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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. Many studies show that lactose intolerance is significantly related to outcome.

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 the one of the leading cause of childhood morbidity and mortality in India. Diarrhoea damages the intestinal mucosa which consequently causes transient lactase deficiency and causes lactose intolerance.[3]

Milk, the main food of infants, has high lactose content. Milk when given as part of rehabilitation of diarrhoea, may worsen the symptoms in children with lactose intolerance. Hence, recognition of this mal-absorption entity gains important practical importance. Unrecognized lactose intolerance complicates the treatment of diarrhoea and hampers the clinical outcomes.

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 thispractice 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.

Many current guidelines encourage caregivers to provide a regular diet for their children. In children with diarrhoea lasting > 1 week, or if milk feeds appear to trigger profuse diarrhoea, lactose prevention is often considered empirically. More recently, good evidence has been published showing that probiotics shorten the duration of diarrhea.[7]

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'.[8] 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.

Many studies in the past have focussed on lactose intolerance following diarrhoea in malnourished or those with chronic diarrhoea. This study attempts to document lactose intolerance in patients with acute diarrhoea seen in both well nourished and mal nourished children.

While many studies indicate guidelines to identify and treat lactose intolerance, especially in children for improving the mortality and morbidity outcomes, their implementation in routine practice should be exacting. Although 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 in children with Acute Diarrhoea having Lactose Intolerance.

Review of literature

Lactose intolerance is a form of carbohydrate mal-absorption caused by lactase deficiency. Lactase is one of the b –galactosidases seen in the small bowel .it is most active in jejunum.[9] during digestion lactose is hydrolysed into 2 monosaccharides: glucose and galactose. In the absence or in deficiency of lactase, sugar lactose hydrolysis is incomplete. Since the sugar is osmotically active, it pulls fluid into the intestine. In addition to other organic acids, hydrogen and lactic acid are produced when colonic bacteria act on undigested sugar.

Lactose

Alpha- lactose or lactose, is disaccharide formed by glucose and galactose. It is found mainly in human and cow milk. It is a sweetening agent used in food, beverages, medications etc.

History [10]

The first crude isolation of lactose, by Italian physician Fabrizio Bartoletti (1576–1630), was published in 1633.In 1700, the Venetian pharmacist Lodovico Testi (1640–1707) published a booklet of testimonials to the power of milk sugar (saccharum lactis) to relieve, among other ailments, the symptoms of arthritis.[11] In 1715, Testi's procedure for making milk sugar was described by Antonio Vallisneri. Lactose was identified as sugar by Carl Wilhelm Scheele in 1780. Over time it was recognized that glucose was a product of hydrolysing lactose and Louis Pasteur crystallised the other galactose from lactose. He in fact named galactose as “lactose”. But in 1860 it was Berthelot who renamed it to “galactose” and the dissacharide of glucose and galactose as “lactose”.

Structure

Lactose is a derived from condensation of galactose and glucose. They form a β-1→4 glycosidic linkage. Glucose can be either α-pyranose or β-pyranose, while galactose can only be β-pyranose, so α- lactose and β-lactose refer only to the anomeric form of the glucopyranose ring. Lactose is hydrolyzed to glucose and galactose, isomerized to a lactulose alkali solution and catalytically hydrogenated to the corresponding polyhydric alcohol lactite.[5] Lactulose is a commercial product for the treatment of constipation.

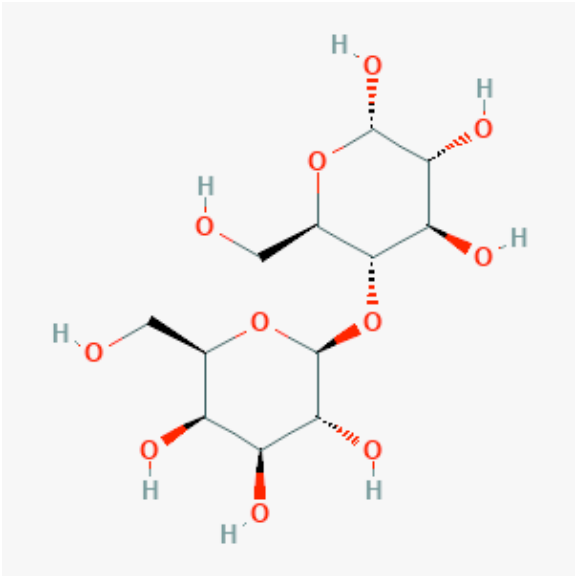

Figure 1 Lactose structure [12]

