

FREQUENCY OF SECONDARY LACTOSE INTOLERANCE IN CHILDREN WITH SEVERE ACUTE MALNUTRITION WITH DIARRHOEA

Sabir Khan, Saira Uzma, Zia Muhammad, Syed Imad Ali Shah, Irshad Ahmad

Department of Pediatrics Khyber Teaching Hospital - Peshawar - Pakistan

ABSTRACT

Objective: To determine the frequency of lactose intolerance in children with severe acute malnutrition presenting with diarrhea.

Material and method: This study was conducted in nutritional rehabilitation unit, Khyber teaching hospital Peshawar from June 2014 to December 2014. It was a descriptive cross sectional study comprising of 150 paediatric patients ranging from 5 months to 5 years of age who met the WHO criteria of acute severe malnutrition having Z-score of $< -3SD$ with weight for height/length, age and sex presenting with diarrhea. Then stool was tested for reducing substances in freshly collected sample.

Results: Of the total 150 patients of 5-60 months of age (mean age 17.7 ± 11.91 SD), 82 (54.7%) were male and 68 (45.3%) were female. Overall 41 (27.3%) were lactose intolerant (having diarrhea with positive stool reducing substances) among them 21 were male (51.2%) while 20 were female (48.7%), 32 patients (78.04%) were having kwashiorkor and 9 patients (21.9%) were marasmic. Perianal rash, abdominal distention were present in 37 (90.2%) and, 38 (92.6 %) patients respectively. The findings which were significantly observed in children with lactose intolerance were edematous malnutrition (p-value 0.003), perianal rash (p-value 0.00), and abdominal distention (p-value 0.00).

Conclusion: Secondary lactose intolerance is a common problem of children with acute severe malnutrition presenting with diarrhea. Clinical signs of lactose intolerance in severely malnourished children are perianalexcoriation of skin and abdominal distention.

Key words: Child, lactose intolerance, Kwashiorkor, nutrition disorders, Diarrhea.

This article may be cited as: Khan S, Uzma S, Muhammad Z, Shah SIMA, Ahmad I. Frequency of secondary lactose intolerance in children with severe acute malnutrition with diarrhea. *J Med Sci* 2018; 26: (4) 326-330.

INTRODUCTION

One of the common complications of diarrhea is lactose intolerance especially in infants with severe malnutrition leading to failure of subsequent management.¹ Recognition of this relatively common condition is important, as it can be easily managed by simple dietary measures. It is the failure to digest significant quantity of lactose, the milk sugar. This non-digestion results from a shortage of lactase enzyme which is normally produced by enterocytes of small intestine². Normally lactose is digested by intestinal lactase to glucose and

galactose on the microvillus membrane of enterocytes of small gut³. The liver converts galactose into glucose which is reabsorbed into blood. When lactose is not absorbed by small intestine, it attracts water in the bowel lumen as a result of high osmolality of the intraluminal sugar and passes rapidly into large gut, where lactose is converted to short chain fatty acids and gas (CO₂, hydrogen and methane) by the bacterial flora thus resulting in osmotic diarrhea, perianal excoriation by acidic stool and flatulence along with passage of flatus⁴⁻⁶.

In majority of the human beings a decrease in the activity of enzyme lactase occurs during mid-childhood resulting in low levels of this enzyme in adult population.⁵ Usual manifestations of lactose intolerance include, abdominal cramps, bloating, gas, nausea and loose motions which begin half hour to 2 hours after ingesting lactose containing food.

Dr. Sabir Khan (Corresponding Author)
Associate Professor
Pediatrics KTH
E-mail: Drsabirkhan66@yahoo.com
Contact: 0333-9112613

Date Received: June 06, 2018
Date Revised: Aug 28, 2018
Date Accepted: Oct 20, 2018

Lactose intolerance is usually categorized into primary and secondary lactose intolerance. Primary lactose intolerance is characterized by the congenital absence of enzyme activity in the enterocytes of small intestine, with normal histology of small bowel mucosa and normal levels of other disaccharidases,⁶ while secondary intolerance is defined as the inability to digest significant amount of disaccharide lactose secondary to certain diseases such as , celiac disease, infectious enteritis, bacterial overgrowth, giardiasis, drug induced enteritis, mucosal injury, inflammatory bowel disease and radiation enteritis⁷⁻⁹. Various studies have shown the prevalence of secondary lactose intolerance ranging from 26% to as high as 100% in affected pediatric population¹³⁻¹⁵

