyme lactase which is normally produced by cells that line the small intestine<sup>3</sup>. Lactose is hydrolyzed by intestinal lactase to glucose and galactose on the microvillus membrane of the intestinal absorptive cells<sup>4</sup>. The liver changes galactose into glucose which is reabsorbed into blood stream. When lactose is not absorbed by small bowel, it passes rapidly into colon as a consequence of high osmolality of the intraluminal disaccharide. In colon, lactose is converted to short chain fatty acids and gas (hydrogen, methane, CO<sub>2</sub>) by the bacterial flora.<sup>5</sup> In most of the human population a decrease in lactase activity occurs during mid-childhood leading to low levels in adulthood.<sup>6</sup> Common symptoms of lactose intolerance include nausea, abdominal cramps,

bloating, gas and diarrhea which begin 30 minutes to 2 hours after eating or drinking foods containing lactose.

Lactose intolerance may be classified into primary lactose intolerance and secondary lactose intolerance. Primary lactose intolerance is the inability to digest significant amount of lactose with no identifiable underlying cause. In primary lactose intolerance, the body begins to produce less lactase after about the age of two years, depending on an individual's racial or ethnic background. It may be racial, developmental or congenital in origin. It is the most prominent in Asian and African populations, in contrast, the majority of the Caucasians, particularly of Scandinavian background, have preservation of intestinal lactase activity into adulthood, inherited as an autosomal dominant trait. Developmental lactose malabsorption results from low lactase levels and is a consequence of prematurity. Congenital lactase deficiency is a rare autosomal recessive disorder. This disorder is characterized by the absence of lactase activity in the small intestine, with normal histologic findings and normal levels of other disaccharidases<sup>7</sup>.

Secondary lactose intolerance defined as the inability to digest significant amount of lactose secondary to some disease such as bacterial overgrowth, infectious enteritis, mucosal injury, celiac sprue, drug induced enteritis, inflammatory bowel disease, radiation enteritis and giardiasis,<sup>8-10</sup> in which the production of lactase may be permanently disrupted. However, a significant percentage of the adult population develops a deficiency of intestinal lactase after weaning.<sup>11</sup> Prevalence of lactose intolerance in adult population is high and varies from 5% to 15% in Northern European and American countries and 50% to 100% in African, Asian and South American countries<sup>6</sup>, 50% in Indians and 15% in Russians<sup>12-14</sup>. Italians have also poor lactose intolerance (41%)<sup>7</sup>.

The most common non-invasive tests used to measure the absorption of lactose in the digestive system are lactose tolerance test, hydrogen breath test and stool pH. Stools are acidic owing to bacterial fermentation of malabsorbed carbohydrates. Stool pH below 5.5 in a freshly passed stool is a highly suggestive, although rather insensitive indicator of carbohydrate malabsorption.<sup>15</sup> Lactose tolerance test begins with the individual fasting before the test and then drinking a liquid that contains 50g of lactose. Blood glucose levels are monitored at 0, 60 and 120 minutes. In normal subjects, plasma glucose rises by greater than 20 mg/dl over a 2-hour period after an oral dose of 50g of lactose, whereas an increase in blood glucose by less than 20 mg/dl plus the development of symptoms is diagnostic of lactose intolerance. Lactose tolerance test has a sensitivity of

75% and specificity of 96%. It has largely been replaced by lactose hydrogen breath test<sup>16</sup>.

Hydrogen breath test is simple, safe and based on the fact that there is no source for pulmonary excretion of hydrogen in humans other than bacterial metabolism of carbohydrates.<sup>17</sup> Hydrogen breath test measures the amount of hydrogen in the breath through hydrogen breath analyzer<sup>18</sup>.

The study was conducted to determine the frequency of primary and secondary lactose intolerance in adult population and to compare the primary and secondary lactose intolerance in adult population in terms of age of onset, duration and sex.

## MATERIALS AND METHODS

Hundred adults aged between 18-60 years of both sexes presented with diarrhea, abdominal distension or bloating, abdominal cramps, nausea or vomiting and altered bowel habits were included. Those with inadequate pretest fasting within 12 hours, smoked recently, used antibiotics within 2 weeks prior to hydrogen breath test and with lung disorders were excluded. Detailed history from a patient enrolled in the study was taken. Data pertaining to diarrhea, bloating/distention, vomiting, abdominal cramps, nausea, and altered bowel habits was recorded in a specially designed proforma. Hydrogen breath test was performed, and during this test exhaled air was collected before and after every 30 minutes upto 3 hours after ingestion of 50 g of lactose in 250 ml of water. Hydrogen levels in exhaled air were measured using hydrogen breath analyzer (Bedfont Scientific Limited, UK) and levels exceeding 20 parts per million above the fasting values were considered abnormal. If hydrogen breath test showed positive result then specific investigations like H. pylori antibodies, FT4, TSH, upper GI Endoscopy, flexible sigmoidoscopy/colonoscopy, anti-transglutaminase antibodies and ultrasound were done to rule out secondary causes of lactose intolerance i.e. bacterial overgrowth, celiac sprue, inflammatory bowel disease, infectious enteritis, giardiasis and gall stone disease as indicated clinically. All the findings were recorded in specially designed proforma.

