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Study on Lactose Intolerance in Children with Acute Diarrhoea

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Abstract
Diarrhoea is a major cause of mortality and morbidity among children in India. Mortality rates are exacerbated by multiple risk factors like malnutrition, infection, the lack of adequate health care and other factors like lactose intolerance. Few studies have been done in India relating to lactose intolerance in acute diarrhoea. This study aims to estimate the frequency of lactose intolerance in children with acute diarrhoea and to assess the factors affecting the outcome of lactose intolerance. In this prospective study, in 150 cases with acute diarrhoea, diagnosis of lactose intolerance was made on the basis of stool pH (<5.5) and presence of reducing substances. 54 cases were diagnosed as lactose intolerant. Cases with lactose intolerance had longer stay in hospital compared to the lactose tolerant counterparts (6.01 ± 2.24 days and 5.13 ± 1.24 days respectively). Among these lactose intolerant cases, those who were fed on low-lactose feeds had shorter duration of stay compared to those on normal feeds (4.82 ± 1.05 days and 7.59 ± 1.13 days respectively). Lactose intolerance was more common in cases with malnutrition (p value=0.011). There was no positive correlation with degree of dehydration. Lactose intolerance is very common in cases with acute diarrhoea and is often underemphasized. Treatment of lactose intolerance with low lactose feeds has the potential for speedier recovery and improved outcomes in cases with diarrhoea. There is need for considering lactose intolerance in formulating better diarrhoea treatment guidelines in India.
Keywords: *Lactose intolerance, Acute diarrhoea, Low Lactose feeds.*

Introduction
More than 10 million cases and more than 1000 deaths are reported every year due to diarrhoea in India.[1] There are many risk factors behind this large number of cases, but almost 90% are attributed to unsafe drinking water, poor sanitation and poor hygiene. In developing countries, mortality rates are further exacerbated by the vicious cycle between malnutrition and infection, the lack of adequate health care and transport facilities and other factors like lactose intolerance.

Lactose intolerance is a clinical syndrome of 1 or more of the following: abdominal pain, diarrhoea, nausea, flatulence, and/or bloating after the ingestion of lactose or lactose-containing food substances. The amount of lactose that causing symptoms varies among individuals depending on

the amount of lactose consumed, the degree of lactase deficiency, and the form of food substance in which the lactose is ingested.[2] Lactose is a disaccharide only found in mammalian milk. During digestion, it is hydrolysed into 2 monosaccharide's glucose and galactose by the enzyme lactase. Lactase is formed in the brush border of enterocytes on the villous tip of small intestine. Affected expression of lactase producing gene or affected intestinal mucosa form the major patho-physiological processes causing lactose intolerance. Diarrhoea is one of the leading causes of childhood morbidity and mortality in India. Diarrhoea damages the intestinal mucosa which consequently causes transient lactase deficiency and causes lactose intolerance.[3]

Successful gastroenteritis management in children depends primarily on maintaining or restoring adequate hydration and electrolyte balance and maintaining adequate nutritional intakes. The current treatment guidelines reflect this goal of replacing fluids and electrolytes that have been lost. The WHO recommends commercially prepared oral rehydration solutions (ORS) in order to replace losses of mild to moderate dehydration.[4] ORS is widely available, easy to administer, well tolerated, has adequate glucose and electrolyte concentrations and is cost - effective. Infants with breastfeeding should continue to feed breast milk for hydration and nutritional benefits. Once children have been rehydrated, the current guidelines recommend that an unrestricted age - appropriate diet be introduced early, which may include milk products containing lactose.[5] Historical evidence showed that this practice is safe with no or mild dehydration in children.[6] Early feeding improves enterocyte regeneration and restores the production of digestive enzymes, ultimately shortens the length of diarrhoea and improves the absorption of nutrients. Transient lactase deficiency due to intestinal inflammation or injury following diarrhoea is common and underlies the rationale behind the recommendation of some practitioners to avoid products containing lactose during a diarrheal episode. It is thought that the duration and severity of diarrhoea could be reduced.

Evidence is suggesting that lactose prevention can shorten the duration of diarrhoea by an average of 18 h and also that lactose prevention reduces chances of treatment failure.[7] Some studies also show that dilution of products containing lactose did not significantly reduce the duration of diarrhoea and that the chances of treatment failure were reduced.