Lactase activity is diminished in many patients with edematous malnutrition even at early ages, and lactose intolerance occurs more frequently in infants and children with kwashiorkor (48.3%) than in those with marasmic-kwashiorkor (20%), marasmus (15%), and healthy controls (23.5%).^{16,17} Prevalence of secondary lactose intolerance is 25.5% in severely malnourished children presenting with diarrhea. The prevalence of lactose intolerance in Pakistani children as reported by one study is 31%.¹⁸ Approximately 20% of Asian, Hispanic, and black children less than 5 years of age have evidence of lactase deficiency.¹⁹

Diarrheal disease is a leading cause of infantile and childhood morbidity and mortality in the world, and usually results from contaminated water and food sources. Worldwide, 780 million individuals lack access to clean drinking-water and up to 2.5 billion people lack improved sanitation. Diarrhea due to infection is prevalent throughout developing countries. In the developing world, children under three years of age experience on average three episodes of diarrhea per year.²⁰ Each episode deprives the child of the nutrition necessary for development and growth. As a result, diarrhea is one of the major causes of malnutrition, and malnourished children are more prone to fall ill from diarrhea. Children who die from diarrhea often have underlying protein calorie malnutrition, which makes them more vulnerable to diarrhea. There is a vicious circle that each episode of diarrhea, in turn, makes their existing malnutrition even more badly.

The rationale for this study was that limited local studies have been done to highlight this common problem of malnourished children presenting with diarrhea not responding to routine management. This study will highlight the issue and will improve the management outcome of such patients overall.

MATERIAL AND METHODS

This study was conducted in nutritional rehabilitation unit, Khyber teaching hospital Peshawar-Pakistan from June 2014 to December 2014. It was a descriptive cross sectional study comprising of 150 children from five months to five years of age who met the WHO criteria of acute severe malnutrition having Z-score of $< -3SD$ with weight for height/length, age and sex presenting with diarrhea. Children already on lactose free diets were excluded from the study as it act as confounder and if included would have introduced bias in the study result. Permission was taken from ethical board before starting the study. All those fulfilling our inclusion criteria were enrolled after informed consent from the parents. Detailed history and physical examination was performed to look for signs and symptoms of secondary lactose intolerance (diarrhea, abdominal distension, and perianal excoriation) in addition to signs of severe acute malnutrition (wasting, wrinkling, thinning and brittleness of hair, nutritional edema and dermatitis). Then stool for reducing substances in freshly collected sample were done from Khyber medical college Peshawar.

Operational definition

Acute severe malnutrition: Malnutrition of less than 3 months duration with WHO weight for length/height Z-score < -3 .²¹

Secondary lactose intolerance: Previously normal child since birth, who develops diarrhea with signs and symptoms of lactose intolerance (diarrhea, abdominal distension, and perianal excoriation) with positive stool for reducing substances later in life.

Diarrhea: Diarrhea is defined as the passage of three or more than three loose watery stools per day.²²

All the information was recorded in predesigned proforma. Exclusion criteria was strictly followed to control confounders and bias in the results. Data collected and analyzed in SPSS version 20. Mean \pm SD was calculated for numerical variables like age. Frequency and percentages were calculated for categorical variables like gender, secondary lactose intolerance and reducing substances. Stratification of secondary lactose intolerance was done for age and sex. All results were presented in descriptive form, tables and graphs.

Kwashiorkor and marasmus were defined according to Welcome classification.

Kwashiorkor: Weight between 60-80 % with edema.

Marasmus: Weight less than 60 % without edema.

Marasmic Kwashiorkor: Weight below 60 % with edema.

RESULT

Of the total 150 patients of 5-60 months of age (mean age 17.7 ± 11.91 SD), 82(54.7%) were male and 68(45.3%) were female. Overall 41 (27.3%) were lactose intolerant (having diarrhea with positive stool reducing substances) among them 21 were male (51.2%) while 20 were female (48.7%), 32 patients (78.04%) were having kwashiorkor and 9 patients (21.9%) were marasmic. Perianal rash, abdominal distention were

present in 37 (90.2%) and 38 (92.6 %) lactose intolerant patients respectively. The findings which were significantly observed in children with lactose intolerance were edematous malnutrition (p-value 0.003), perianal rash (p-value 0.00), abdominal distention (p-value 0.00) and abdominal pain (p-value 0.03).