Data was analyzed by Statistical Package for Social Sciences (SPSS) version 15. Frequency of the variables include age, sex, altered bowel habits, abdominal pain, bloating/distention were assessed and reported as percentage. The frequency of primary and secondary lactose intolerance was calculated and reported as percentage. Age mean $\pm$ SD was calculated and compared by applying t-test between two groups i.e. primary and secondary lactose intolerance. Duration of illness, and sex distribution were calculated and reported as percentage and

compared in two groups by applying Chi square test. P value <0.05 was considered significant.

## RESULTS

This study includes 100 adults aged 18-60 years, who presented to Gastroenterology Outdoor Patient Department, Shaikh Zayed Hospital, Lahore. There were 54 males (54%) and 46 females (46%). Male to female ratio was 1.2:1. Patients were divided into 4 age groups. There were 32% patients aged 18-28 years, 33% aged 29-38 years, 21% aged 39-48 years and 14% aged 49-58 years. The mean age was 37.04±12.06 years. The patients were divided into three groups for age at onset of symptoms. There were 19% patients having age of onset 15-30 years, 56% at 31-45 years, and 25% in the age 46-59 years. The mean age at onset of symptoms was 33.85±12.15 years. The frequency of diarrhea was noted in 65% of cases, abdominal distension/bloating in 60%, abdominal cramps in 37%, Nausea/vomiting in 16% and altered bowel habits in 5%. Lactose intolerance was seen in 40% of the patients, of these cases, 80% were found to have primary lactose intolerance and 20% showed secondary causes. Cause-wise frequency distribution of secondary lactose intolerance was celiac sprue in 7 (87.5%) and bacterial overgrowth in 1 (12.5%). These were diagnosed on the distal duodenal biopsy, duodenal aspirate, presence of duodenal diverticuli on esophagoduodenoscopy (EGD), macrocytic anaemia, symptoms of weight loss, abdominal bloating and diarrhea, which was settled after antibiotic treatment.

Table 1: Comparison of primary and secondary lactose intolerance in term of age of onset, duration, sex and ethnic origin

Comparison	Primary lactose		Secondary lactose	
	Frequency	%age	Frequency	%age
<b>Age onset (years)</b>				
15 – 30	8	25.0	1	12.5
31 – 45	10	31.3	6	75.0
46 – 59	14	43.7	1	12.5
P value	< 0.05			
<b>Duration of symptoms (years)</b>				
1 – 5	20	62.5	4	50.0
6 – 10	9	28.1	2	25.0
11 – 15	2	6.3	1	12.5
16 – 20	1	3.1	1	12.5
P value	> 0.05			
<b>Sex</b>				
Male	15	46.9	3	37.5
Female	17	53.1	5	62.5

Chi square value" > 0.05

There was significant association of primary and secondary lactose intolerance with age of onset of disease, p-value < 0.05. The primary cause was most

prevalent in 45–60 years age and not less in other groups, while secondary causes were mostly seen in 31–45 years age. There was no association observed for duration of symptoms and gender with primary and secondary lactose intolerance, both with p-values > 0.05 (Table 1).

## DISCUSSION

Lactose intolerance is a common problem. There is no cure to the lactose intolerance. People who have trouble digesting lactose can learn which dairy products and other foods they can eat without discomfort and which ones they should avoid. Many people can enjoy milk and ice cream, if they eat these in small amount. Frequency of lactose intolerance varies widely among populations but is high in nearly all but those of European origin.<sup>19</sup> In Europe and United States, the prevalence varies from 5% to 15% and 50% to 100% in Africans, Asians and South American countries.<sup>6,20</sup> This study was performed in adults as the first study of lactose intolerance in our region. In this study, out of 100 subjects studied, mean age 37.40±12.06 years were comparable with the study conducted by Rana<sup>13</sup> Forty subjects (40%) reported lactose intolerance which is similar to the results obtained by Heyman<sup>7</sup>, Rana<sup>13</sup>, and Cavalli-Sforza.<sup>21</sup> Shamim<sup>22</sup> reported 22 (44%) cases of lactose intolerance in Pakistani adults.

