Review Article

Lactose intolerance in Indonesian children

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"Lactose intolerance (LI)" is considered a common problem in Asians, and in many parts of the world. Its prevalence and age of manifestation varies between by Asian country, for possible genetic or cultural reasons. Studies in Indonesian children 3-15 years old (y) are available within the past two decades, using a pure lactose tolerance test. The prevalences of lactose malabsorption (LM) in pre-elementary (3-5 y), elementary (6-11 y), and junior high (12-14 y) school-children were 21.3%, 57.8%, and 73%, respectively. An increasing trend for LM prevalence was seen within the pre-elementary group, from 9.1% at 3 y to 28.6% at 5 y. The most frequent symptoms of LI in junior high school (JHS) group were abdominal pain (64.1%), abdominal distention (22.6%), nausea (15.1%), flatulence (5.7%), and diarrhea (1.9%), mostly within one hour of lactose ingestion. In children with regular and irregular milk drinking, LM occurred in 81.2% and 69.6%; LI was found in 56.2% and 52.1%, respectively. Most JHS children with dairy-associated recurrent abdominal pain (RAP) symptoms proved to be malabsorbers. Dairy products most related to RAP were milk and yogurt. LI was found in 81% of RAP children with abdominal pain most frequently, followed by nausea, bloating, diarrhea, borborygmi, and flatulence. Symptom onset occurred 30 minutes after lactose ingestion, especially nausea, bloating, and abdominal pain. In RAP children LI symptoms mostly found in breath hydrogen concentration >20 ppm. More LI symptoms were found in lactose malabsorbers, but symptoms were mild and generally disappeared in 7 hours, and in most by 15 hours.

Key Words: lactose intolerance, lactose malabsorption, children, lactase deficiency, Indonesia

INTRODUCTION

Lactose intolerance, the inability to digest lactose in the diet, is considered a common medical condition in Asian countries and may have an impact on the quality of life. It is characterized by symptoms such as abdominal pain, bloating, flatulence, and diarrhea.[1,2] Because lactase activity progressively decreases following weaning, only a minority of children maintain high lactase levels until adulthood. Lactose intolerance is considered an irreversible and developmental phenomenon, and appears to be attributable to genetic factors and influenced by cultural factors.[1,2]

Lactose intolerance is more prominent in older children, particularly in Asian countries, because of the decrease in lactase activity beginning at ages of 2–3 years. The prevalence and age of manifestation vary among Asian countries. Genetic factors are proposed to contribute to this primary lactase deficiency. Not all children with lactose malabsorption experience symptoms, because it depends on several factors such as the rate of gastric emptying, motility of the small intestine, sensitivity of colonic flora, and the amount and manner of lactose ingestion.[2]

Lactose intolerance, though frequently observed, has not been studied widely in Indonesia. Data on lactose malabsorption and intolerance in Indonesian population are not as readily available as those in the international population. However, lactose malabsorption in Indonesian children aged 3–15 years was studied between 1997 and 2004. Data on the incidence of lactose malabsorption and lactose intolerance in crucial age groups and subgroups; the onset, type, and duration of symptoms; the association with food and various types of dairy products; and recurrent abdominal pain (RAP) are presented in this review article.

VARIATION OF LACTASE ACTIVITY AMONG POPULATIONS

Lactase activity varies among geographical locations and populations worldwide. The frequency of lactase persistence is 100% in the Dutch population and 99% in the Swedish population. By contrast, the frequency of lactase nonpersistence is 80%–100% in some Asian and African countries, particularly 60% in Pakistan, 90% in Thailand, and 90% in China, whereas it is merely 4% in Denmark and 16%–23% in Russia.[1]

The prevalence of lactose intolerance has been shown to be age related. The prevalence of lactose intolerance was 12.2%, 33.1%, and 30.5% in Chinese children at the ages of 3–5 years, 7–8 years, and 11–13 years, respectively.[3] The prevalence of lactose intolerance in Malaysia was 88% in Malay, 91% in Chinese, and 83% in Indian ethnic groups.[3] According to US data, Hispanics were 43% more likely to report symptoms of lactose intolerance following

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a lactose challenge than white non-Hispanics, and the prevalence was higher in African–American children than in Caucasian children.[4]

The high percentage of lactase persistence in the northern European population and a few other ethnic populations is strongly correlated with the dairying history of the population, where the culture of dairying creates a strong selective advantage for those who can drink milk and nutritionally benefit from the milk. Some studies have suggested that such individuals are heterozygous. This genetic polymorphism may be a factor determining whether an individual is tolerant or intolerant to lactose. Moreover, family studies have suggested that lactose intolerance is inherited as an autosomal recessive trait. Individuals with both hypolactasia and lactase persistence have identical coding sequences and thus identical lactase activity. Random mutations have occured in regions upstream from the *LCT* gene that have an enhancer effect on the LCT promoter, which enables carriers with a lactase-persistence phenotype to exist in human populations.[1] A population genetics analysis suggested that low lactase activity might be an autosomal recessive trait, whereas high lactase activity is an autosomal dominant trait.[5]

CLINICAL VARIATIONS AND TERMINOLOGY ASSOCIATED WITH LACTASE DEFICIENCY

Lactose malabsorption is inefficient lactose digestion because of reduced expression or impaired activity of the lactase enzyme. In some people, it results in symptoms, with the most frequent being abdominal pain, bloating, flatulence, and diarrhea. These clinical symptoms caused by the lack of lactase are collectively defined as lactose intolerance.

Diagnosing lactose intolerance is difficult because it depends on self-reported symptoms that are variable and thus may not be assessed objectively. The diagnosis is based on a combination of clinical findings and the results of an appropriate test. The breath hydrogen test (BHT) is the primary procedure for determining the presence of lactose malabsorption in Indonesia.[6] Children drink a lactose bolus (2 g/kg body weight; max 50 g), and the lactose BHT is conducted to measure the hydrogen gas partially excreted in the breath. This test is sensitive and noninvasive. A >20 ppm or 10–19 ppm increase in the hydrogen level expired after approximately 60 minutes, along with the characteristic symptoms, is consistent with lactose malabsorption.[7,8] The test suffers from the limitation that lactose is ordinarily not consumed as the isolated sugar in the human diet, but rather as a foodstuff likely to modify the response.