Age recorded reducing substance positivity is given in Table 1. Baseline features of study population and lactose intolerance are given in Table 2.

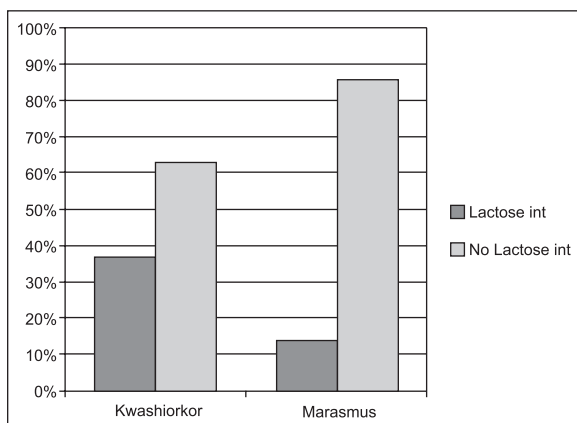


Figure 1: Percentage of secondary lactose intolerance in kwashiorkor and marasmus

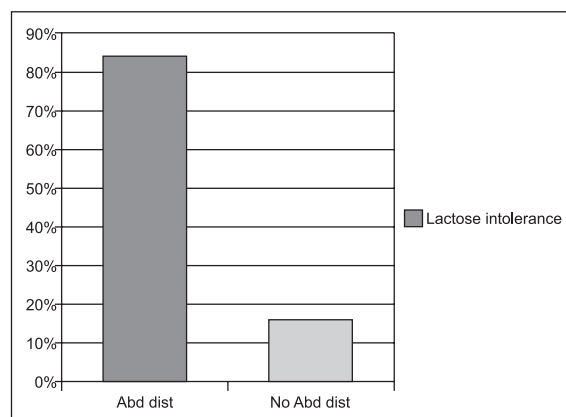


Figure 2: Showing abdominal distention % in secondary lactose intolerance

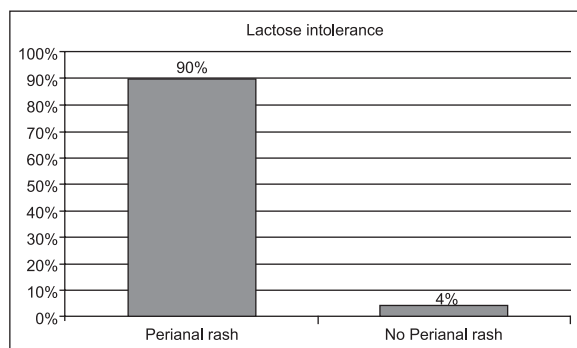


Figure 3: Percentage of perianal rash in secondary lactose intolerance.

Table1: Age recorded Reducing Substance

		Reducing Substance		Total
		Yes	No	
Age recorded	5 to 12 months	35	64	99
	13to28 months	3	36	39
	29to42 months	1	4	5
	43 to60months	2	5	7
	Total	41	109	150

Table 2: Baseline features of study population and lactose intolerance.

Characteristics	Total patients= %	Lactose intolerant(no of patients= in %)	Lactose tolerant (no of patients=in %)	P value
Sex	Male: 82 (54.66%)	21 (25.6%)	61 (74.4%)	
	Female: 68 (45.33%)	20 (29.4%)	48 (70.6%)	
Kwashiorkor	87 (58%)	32(36.8%)	55(63%)	.003
Marasmus	63(42%)	9(14.3%)	54(85.7%)	
Perianal rash	43 (28.7 %)	37(86%)	6(14%)	0.00
Abdominal distention	45(30%)	38(84 .4%)	7 (15.5%)	0.00

DISCUSSION

Secondary lactose intolerance is a relatively common problem of children, especially infants with acute severe malnutrition presenting with diarrhea and a cause of failure to therapy in subsequent management.¹

The 27.3% secondary lactose intolerance in severely malnourished 150 children presenting with diarrhea is approximately close to previous findings in Senegalese study (26%) and Z. A Bhutta study held in Karachi (25%)²⁴ but lower than that found in other studies²³⁻²⁵ the difference might be due to sample size and study population. However 27.3% frequency is still very high in malnourished child population leading to worsening of diarrhea and its related complications, becoming a great challenge in management of malnourished children with routine UNICEF's high lactose containing nutritional formulae (F-75, F-100).

