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ORIGINAL ARTICLE

# Lactase deficiency and lactose intolerance in a multiracial Asian population in Malaysia

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**Key words**
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## Abstract

**Background and Aims:** There have been few reports on lactase deficiency (LD) and lactose intolerance (LI) in Malaysia, which has a peculiar mix of three distinct major Asian races—Malay, Chinese, and Indian. The aim of this study was to determine the prevalence of LD and LI in a young multiethnic Malaysian population.
**Methods:** Lactase activity was measured with a $^{13}CO_2$ lactose breath test using an infrared spectrometer. Each subject took 25 g of lactose naturally enriched in $^{13}CO_2$ together with 250 mL of water after an overnight fast. Breath samples were collected at baseline and at 15-min intervals for 180 min. Subjects were asked to report gastrointestinal (GI) symptoms following ingestion of the lactose test meal.
**Results:** Of the 248 subjects tested, 216 (87.1%) were lactase deficient. We found no significant differences in the presentation of LD between gender and races. LD was found in 87.5% of males and 86.8% of females ($P = 0.975$) and in different races: Chinese (88.5%) *versus* Malay (83.1%) ($P = 0.399$), Indian (90.5%) *versus* Malay ($P = 0.295$), and Chinese *versus* Indian ($P = 0.902$). LI was diagnosed in only 49 (19.8%) subjects; 35 patients had diarrhea, while the remainder had at least two other GI symptoms after the lactose meal.
**Conclusion:** The prevalence of LD was high in all three major ethnic groups—Malays, Chinese, and Indians. Ironically, the prevalence of LI was low overall.

## Introduction

Lactose intolerance (LI) is a syndrome whereby a person develops gastrointestinal (GI) symptoms from the maldigestion of lactose. This is due to an insufficiency of the enzyme lactase in their GI tract. This disorder is characterized by osmotic diarrhea, weight loss despite sufficient caloric intake, abdominal pain, and bloating.[1]

It is thought that Asian populations have decreased amounts of lactase in adulthood compared to Caucasian populations, especially those of northern European descent.[2] There have been a paucity of reports on the prevalence of LI and lactase deficiency (LD) in Asian patients.[3–6] Most of these papers focused on children and were published many years ago.

There have been a few reports on LD and LI in Malaysia, which has a peculiar mix of three major Asian races—Malay, Chinese, and Indian—living together. It has been a popular notion that, within our multiracial population, because Indians consume far larger amounts of milk and milk products in their daily diet, they have a higher lactase activity and are more tolerant to lactose compared to Chinese and Malays. However, there has been no study carried out in Malaysia on LD and LI in our local population.

In this study, we sought to determine the prevalence and differences of LD and LI in a young multiethnic Malaysian population.

## Patients and methods

A prospective study was conducted on consecutive young healthy medical subjects who volunteered for the study. Informed consent was obtained from all tested subjects. The study was approved by the ethics committee of the University Malaya Medical Centre, Kuala Lumpur, and the study was performed according to GCP/ICH guidelines. All subjects were interviewed by two investigators, followed by a $^{13}CO_2$ lactose breath test as described below.

Subjects with a previous history of GI surgery or any other condition that may affect gut transit were excluded from the study, as were subjects with any chronic GI symptoms and diseases.

***Analysis of breath samples.*** Before the breath testing, subjects were asked to refrain from consuming foods naturally enriched in $^{13}C$, such as cane sugar, corn, corn products, and pineapple, for 2 days before the experiment. All subjects were then tested with the $^{13}CO_2$ lactose tolerance test as previously

described by Hiele *et al*.[7] Each subject took 25 g of lactose naturally enriched in $^{13}CO_2$ together with 250 mL of water after an overnight fast. Breath samples were collected at baseline and then every 15 min for 180 min. The collected $^{13}CO_2$ breath was analyzed using an infrared isotope spectrometer (IRIS, Analyzer Wagner AnalysenTechnik™, Worpswede, Germany). Its computer analyzer software is able to plot curves of $^{13}CO_2$ concentrations in the breath and provide an index of the patient's ability to digest lactose. Patients with LD will produce minimal amounts of $^{13}CO_2$ in their breath. Cumulative excretions of $^{13}CO_2$ in the subject's breath were charted against four selected test time intervals of 0, 60, 120, and 180 min to determine the lactose tolerance in the subjects. A subject was considered lactase deficient if the cumulative excretion of $^{13}CO_2$ at 180 min was below the normal value of a control population previously determined by the manufacturer of the instrument.

***Assessment of LI and GI symptoms.*** Patients were asked for specific classical lactose intolerance GI symptoms, which included nausea, abdominal pain, bloating, borborygmi, and diarrhea. LI was defined as arbitrarily present when patients experienced diarrhea or at least two other classical LI GI symptoms 20–30 min after ingestion of the lactose meal.