LACTOSE MALABSORPTION IN INDONESIAN CHILDREN

Primary lactase deficiency or lactase nonpersistence is the downregulation of lactase activity; it is genetically determined and considered as a developmental phenomenon. Brush border lactase activity is only a small fraction of the infantile level based on brush border biopsy. It occurs soon after weaning from breast milk in most ethnic groups, but the prevalence and age of manifestation vary among ethnic populations. Several studies have examined lactose malabsorption and intolerance in Indonesian children. Data on the Indonesian population show the prevalence of lactose malabsorption in pre-elementary school (age, 3–5 years),[9] elementary school (age, 6–11 years),[10] and junior high school (age, 12–14 years) children to be 21.3%, 57.8%, and 73%, respectively (Figure 1).[11]

A thorough analysis of each subgroup shows an increasing trend in the prevalence of lactose malabsorption in pre-elementary school children (age, 3–5 years). The prevalence was only 9.1% at 3 years of age and constantly increased to 28.6% at 5 years of age (Figure 2).[9]

In elementary school children (age, 6–11 years), no significant difference in the incidence rate of lactose malabsorption was observed among all age groups. Hegar et al reported an incidence rate ranging between 57.1% and 58.6% (Figure 3).[10]

The incidence rate of lactose malabsorption increased in junior high school children, with 69% of the population showing the hydrogen concentration in the breath to be >20 ppm (Figure 4).[11]

Not all lactose-intolerant children exhibit the aforementioned symptoms.[3] Therefore, they may not realize that they are lactose intolerant. Undigested lactose acidifies the colon and increases the osmotic load, resulting in loose stool and diarrhea.[6] Considerable intraindividual and interindividual variation in the severity of symptoms is observed according to the amount of lactose ingested and the ability of a patient to digest it as well as the individual perception of abdominal pain and discomfort.

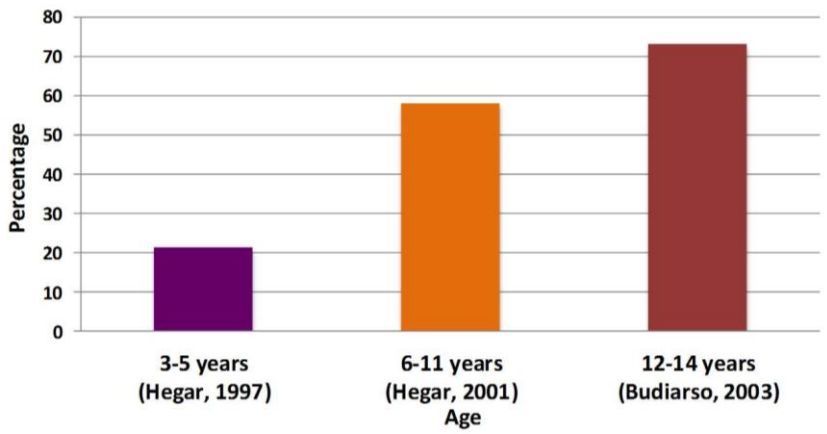

Figure 1. Lactose malabsorption in Indonesian children.[9-11]

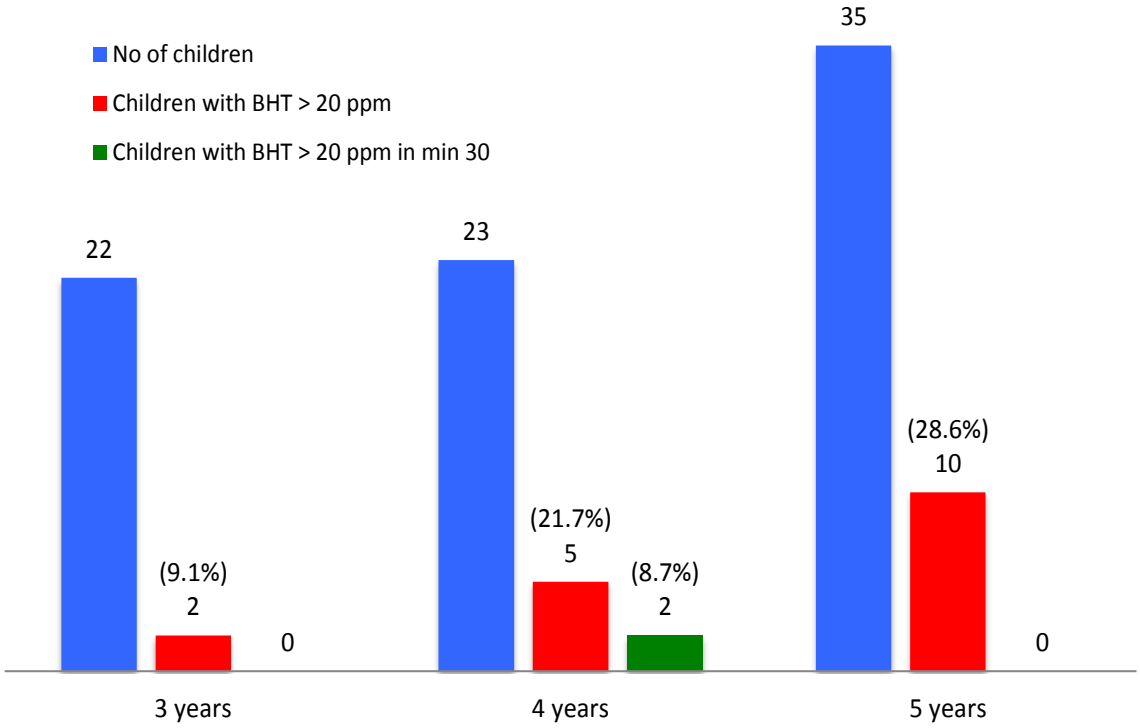

Figure 2. Prevalence of lactose malabsorption in pre-elementary children (age 3-5 years).[9]