Although the aim of the present study is to estimate the frequency of Lactose Intolerance and to assess the factors affecting it, in children with acute diarrhoea, the intention of the study is to reemphasize the need to include investigations and treatment of lactose intolerance routinely in daily practice regarding management of acute watery diarrhoea in children.

Aims and Objectives

1. To estimate the frequency of Lactose Intolerance in Children with Acute Diarrhoea.
2. To assess the factors affecting the outcome of Lactose Intolerance in Children with Acute Diarrhoea.

Methodology

The study included 150 children below 5 years of age suffering with Acute Diarrhoea. The patients were selected from those admitted from June 2017 - November 2018 in the paediatric ward of a tertiary care hospital. After selection, detailed history and physical examination was done. History included age, duration of illness, number and character of stool, vomiting, feeding history and past history of diarrhoea. In physical examination body weight, height, weight/ height ratio and head circumference was measured. Examination for abdominal distension was done. Stool (3ml) was collected in a clean container. Physical character of stool and then pH of stool by pH meter was noted. Reducing sugar was determined in watery portion of stool with Benedict's reagent.
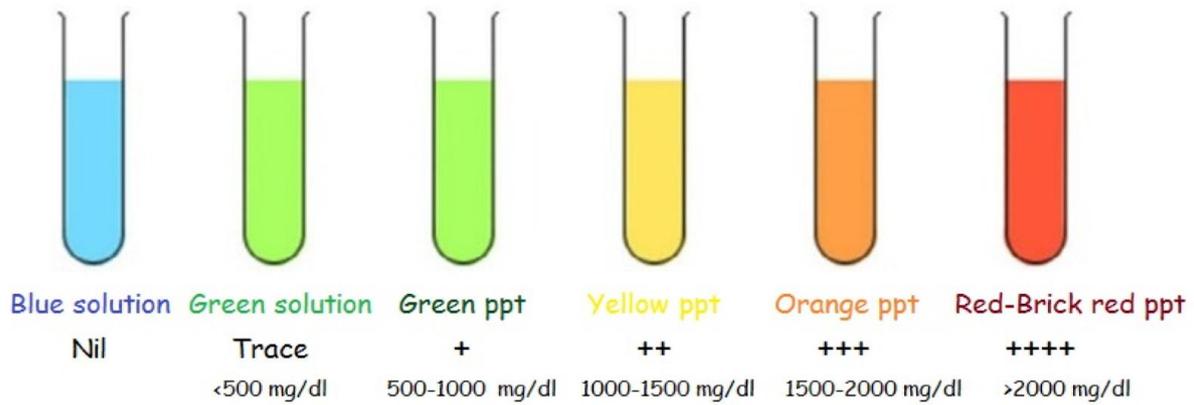
Figure 1 Benedict's test interpretation

Patients with diarrhoea, vomiting, abdominal distension, having pH $\leq$5.5 and reducing sugar > 0.5 - 1 gm % (+) were classified as sugar intolerance. The various factors affecting the outcome such as Dehydration, Anaemia, Malnutrition, and the use of any lactose formula feeds was assessed. WHO classification of dehydration in acute diarrhoea is used for assessing dehydration. Anaemia is assessed using the Haemoglobin values of -2 Standard Deviation.IAP Classification of Malnutrition is used to assess children with malnourishment. Commercially available Low Lactose Formula feed is used to assess the effect of Lactose free diet on the duration of Illness.

Inclusion Criteria

- The children aged 1month to 5 years suffering with acute diarrhoea (<14days) will be included in the study after taking consent from parents or guardian.

Exclusion Criteria

- Children with diagnosed malabsorption syndromes
- Children with dysentery

Results

The study entitled "Study on lactose intolerance in children with acute diarrhoea" was conducted in the institute from June 2017 to November 2018. Subjects were selected according to the inclusion criteria for recruitment in the study. The study protocol was approved by the institutional ethical committee. Informed written consent was obtained from parents/guardians of all the study subjects enrolled in the study

Incidence of lactose intolerance

Table 2 Incidence of lactose intolerance

	number of cases	% of n=150
lactose intolerant	54	36
lactose tolerant	96	64

Table 2 shows the incidence of lactose intolerance. Among the 150 cases of acute diarrhoea, 54 were diagnosed as having lactose intolerance and 96 cases were lactose.