In our study secondary lactose intolerance was more frequently encountered in kwashiorkor (36.8%) as compared to marasmus (14.3%) a finding consistent with Nyeko et al study conducted in Uganda. The reason behind this may be the fact that kwashiorkor is associated with variable degrees of malabsorption of nutrients resulting in carbohydrates, protein, vitamin and mineral deficiencies of variable severity that contributes to intestinal mucosal damage, in addition to oxidative stress. Passage of lipopolysaccharide to the systemic circulation, failure of the intestinal barrier from bacterial overgrowth and uncontrolled stimulation of the inflammatory mechanisms probably also have a part to play.²⁶

In our study secondary lactose intolerance was more frequently found in infantile age group (5-12 months). It was 35.3 % though it was far more lower than that found in Nyeko et al study at Mulago (68%)²⁶, such a huge difference may be attributed to the difference in sample size and study population. There was gradual decline in lactose intolerance to 7 % in age group (13-28 months) which gradually increased to 20% in age group (29-42 months) and 28 % in age group (43-60 months) subsequently.

Children with secondary lactose intolerance were most likely having perianal rash (p value 0.00) and abdominal distention (p value, 0.00). This is not surprising since undigested and unabsorbed lactose that is not metabolized is a nutritive source for intestinal bacteria, especially in the large bowel. Metabolism of lactose by bacteria of large gut results in formation of volatile fatty acids and gases (carbon dioxide, methane and hydrogen), leading to flatulence. The fatty acids decrease the pH of stool, causing excoriated rash on contact with perianal region. When significant intestinal gas is produced by the intestinal bacteria, abdominal distention occurs.²⁶

LIMITATIONS

We did not use the breath hydrogen test which is

the gold standard because it is cumbersome to use on a large scale, it is expensive and requires the patient to fast, in addition to the side effects of using of a lactose load (procedures not desirable in severely malnourished children on highly regulated dietary management). As our study was performed in a single teaching hospital of our province, further multicenter studies should be conducted for more statistically more significant results.

CONCLUSION

Secondary lactose intolerance is a common problem of children with acute severe malnutrition presenting with diarrhea. Clinical signs of lactose intolerance in severely malnourished children included perianal skin erosion and abdominal distention and positive stool examination for reducing substances.

RECOMMENDATIONS

The frequency of secondary lactose intolerance in acute severe malnourished children presenting with diarrhea is high, so we recommend:

Every child presenting to nutritional rehabilitation unit with severe acute malnutrition and diarrhea should be screened for reducing substances in stools for lactose intolerance.

Lactose intolerant malnourished children above 6 months of age should be supplemented with lactose free diet like rice, banana and yoghurt.

High lactose containing nutritional formulae (F-75 and F-100) should be used cautiously for such children to avoid deleterious effects of lactose intolerance or alternatively lactose free milk containing nutritional formulas having same caloric values as F-75 and F-100 should be manufactured for malnourished children with lactose intolerance.

Breast fed infants with secondary lactose intolerance should be supplemented with lactase enzyme for digestion of lactose. Breast feeding should not be stopped or substituted with lactose free milk formula.

REFERENCES

1. Campbell AK, Waud JP, Matthews SB. The molecular basis of lactose intolerance. *Sci Prog.* 2009;92:241-87.
2. Buller HA, Grand RJ. Lactose intolerance. *Ann Rev Med* 2003; 41: 141-8.
3. Maiuri L, Raia V, Potter J. Mosaic pattern of lactase expression by villus enterocytes in human adult-type hypolactasia. *Gastroenterology* 2002; 100: 359-69.
4. He T, Venema K, Priebe MG, Welling GW, Brummer RJ, Vonk RJ. The role of colonic metabolism in lactose intolerance. *Eur J Clin Invest* 2008; 38: 541-7.
5. Di Stefano M, Veneto G, Malservisi S et al. Lactose malabsorption and intolerance in the elderly. *Scand J Gastroenterol* 2002; 36: 1274-8.
6. Heymann MB, Lam T, Tom V. Lactose intolerance in