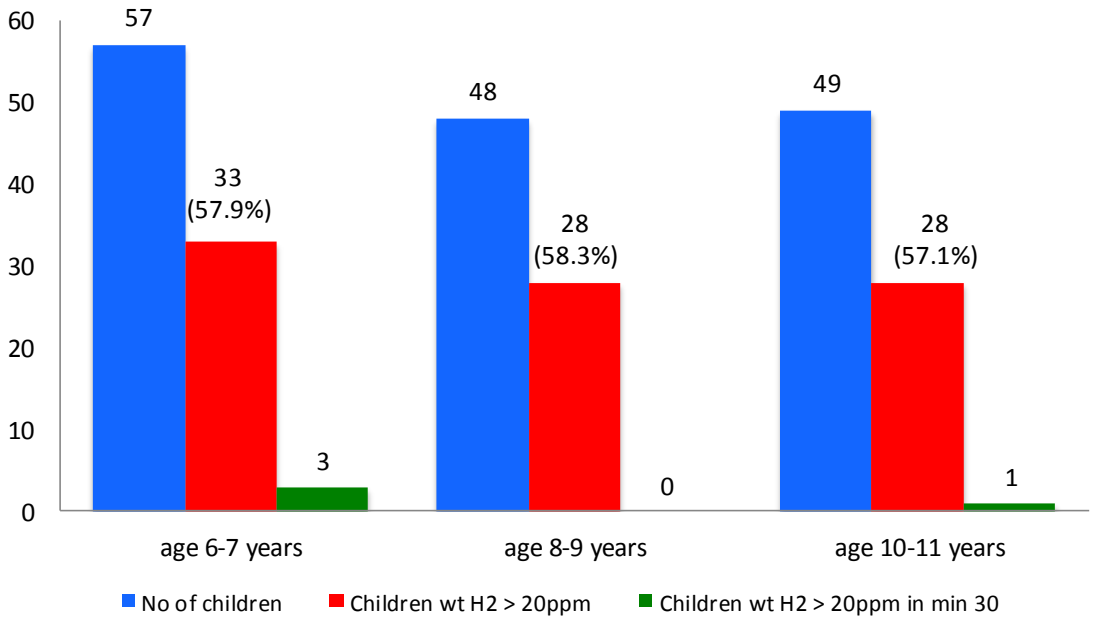

Figure 3. Prevalence of lactose malabsorption in elementary school children (age 6-11 years).[10]

Boediarso et al reported that lactose intolerance occurred in 53 of 98 children (54%) aged 12–14 years, and the most frequent symptom was abdominal pain (64.1%), followed by abdominal distention (22.6%), nausea (15.1%), flatulence (5.7%), and diarrhea (1.9%). Five children exhibited two symptoms. The symptoms of lactose intolerance mainly occurred 1 hour after ingestion of a test dose of a lactose solution. Only diarrhea occurred within 2 hours. Lactose malabsorption was not always followed by the symptoms of lactose intolerance (Figure 5).[11]

The disappearance of symptoms in patients with lactose intolerance led scientists to believe that lactase induction occurred. Several studies have shown an increase in lactase activity after high lactose intake.[12–14] However, the increase was smaller than the decrease that occurs around the weaning period. A US study reported no difference in milk consumption by both lactose-tolerant and lactose-intolerant children.

The severity of symptoms varies depending on the amount of lactose that can be tolerated by each child. In children with lactose malabsorption who exhibit clinical symptoms, the increase in expired hydrogen levels tends to occur earlier and be greater after lactose ingestion

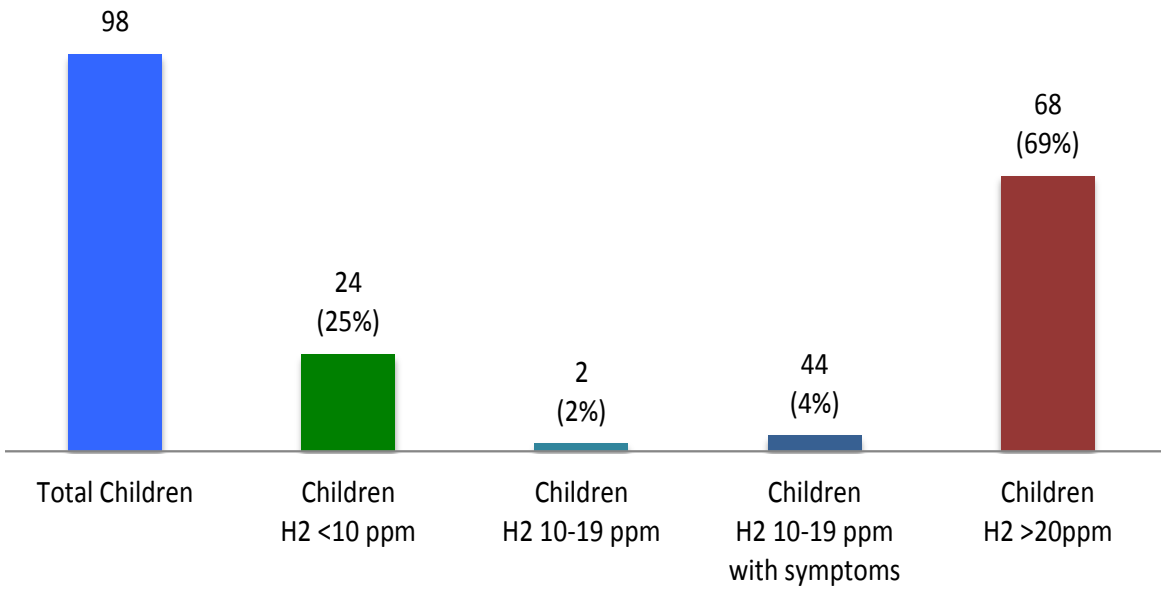

Figure 4. Prevalence of lactose malabsorption in junior high school children (age 12-14 years).[11]