***Statistical analysis.*** All data were entered into SPSS (Statistical Packages for the Social Sciences, version 19, Chicago, IL, USA) program for analysis. Fisher's exact tests and chi square tests were used to compare categorical data. A two-tailed test was used in all analyses, and a *P*-value of <0.05 was considered statistically significant.

## Results

A total of 248 subjects volunteered for this study; 104 were males (42%), and 144 were females (58%), with 89 Malays (35.9%), 96 Chinese (38.7) and 63 Indians (25.4%). The mean age of subjects was 21.7 ± 2.9 (S.D.)

***Lactase deficiency.*** Of the 248 subjects tested, 216 (87.1%) were lactase deficient. Amongst males, 87.5% were lactase deficient compared to 86.8% amongst the females. There was no statistical difference between males and females ($P = 0.975$). There were also no significant differences between the different races: Chinese (88.5%) *versus* Malay (83.1%) ($P = 0.399$), Indian (90.5%) *versus* Malay ($P = 0.295$), and Chinese *versus* Indian ($P = 0.902$). Subanalysis according to race and gender is as shown in Table 1. Although the prevalence in Indian males (91.4%) was numerically higher than in Malay males (73.7%), there was no significant difference ($P = 0.082$).

LI was diagnosed in 50 (20.2%) subjects. All were found to be lactase deficient; 35 patients had diarrhea after the lactose meal, while the remainder had at least two other GI symptoms: abdominal pain, bloating, or borborygmi. However, the majority of those who were lactase deficient did not exhibit LI symptoms—76.9% ($n = 166/216$).

**Table 1** Prevalence of lactase deficiency according to race and gender

| | Lactase deficient, *n*(%) | | | |
|---|---|---|---|---|
| | Male | Female | Total | Male *vs* female *P*-value |
| Malay | 14/19 (73.7) | 60/70 (85.7) | 74/89 (83.1) | 0.217 |
| Chinese | 45/50 (90.0) | 40/46 (87.0) | 85/96 (88.5) | 0.642 |
| Indian | 32/35 (91.4) | 25/28 (89.3) | 57/63 (90.5) | 0.775 |
| Total | 91/104 (87.5) | 125/144 (86.8) | 216/248 (87.1) | |

*Male*: Malay *versus* Chinese—$P = 0.088$; Malay *versus* Indian—*P* value = 0.082; Chinese *versus* Indian—$P = 0.825$.
*Female*: Malay *versus* Chinese—$P = 0.850$; Malay *versus* Indian—*P* value = 0.640; Chinese *versus* Indian—$P = 0.808$.

## Discussion

Lactose is a disaccharide commonly found in milk and is comprised of a galactose and glucose molecule linked by a beta 1,4 glycosidic bond. Intestinal absorption of lactose requires initial hydrolysis to its component monosaccharide by the intestinal beta-galactosidase enzyme, more commonly known as lactase. There are three main types of lactase deficiencies: primary, secondary/acquired, and congenital. The most common form of LD is primary adult hypolactasia. Lactase concentrations in the body are the greatest at birth and rapidly decline after weaning such that the majority of adults would be lactase deficient. Published studies in Chinese and Japanese patients have shown a steady decline in lactase activity in children with increasing age.[3–5] The timing and rate of decline is genetically determined[8] and varies between individuals and ethnic groups. It has been shown in Western populations that lactase activity persists into adulthood.[9] This is believed to be associated with two single-nucleotide polymorphisms in the lactase gene, which is located on chromosome 2.[10]

Some GI disorders that cause damage to the brush border or significantly increase transit time in the jejunum mucosa may result in the development of secondary or acquired hypolactasia.[8] Congenital hypolactasia is a rare disorder with severe symptoms, particularly in neonates. This is the result of mutations of the lactase-phlorizin hydrolase gene, which causes a deficiency of intestinal lactase activity. Symptoms begin as early as the first week of life due to the ingestion of lactose-containing breast milk or formula.[1] This condition is life threatening if not diagnosed and treated early as it may result in significant dehydration and electrolyte loss.[11]

LD, however, does not equate to LI. LI is defined as being present when abdominal symptoms—nausea, bloating, diarrhea, borborygmi, and abdominal pain—occur after ingestion of lactose. However, the key to diagnosis is the correlation to lactose intake. In our study, we have used stringent criteria of diagnosis—patients should experience diarrhea postlactose ingestion or, in the absence of diarrhea, patients must have at least two other GI symptoms stated above.