- infants, children and adolescents. *Pediatrics* 2006; 118: 1279-86.
7. Kirschner BS, DeFavaro MV, Jensen W. Lactose malabsorption in children and adolescents with inflammatory bowel diseases. *Gastroenterology* 2002; 81: 829-32.
 8. Wedlake L, Thomas K, McGough M. Small bowel bacterial overgrowth and lactose intolerance during radical pelvic radiotherapy. *Eur J Cancer* 2008; 44: 2212-7.
 9. Ghoshal UC, Ghoshal U, Misro A, Choudhuri G.. Partially responsive celiac disease resulting from small intestinal bacterial overgrowth and lactose intolerance. *BMC Gastroenterol* 2004; 4: 10.
 10. Branski D. Disorders of malabsorption. In: Kliegman RM, Stanton BF, Behrman G, editors. *Nelson textbook of Pediatrics*. 19th ed. USA: Fletcher J; 2011.p.1317-8.
 11. Chandrika R, Anurag T, Radhakrishna H. Thin layer chromatography in children with sugar intolerance in acute diarrhoea. *Indian J Gastroenterol*. 2006;25:103.
 12. Shaw AD, Davies GJ. Lactose intolerance: problems in diagnosis and treatment. *J Clin Gastroenterol*. 2008;28:208.
 13. Fajardo LF, Leal H, Victoria F et al: Milk intolerance in Colombian children, its prevalence and relation to lactose malabsorption. *ArchLatinoam Nutr* 1979, 29(3):329-39.
 14. Tolboom JJ, Ralita pole-Maruping AP, Mothebe M et al: Carbohydrates malabsorption in children with severe protein energy malnutrition. *Trop Geogr Med* 1984, 36(4):355-65.
 15. Nyeko et al., Lactose intolerance among severely malnourished children with diarrhoea admitted to the nutrition unit, Mulagohospital, Uganda *BMC Pediatrics* 2010, 10:31
 16. Prevalence of lactose intolerance in asymptomatic school children in Karachi Pakistan. [Online]. [Cited on March 12, 2012]. Available at http://www.pmr.org.pk/lactose_intolerance_report.htm.
 17. Melvin B, Heyman MD. Lactose intolerance in infants, children and adolescents. *J Am Acad Pediatr*. 2006;1279-86.
 18. De Onis M, Monteiro C, Akre J. The worldwide magnitude of protein-energy malnutrition: an overview from the WHO Global Database on Child Growth. *Bull World Health Organ*. 1993;71(6):703-712.
 19. Defining pediatric malnutrition, a paradigm shift toward etiology-related definitions [online] .[cited on June 14 2013]. Available at <http://www.sagepublications.com>
 20. <http://www.who.int/en/news-room/fact-sheets/detail/diarrhoeal-disease>
 21. <http://www.who.int/nutgrowthdb/about/introduction/en/index4.html>
 22. Guarino A. Chronic diarrhoea. In: Stanton K. *Nelson textbook*. 19th ed. USA: Fletcher J; 2011.p.1339.
 23. Beau JP, Fontaine O, Garenne M: Management of malnourished children with acute diarrhoea and sugar intolerance. *J Trop Pediatr* 1989,35(6):281-4.
 24. Bhutta, Z.A. Nizami S.Q. Lactose intolerance in persistent diarrhoea during childhood. Comparison of a traditional rice-lentil based diet with soy formula . *Pediatrics*, 1991;88:1010-20-24.
 25. Fagundes-Neto U, Viaro T, Lifshitz F: Tolerance to glucose polymers in malnourished infants with diarrhoea and disaccharide intolerance. *Am J Clin Nutr* 1985, 41(2):228-34.
 26. Nyeko et al., Lactose intolerance among severely malnourished children with diarrhoea admitted to the nutrition unit, Mulagohospital, Uganda *BMC Pediatrics* 2010, 10:31
 27. Sánchez-Ávila MT, Chávez Caraza KL, González Gil AM et al. Correlation between the presence and intensity of symptoms and the results of hydrogen breath tests in the diagnosis of carbohydrate intolerance. *Rev Gastroenterol Peru*. 2016 Jul-Sep;36(3):225-230.
 28. Ruzsanyi V, Heinz-Erian P, Entenmann A. Diagnosing lactose malabsorption in children: difficulties in interpreting hydrogen breath test results. *J Breath Res*. 2016 Mar 2;10(1):016015. doi: 10.1088/1752-7155/10/1/016015.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

- Khan S:** Main idea and article writing.
Uzma S: Data collection.
Muhammad Z: literature searching & Writing References.
Shah SIA: Searching & Writing References.
Ahmad I: Statistical analysis and review.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.