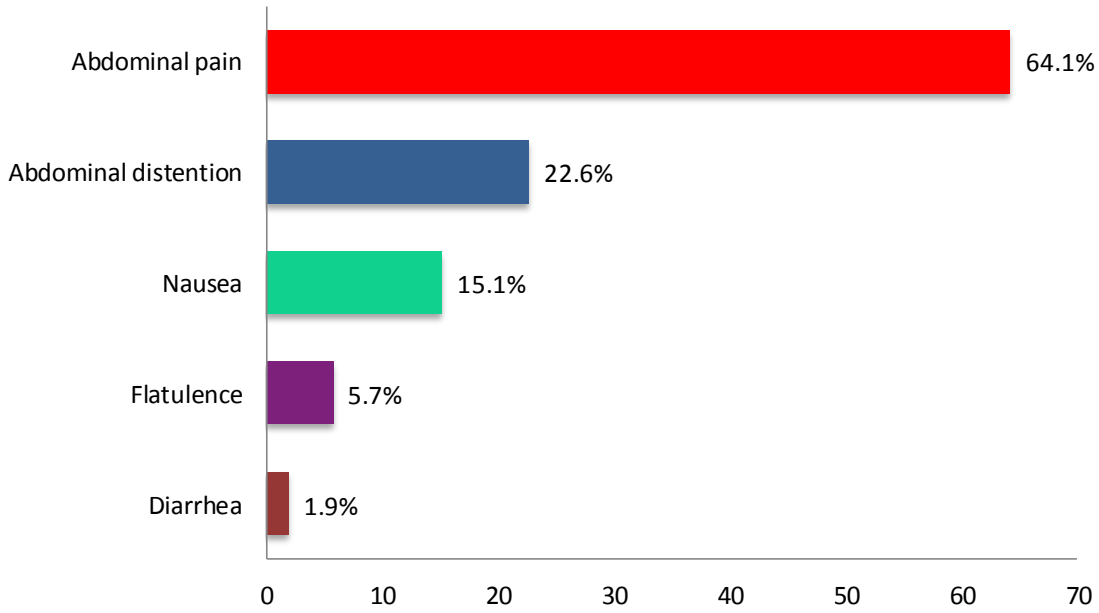

Figure 5. Symptoms after ingestion of lactose solution in 98 junior high school children.[11]

compared with that in children with malabsorption who exhibit no clinical symptoms.

A regular milk-drinking habit was reported in 33% of junior high school children. Lactose malabsorption occurred in 81.2% children of this age group with a regular milk-drinking habit and 69.6% children of this age group with an irregular milk-drinking habit (Figure 6).[11]

Lactose intolerance was observed in 56.2% of junior high school children with a regular milk-drinking habit and 52.1% of those with an irregular milk-drinking habit (Figure 7).[11]

LACTOSE MALABSORPTION AND RECURRENT ABDOMINAL PAIN

RAP is the most commonly observed symptom of lactose intolerance, and each RAP complaint from a patient should be carefully assessed.[15-20] Lactose malabsorption as a contributing factor for RAP in children was studied in 85 Indonesian children aged 12–14 years by using the BHT, and the prevalence of lactose malabsorption was found to be 80%.[6] Four children exhibited a hydrogen concentration in the breath >20 ppm within the first 30 minutes after lactose ingestion (Figure 8), probably because of the overgrowth of bacteria; bacteria from the colon overflowed to the small intestine, leading to early fermentation of lactose in the intestine and, consequently, increased hydrogen gas production within 20–30 minutes (early peak).[21]

The dairy products most frequently reported as the cause of RAP are milk and yogurt, followed by ice cream, chocolate, cheese, and biscuits. In one study, most children with a history of RAP thought to be associated with dairy product consumption were lactose malabsorbers (Figure 9).[6] A possible reason for this condition was the

extremely high prevalence of lactose malabsorption (80%).

In the study by Yohmi,[6] yogurt seemed to cause RAP in children instead of alleviate it, whereas several studies have demonstrated that lactose tolerance is enhanced after yogurt consumption. Thus, yogurt has widely been used for treating lactose intolerance. This difference was probably due to the difference between fresh yogurt and pasteurized yogurt. Pasteurization of yogurt, which reduces its β-galactosidase activity, can also diminish multiple beneficial effects of lactose digestion. Slower gastric emptying; a longer orocecal transit time, which is proposed to be due to osmolality; and the physical form of yogurt are also suggested to play a role.[22]

The progression of lactose intolerance after lactose ingestion varies in each individual. Lactose intolerance during BHT was reported in 81% of children. The most frequent symptom was abdominal pain (56 children), followed by nausea, bloating, diarrhea, borborygmi, and flatulence. Several symptoms began to appear 30 minutes after lactose ingestion, particularly nausea, bloating, and abdominal pain (Figure 10).[6] A previous study reported that nausea and bloating usually occurred within 30 minutes after lactose ingestion, whereas abdominal pain, flatulence, borborygmi, or diarrhea usually appeared later, within 1–2 hours after lactose ingestion.[23]