The main symptoms were diarrhea, abdominal bloating and abdominal cramps that can be compared with study conducted by Saberi-Firoozi et al.<sup>23</sup> and Shamim.<sup>22</sup> However 32 (80%) patients were found to have primary lactose intolerance and 8 (20%) patients were found to have secondary cause in favour of secondary lactose intolerance. Primary lactose intolerance is a common form of lactase deficiency worldwide which is significantly seen in adulthood.<sup>24</sup> High prevalence of celiac disease in patients with secondary lactose intolerance 7 (87.5%) was seen, which is compared with the study conducted by Ojetti et al.<sup>25</sup> Bacterial overgrowth (12.5%) was diagnosed on EGD<sup>26</sup> and clinical criteria.<sup>27</sup> Lactose intolerance associated with celiac disease is temporary and ceases after the patient has been on a gluten free diet long enough for the villi to recover. Level of breath hydrogen significantly increased in age of onset group ranging from 46-59 years in primary lactose intolerance with frequency 43.7% and in secondary lactose intolerance ranging from 31-45 years with frequency 75%. Results of this study indicate that the frequency of lactose intolerance significantly increases with age as compared to the study conducted by Rao et al.<sup>28</sup> This study revealed significant difference in terms of age of onset between primary and secondary lactose intolerance. Increased

frequency of primary and secondary lactose intolerance in terms of duration of symptoms were seen between 1-5 years in primary lactose intolerance 62.5% and in secondary lactose intolerance 50% but statistically there was no difference found between both groups. This study has revealed increased frequency of primary lactose intolerance among females with frequency of 53.1% and secondary lactose intolerance in females with frequency of 62.5%. It can be compared with the study conducted by Saberi-Firoozi et al<sup>23</sup> and Shamim<sup>22</sup>. In earlier study, performed on small sample size in Pakistani adults at Faisalabad, lactose intolerance was detected by using oral lactose tolerance test, which has been now replaced by hydrogen breath test due to its superior sensitivity and specificity<sup>16</sup>.

In this study, hydrogen breath test was used as the main diagnostic tool. The hydrogen breath test should remain the primary method of lactose intolerance diagnosis because the hydrogen breath test is simple, non-invasive and easily available<sup>29</sup>. Many people are more tolerant of yogurt than milk because it contains lactase produced by the bacterial culture used to make the yogurt<sup>30</sup>. It is important for lactose intolerant people to be specially careful in avoiding products that whilst not apparently dairy (or are dairy but normally contain low amounts of lactose) nonetheless contain lactose. Such products include commercial sausages, medications which may contain lactose as a filler, most meal replacement and protein bars, cottage cheese and even yogurt. Avoidance of milk and other dairy products can lead to reduced calcium intake<sup>31</sup> which may increase the risk for osteoporosis and fractures<sup>32,33</sup>, in addition, the vitamin D status in patients with restricted intake of dairy products should be monitored. In a survey of healthy adolescents, 24% of attendees in an urban hospital in Boston were found to be vitamin D deficient<sup>34</sup>.

Patients should be informed that having lactose malabsorption does not mean they are allergic to milk, dairy products, or dairy foods. A milk allergy is related to the proteins in milk rather than the lactose. The degree of lactose malabsorption varies widely among patients, but most patients do not require a totally lactose-free or severely restricted diet<sup>35</sup>. Dairy products provide approximately 75% of the calcium.<sup>36</sup> Adult patients with lactose intolerance should maintain a calcium intake of 1,200 to 1,500 mg per day, including actual dairy products up to their individual threshold for symptoms. Milk intake commonly has to be limited to less than 250 to 375 mL (8 to 12 oz) per day. Patients should consider drinking lactose-reduced milk or taking calcium supplements. Patients should also be advised to avoid medications that contain lactose as filler and certain food products

that may contain unrecognized lactose. Patient education is usually highly useful in patients with lactose intolerance. Recent evidence<sup>37-38</sup> suggests that patients with medically confirmed lactose malabsorption can ingest the number of servings of milk and dairy products recommended by the American Dietetic Association without experiencing gastrointestinal discomfort. Some patients increase their tolerance to lactose with repeated intake<sup>39,40</sup>

## CONCLUSION

Increased frequency of lactose intolerance seen in females as compared to males. The frequency of lactose intolerance significantly increases with age of onset. Celiac disease was the common cause of secondary lactose intolerance. It is suggested that people with suspected carbohydrate malabsorption should have hydrogen breath test to evaluate for possible lactose intolerance.

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