Symptoms, however, depend on the lactose load that the patient has ingested and are generated from maldigestion of lactose as a consequence of the "fermentation" of lactose in the GI tract. The generation of symptoms is partly dependent on a balance between the production and removal of fermented products. These fermented products include short-chain fatty acids, which are quickly absorbed by the colonic mucosa, as well as gases such as $H_2$ and $CO_2$.[12] These gases may cause symptoms such as bloating

and borborygmi if not removed efficiently via consumption by bacteria or absorption into the bloodstream.[12,13] Occurrence of diarrhea is largely due to the osmotic effect of the undigested lactose, causing net fluid secretion into the gut lumen. Having fluid in the gut lumen will also cause the sensation of distention and bloating.[14] Other factors also play a role in symptom generation. These include diet, GI transit time, flora of the gut, and other physiological factors including visceral hypersensitivity.[9]

The amount of lactose that can be tolerated by a lactose maldigester before onset of symptoms varies from person to person. In many cases, ingestion of dairy products does not result in clinical symptoms, and most people will still be able to ingest a certain amount of lactose.[10] Furthermore, LI symptoms can be subjective and overlap with that of dyspepsia and irritable bowel syndrome.[15]

The high prevalence of LD amongst Asian patients is in keeping with the findings of previous studies carried out in this region. In our study, we have shown a high prevalence of LD in the study population. Regardless of race or gender, the prevalence of LD was in an excess of 80%. However, only about 20% of our study population had symptoms of lactose intolerant (LI). This shows that, although many are unable to digest and absorb lactose, the malabsorption does not necessarily result in clinical symptoms.

We found a high prevalence of LD in all three races and no significant difference between races. This finding is similar to that of Asmawi *et al*.[16] The authors found that the prevalence of LD was 88, 91, and 83% amongst Malays, Chinese, and Indians, respectively, with no significant difference between any of the three races.[16]

Yap *et al*., in a smaller study, investigated the prevalence of LD in Singapore and Canadian adult Chinese using the $H_2$ breath test. In this study, the authors found both groups to have an inordinately high prevalence of LD at 98 and 99% respectively. Interestingly, only 32 and 23% of Singapore and Canadian Chinese, respectively, in this study had symptoms of LI. This is consistent with the findings of our study where only 19.8% of patients were lactose intolerant.[6]

In particular, we did not find a lower level of LD amongst Indian patients who consume more milk and milk products in their daily diet compared to Chinese and Malays. A study from India showed a lower prevalence of LD, but this was confined to the Northern Indians. Babu *et al*. showed, using the lactose hydrogen breath test, that 78.9% of Southern Indians and only 57.1% of Northern Indians ($P = 0.003$) had LD. Similar results were obtained with the lactose tolerance test where 88.2% Southern Indians and 66.2% Northern Indians ($P = 0.001$) were lactase deficient.[17] An earlier published study conducted on northern "Indian" patients in Panjab, Pakistan, showed similar results, with a prevalence of LD of 60%.[18] This difference has some genetic basis as many Northern Indians have a Caucasian background compared to Southern Indians, who are mainly Dravidians. In Malaysia, the overwhelming majority of Indians are Tamilians of Southern Indian descent (Dravidian) rather than Northern Indian. This may explain the high prevalence of LD amongst Indians in Malaysia.

We have chosen to use the $^{13}CO_2$ lactose breath test for our study. Although the $H_2$ breath test has been considered the gold-standard test for lactase activity, it has several drawbacks. It is an indirect method of measuring lactose malabsorption, which may lead to misinterpretation.[19] The basis of this test is that, in those with lactase insufficiency, lactose is not digested in the colon but is fermented by bacteria, which will release $H_2$ gas. Hence, a rise in $H_2$ concentrations in the breath is an indication of lactase insufficiency.[20] Another issue with the $H_2$ breath test is that, in a proportion of people, the gut may be colonized by bacteria that are incapable of producing hydrogen. A drop in pH could also affect the colonic microflora in producing $H_2$.[21]

Because of the many limitations of the $H_2$ breath test, the isotope labeled $^{13}CO_2$ was used to create a lactose breath test to investigate LI. $^{13}C$ was chosen instead of $^{14}C$ to compare with $^{12}C$ as it was nonradioactive, unlike $^{14}C$.[22,23]

There have been few studies of LD and LI in our multiracial Asian population in Malaysia. Our multiracial Asian population consisting of three major Asian races lends itself to study and comparison to determine if there were any differences in lactase activity in young adults between different ethnicities.

Although this study gives us important clear information about the prevalence of lactase insufficiency and LI in our local population, it has some limitations. First, the size of the study population relatively is small and only includes young healthy subjects. A larger study that includes a random sampling of the population, including subjects over a wider age range, would certainly be useful.

## Conclusions

The prevalence of LD was high in all three major ethnic groups—Malays, Chinese, and Indians. However, the prevalence of LI was low overall and in all three ethnic groups.

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