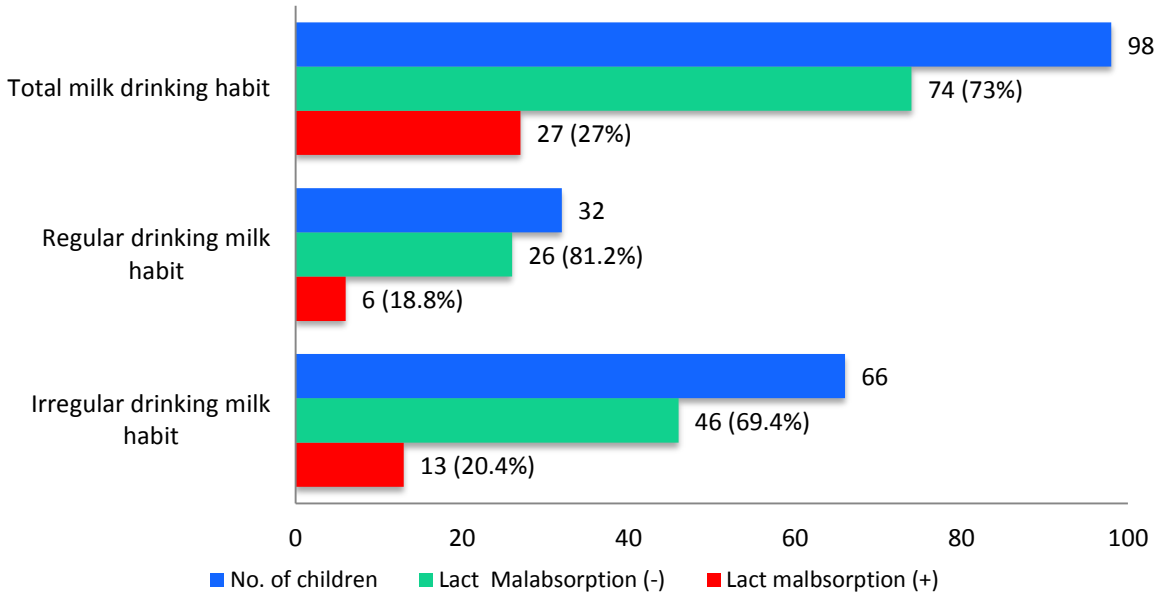

Figure 6. Lactose malabsorption in junior high school children related to milk drinking habit.[11]

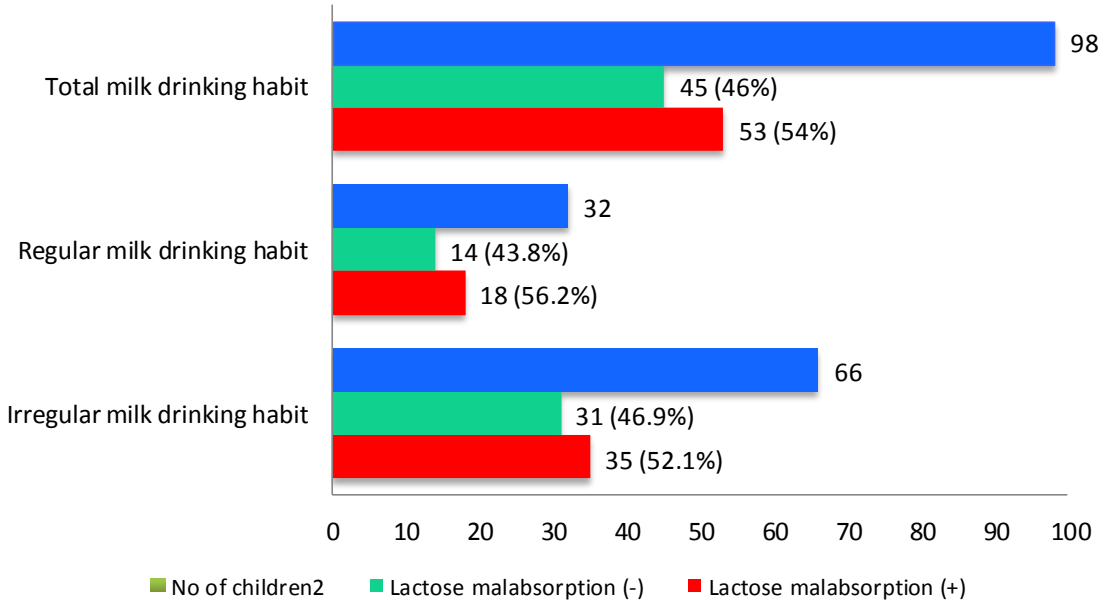

Figure 7. Lactose intolerance in junior high school children Related to milk drinking habit.[11]