Correlation between duration of illness and lactose intolerance

Table 3 Correlation between duration of illness and lactose intolerance

	Mean duration of diarrhoea (days)	Std Dev	T score and p-Value
Lactose intolerant cases	6.01	2.24	-3.100 and p=0.002 (significant)
Lactose tolerant cases	5.13	1.24	

Lactose intolerance was associated with a mean duration of 6.01 $\pm$ 2.24 days of illness and lactose tolerant cases had a mean duration of 5.13 $\pm$ 1.24 days of illness. These results were statistically

significant with a t score of -3.100 and a p-value of 0.002.

Correlation between duration of illness and low lactose feeds

Table 4 Correlation between duration of illness and low lactose feeds

	Mean duration of illness(days)	St dev	T score and p-value
Low lactose feeds	4.82	1.05	12.01 and p=<0.001 (significant)
Normal feeds	7.59	1.13	

Of the 54 children, diagnosed 29 children were fed low lactose feeds and the rest were fed normal feeds in addition to the feeds as suggested by the diarrhoea guidelines. In those who took low lactose feeds mean duration of illness was 4.82 ± 1.05 days compared to 7.59 ± 1.13 days in those who took normal feeds. These results were statistically significant with a p value <0.001.

Correlation between duration of illness and malnutrition

Table 5 Malnutrition vs duration of illness

	Mean	Stdev
Malnutrition	6.00	1.50
Normal	5.35	1.45

In the present study cases with malnutrition had a longer duration of illness with mean of 6 day compared to well nourished counterparts whose mean was about 5.35 days

Correlation between duration of illness and levels of Hb

Table 6 Anaemia vs duration of illness

	mean	stdev
Anaemia	6.00	1.49
No Anaemia	5.42	1.48

In the present study cases with anaemia had a longer duration of illness (mean of 6 days) compared to those with no anaemia (mean of 5.42 days)

Correlation between lactose intolerance and degree of dehydration

Table 7 Correlation between lactose intolerance and degree of dehydration

		lactose intolerant	lactose tolerant	Chi square and p value
Degree of dehydration	no	28	58	3.0465 & p=0.218 (insignificant)
	some	19	33	
	severe	7	5	

Of the 54 lactose intolerant cases 7 had severe dehydration, 19 had some dehydration and 28 had no signs of dehydration. Among those who are lactose tolerant while 5 of them had severe dehydration, 33 had some signs of dehydration, 58 had no signs of dehydration. The chi-square value was calculated to be 3.05 and p value was 0.218, which is statistically insignificant.

Discussion

Lactose intolerance, in spite of having considerable prevalence in the community is under recognized and warrants consideration in formulating treatment guidelines of comorbidities especially diarrhoea.

Stool sample was sent in all the 150 cases and the results were categorised into those having a pH ≤5.5 and those having a pH>5.5. A total of 54 children (36%) had stool pH <5.5 and 96 (64%) had stool pH >5.5. In a study done by M. Karabocuoglu et al,[8] a total of 245 cases of acute diarrhoea were evaluated using faecal pH and presence of reducing substances as diagnostic tools. They found that 52 % had pH <6 in stool. The cut-off value for considering stool as acidic was pH <6 in this study compared to pH <5.5 in the current study hence the higher percentage.

Stool was sent to test for reducing substances. If the reducing substances were more than 0.5 - 1 gm then the sample was noted as "reducing substances Present". Of the total 150 samples reducing substances were present in 61 (41%) cases and absent in 89(59%) cases. The results published in a similar study done by Lifshitz F et al,[9] a total of 3,427 samples were sent to test for

reducing substances. Among them 17.4% had reducing substances positive. Their study had a cut-off value of >2.5 % of reducing substances for diagnosis hence the lesser percentage.

In the present study diagnosis of lactose intolerance was made based on stool pH and presence of reducing substances in the stool. All the cases of acute diarrhoea with stool pH<5.5 and with reducing substances were diagnosed as having lactose intolerance. Of the total 150 children included in the study 54 cases (36%) were lactose intolerant and 96 cases (64%) were lactose tolerant.