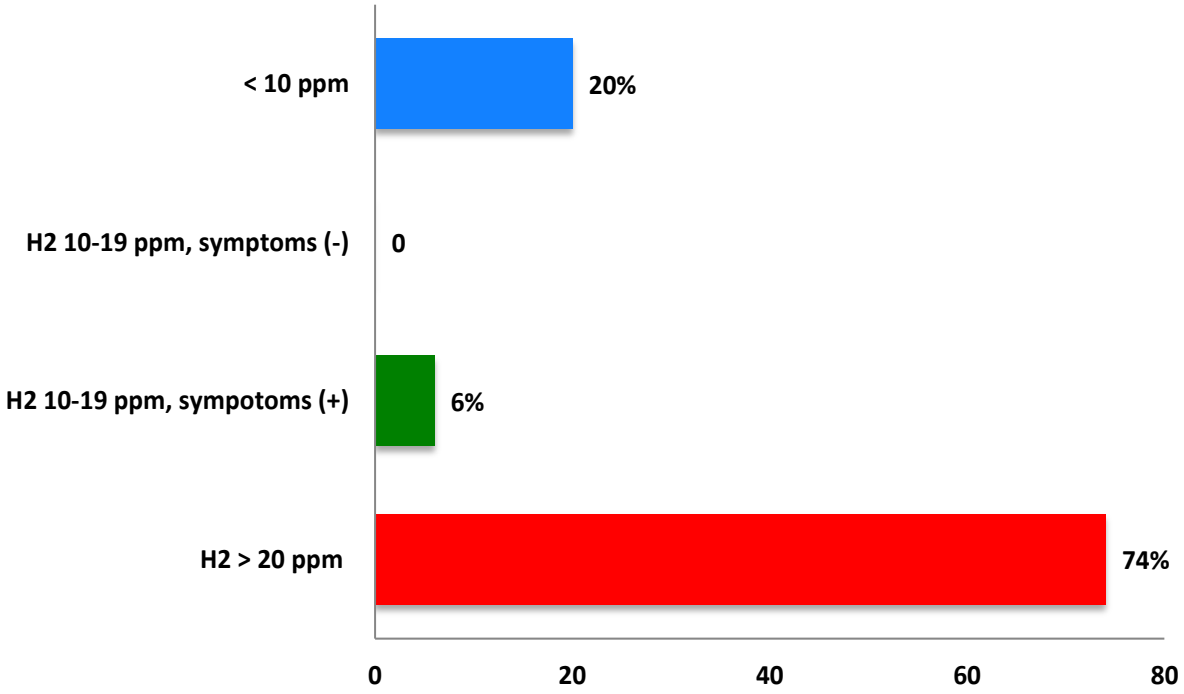

Figure 8. Lactose malabsorption in Indonesian children with recurrent abdominal pain.[6]

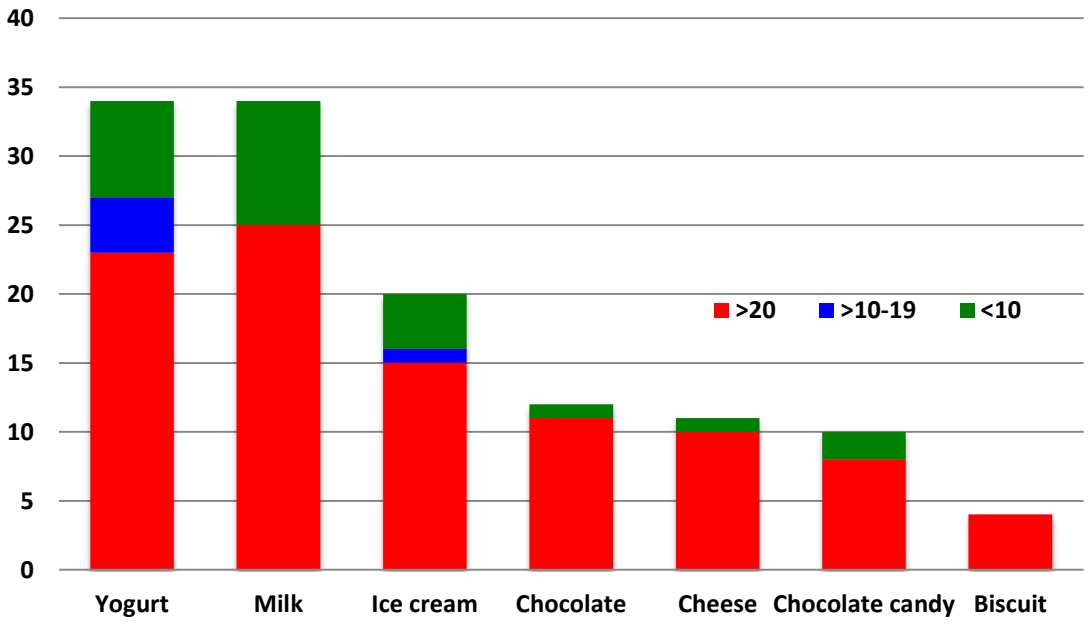

Figure 9. Breath hydrogen concentration in children with recurrent abdominal pain: relation to food-associated symptoms.

The symptoms of lactose intolerance, such as abdominal pain, nausea, bloating, and borborygmi, were frequently observed in children with an increased hydrogen concentration in the breath (>20 ppm). More lactose intolerance symptoms were observed in children with lactose malabsorption than in those with no lactose malabsorption (Figure 11). Few symptoms of lactose intolerance were evident in children showing a <10 ppm increase in the hydrogen concentration in the breath. This is probably because the colonic bacteria present in those children produced not hydrogen but methane gas that could induce symptoms of lactose intolerance. A group of children with an increased hydrogen concentration in the breath (>20 ppm) did not complain of any symptoms. The symptoms of lactose intolerance depend on several factors, such as the rate of gastric emptying, motility of the small intestine, sensitivity of colonic flora, and the amount and manner of lactose ingestion.[24]

The symptoms in junior high school children were relatively mild and disappeared in 7 hours. A follow-up after the lactose load showed that the symptoms disappeared in approximately 15 hours. Only two children exhibited the symptoms 36 hours after lactose ingestion. Most children had recovered from the symptoms within 15 hours after ingestion (Figure 12).[6]

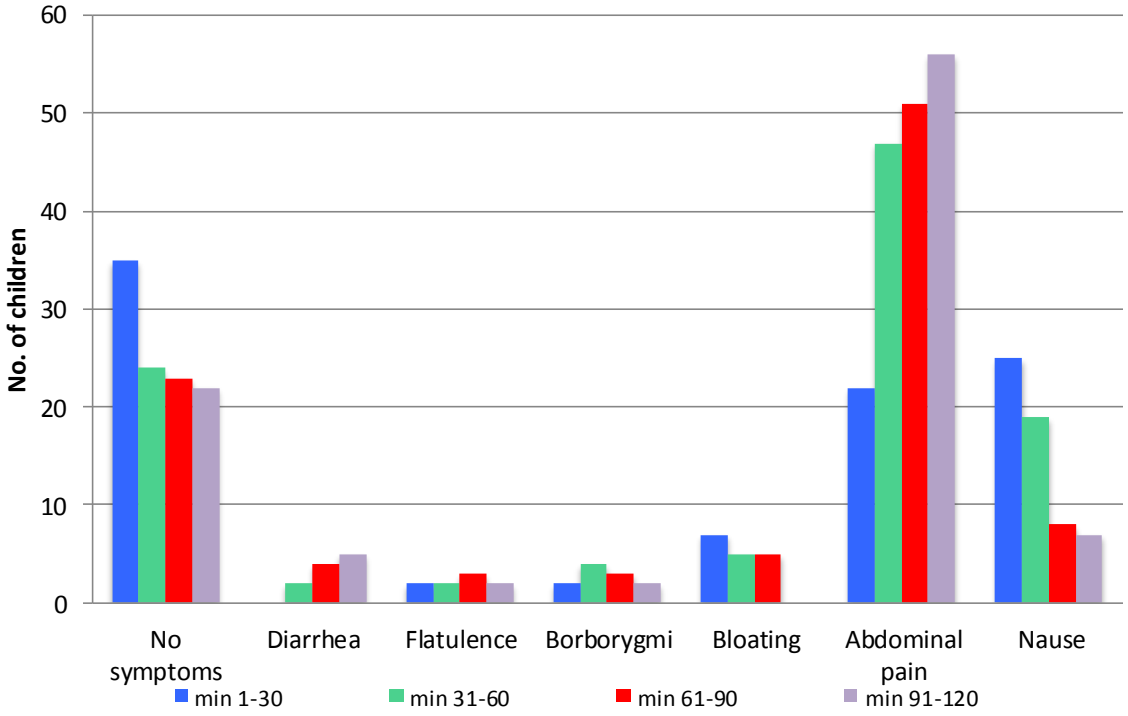

Figure 10. Food-related recurrent abdominal pain symptoms in children with and without lactose malabsorption.[6]

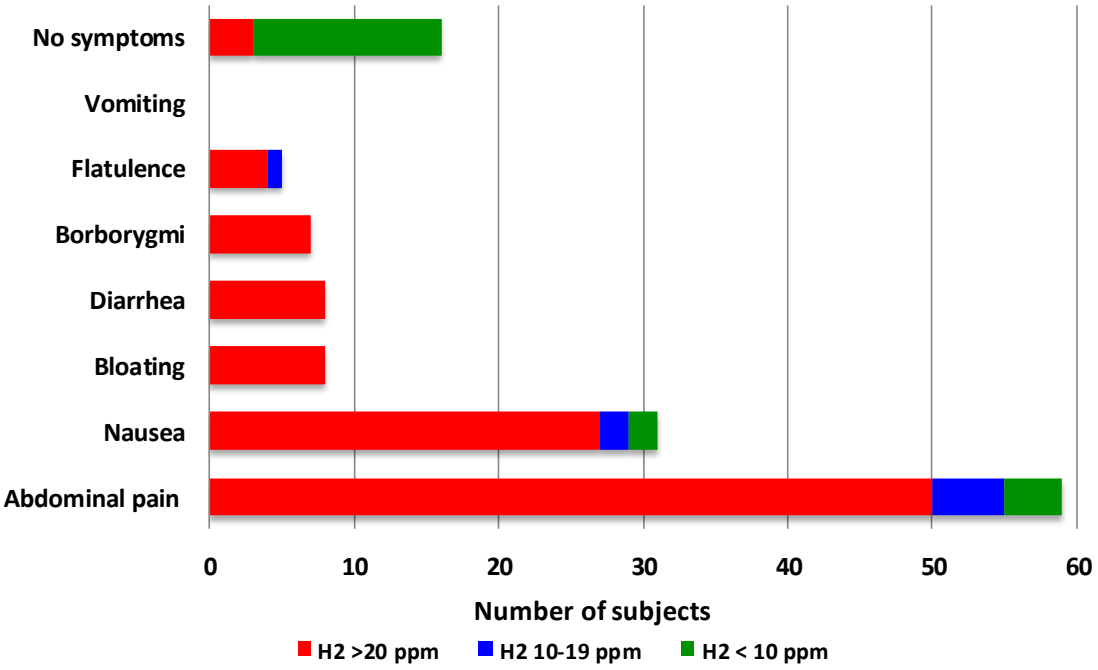

Figure 11. Breath hydrogen concentration in children with recurrent abdominal pain based on lactose intolerance symptoms.[6]

WHAT NEXT?

Multiple challenges are faced in the management of lactose intolerance. Several options can be considered for managing lactose intolerance in the Asian population. The first option is to exclude or lower lactose consumption. This is a logical option for people who know that they always experience uncomfortable symptoms after lactose ingestion. Asian food contains less milk and dairy products than Western food does. However, some lactase-deficient people can tolerate a substantial amount of milk without developing any signs or symptoms of lactose intolerance. Therefore, elimination of dairy products is not necessary for such people.

Complete elimination of dairy products from the diet may lead to adverse consequences, such as osteoporosis, although this is disputed. As an alternative, lactose-intolerant people can try consuming modified forms of dairy products, such as fermented dairy products that contain a reduced amount of lactose, or consuming milk with meals, thus preventing symptoms of lactose intolerance.[25]