In a study done by Hu Y et al,[10] to find out the incidence of infants with rotavirus enteritis combined with lactose intolerance, the incidence of lactose intolerance in non- rotaviral enteritis was 49.2% and in rotaviral enteritis was 67.03%. In a study done in Mexico by Lifshitz F et al,[9] which included 332 cases with acute diarrhoea 77% were found to be lactose intolerant. The variation could be explained by the diagnostic criteria used by Lifshitz F et al, stool pH less than 6 vs the diagnostic criteria used in the present study stool pH< 5.5 to diagnose lactose intolerance and the geographical variations. In a study done by Chandrasekaran R et al,[11] 271 infants with acute diarrhoea were studied among which 110 (40.6%) were diagnosed as lactose intolerant cases, which is comparable to the findings in the present study.

Lactose intolerance is positively correlated with the nutritional status of the patients. All the children were evaluated for signs of malnutrition if any and were classified as normal or graded from 1 to 4. With increasing grade of malnutrition stool acidic pH and reducing substances in stool increased. While 19(35.7%) lactose tolerant were normal 61(63.4%)of the lactose intolerant were normal in PEM grading. Of the total 32 cases in grade 1,13 were lactose intolerant and 19 were lactose tolerant. There were a total of 25 cases categorized as grade 2 cases of which 14 were lactose intolerant and 11 were lactose tolerant. Put together 8 cases were in grade 3, of which 4

belonged to lactose intolerant and 4 to lactose tolerant cases. A total of 6 cases were categorized as having grade 4 PEM, of which 4 were lactose intolerant and 2 were lactose tolerant. These results were statistically significant with a chi square value of 13.01 and a p value of 0.011. In a systematic review and meta-analysis Matilda A. Kvissberg et al.,[12] reviewed 20 studies relating to nutritional status and carbohydrate intolerance. They concluded that carbohydrate malabsorption including lactose intolerance was prevalent in cases with acute malnutrition.

Lactose intolerance prolonged the duration of diarrhoea. Lactose intolerance was associated with a mean duration of 6.01 ± 2.24 days of illness and lactose tolerant cases had a mean duration of 5.13 ± 1.24 days of illness. These results were statistically significant with a t score of -3.100 and a p-value of 0.002. A study conducted by Fima Lifshitz et al,.[13] showed similar results where duration of diarrhoea increased with increasing severity of lactose intolerance with statistically significant results.

Patients who were fed with Low lactose feeds had a lesser duration of illness compared to those who were given normal feeds. Of the 54 children, diagnosed 29 children were fed low lactose feeds and the rest were fed normal feeds in addition to the feeds as prescribed in WHO guidelines for treating. In those who were fed low lactose feeds mean duration of illness was 4.82 ± 1.05 days compared to 7.59 ± 1.13 days in those who took normal feeds. These results were statistically significant with a p value <0.001. In a meta-analysis done by MacGillivray S et.al,[14] 33 trials enrolling 2973 children with acute diarrhoea were studied. It was found that compared to lactose-containing milk, milk products, or foodstuffs, lactose-free products may reduce the duration of diarrhoea by an average of about 18 hours (MD -17.77, 95% CI -25.32 to -10.21, 16 trials, 1467 participants, low quality evidence).

Summary

This is a prospective study of lactose intolerance in 150 cases with acute diarrhoea. Diagnosis of lactose intolerance was made on the basis of stool pH and presence of reducing substances in stool. Although a total of 61 cases had reducing substances in the stool only 54 of them had stool pH <5.5 and hence 54 cases were diagnosed as having lactose intolerance. Some of the factors influencing lactose intolerance were studied. Lactose intolerance was more common in cases with malnutrition. The results were statistically significant and correlated with the severity of malnutrition. There was no positive correlation between degree of dehydration and prevalence of lactose intolerance. Factors affecting the duration of acute diarrhoea were studied. Cases with lactose intolerance had longer stay in hospital compared to the lactose tolerant counterparts. Among the cases with lactose intolerance, those who were fed on low-lactose feeds had shorter duration of stay compared to those on normal feeds.

Conclusion

- Acute diarrhoea is one of the most common causes of admission in children with varied causations and outcomes.
- Lactose intolerance is very common is cases with acute diarrhoea and is often underemphasized.
- Treatment of lactose intolerance with low lactose feeds has the potential for speedier recovery and improved outcomes in cases with diarrhoea.
- By improving the nutritional status, the morbidity associated with diarrhoea can be curtailed.
- There is a need for considering lactose intolerance in formulating better diarrhoea treatment guidelines in India.

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