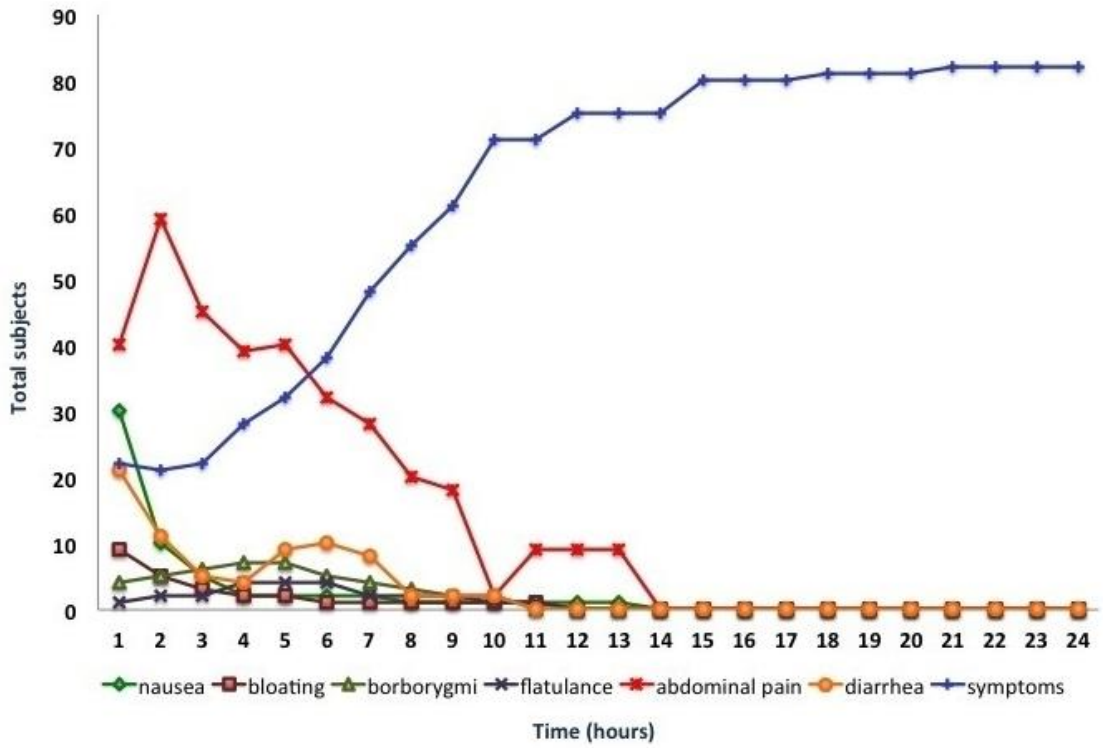

Figure 12. Duration of lactose intolerance symptoms after lactose load in children with recurrent abdominal pain.[6]

Prehydrolyzed milk products treated with β-galactosidase by microorganisms are available. Adding this enzyme to milk improves both the absorption of and tolerance to lactose. In addition, yogurt contains beneficial bacteria, organisms that consume some lactose while passing through the gastrointestinal tract and are active in the duodenum.[3,26] A slight difference is observed in the lactase level after consumption of various commercial yogurts, which usually contain *Lactobacillus bulgaricus* and *Streptococcus thermophilus* in a sufficient quantity (10^8 bacteria/mL). *Lactobacillus acidophilus* is unique because it has no lactase activity, but it can disrupt cell membrane to release lactase from the cells.[27] In a study in Jakarta, Yohmi et al observed that commercial yogurt is the second most common product causing the symptoms of lactose intolerance, raising the question regarding whether the Indonesian population has a lower lactase level than that of other Asian populations.[6]

Frequent exposure to milk products may reduce the severity of residual symptoms in children with lactose intolerance.[3] Repeated daily consumption of milk and dairy products that contain lactose may increase the ability of bacteria in the colon to ferment to produce nutritious products from lactose. For asymptomatic people, a cup of milk should be well tolerated and preferably consumed with other food to slow the intestinal transit time, allowing additional time for lactose digestion.

Of fundamental importance in the interpretation of studies of 'lactose intolerance' is that its formal evaluation by symptoms and breath hydrogen has been in relation to a dose of lactose itself rather than dairy products or the episode of eating in which lactose is consumed. The failure to use food-based methodology may have led to an over-attribution of RAP to lactose intolerance.

CONCLUSION

An increasing prevalence of lactose malabsorption is evident in older Indonesian children. Lactose malabsorption has been detected in numerous children with RAP. Milk-drinking has been of concern as responsible for RAP on account of lactose malabsorption. Milk and yogurt have been the products most frequently considered as causal of RAP in children who were mostly lactose malabsorbers. The available Indonesian data were collected more than a decade ago (those on pre-elementary school children aged 3–5 years are particularly outdated), and the prevalence may have been changed considering the potential adaptive responses in children with lactose intolerance. Moreover, it is now necessary to re-evaluate the purported associations between dairy foods and RAP with tests using the foods themselves rather than lactose alone.

AUTHOR DISCLOSURES

The authors declare that there are no conflicts of interest.

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Review Article

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印尼兒童的乳糖不耐症

在亞洲及世界的許多地區，“乳糖不耐症（LI）”被認為是一個常見的問題。它的盛行率及好發年齡依亞洲國家而有所差異，這可能與基因或是文化因素有關。過去二十年來，印尼有 3-15 歲兒童採用純的乳糖耐受性試驗的研究，可作為探討此議題之用。乳糖吸收不良（LM）的盛行率在學齡前（3-5 歲）、國小（6-11 歲）及初中（12-14 歲）學童分別為 21.3%、57.8%及 73%。LM 盛行率在學齡前兒童有增加的趨勢，從 3 歲的 9.1%至 5 歲的 28.6%。初中生組（JHS）LI 最常見的症狀為腹痛（64.1%）、腹部脹氣（22.6%）、噁心（15.1%）、腸胃脹氣/排氣（5.7%）及腹瀉（1.9%），大部分是在攝取乳糖一個小時內出現。規律與不規律飲用牛奶的兒童，LM 發生分別為 81.2%及 69.2%；LI 則為 56.2%及 52.1%。大部分初中生如有乳製品相關再復發腹痛（RAP）症狀者，即認為是吸收不良者。與 RAP 最相關的乳製品是牛奶及優格。81%的 RAP 兒童被發現有 LI，其中以腹痛最常發生，再來是噁心、腹脹、腹瀉、腹鳴及腸胃脹氣/排氣。通常在攝取乳糖 30 分鐘後，開始有症狀，特別是噁心、腹脹及腹痛。在 RAP 學童，LI 症狀最常發生在 BHC 大於 20 ppm。很多 LI 症狀可在吸收不良者發現，但症狀輕微且通常於 7 小時內消失，至多為 15 小時。

關鍵字：乳糖不耐症、乳糖吸收不良、兒童、乳糖酶缺乏、印尼