***Lactose synthesis*[13]**

Lactose synthesis takes place only in the mammary glands and produces lactose (4-O-B-D-galactosylpyranosyl-a-D-glucopyranoside), the main sugar in milk. Lactose is produced by combining two monosaccharides with a B1,4-glycoside bond. Glucose is first converted into UDP-galactose by the enzyme galactose-1-phosphate-uridylyltransferase. UDP galactose is then transported from the UDP galactose translocator to the Golgi, an antiporter that uses simplified transport to transport UDP galactose to the Golgi and export UMP. Inside the Golgi, the UDP galactose and glucose (which enters the Golgi via the GLUT-1 transporter) become substrates for the lactose synthase enzyme complex, consisting of the enzymatic subunit galactosyltransferase with its regulatory subunit alpha-lactalbumin. Lactose synthase produces lactose by binding galactose from UDP to glucose via a glycosidic bond. Although GT is found in many tissues of the body, alpha-lactalbumin is found only on the inner surface of the Golgi in the mammary glands, making lactose production exclusive to mammals.

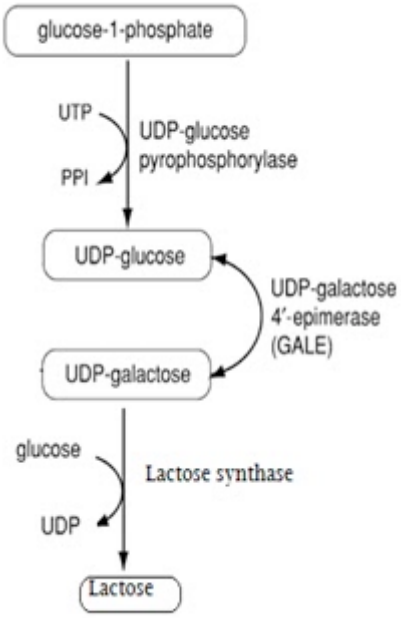

Figure 2 lactose synthesis

Lactose metabolism

If lactose is ingested, it cannot be used as such, it must first be hydrolyzed into the sugar glucose and galactose. This is achieved by lactase phlorizin hydrolase (LPH) (more commonly known as lactase), a disaccharidase that has its highest activity in the jejunum. Lower levels of activity occur in the duodenum and ileum.[14] This enzyme is located in the brush border of the intestinal epithelium and has an optimum pH of 5.5 to 6.0. The activity of LPH is genetically determined.[15] The gene was found to be localized on chromosome 2.[16]

Lactose metabolism in normolactasia

In normolactasia, the activity of lactase remains until adulthood and enables people to consume large quantities of milk without abdominal discomfort. After hydrolysis, galactose and glucose are actively absorbed from the gut, but they have separate

mechanisms in the mucosa. Galactose is absorbed somewhat more efficiently than glucose: the absorption coefficients are 122 and 100 respectively. Glucose enters and is used in the body glucose pool. While galactose is treated like a poison, the body will try to get rid of it through various mechanisms. Galactose is metabolized mainly in the liver via the Leloir pathway to glucose.[17] This route is very efficient because half of the galactose administered reaches the body's glucose pool within 30 minutes. The regulating enzyme of the pathway is UDP-galactose-4-epimerase. In normal individuals, liver extraction is 94 percent of the amount administered. When galactose escapes liver metabolism, it is either metabolized by erythrocytes[18] or excreted in urine. Since there is no renal threshold for galactose and the tubular reabsorption of galactose is less efficient than for glucose, large amounts of galactose are excreted in the urine. Galactose concentrations in urine are about ten times higher than in blood.[19]

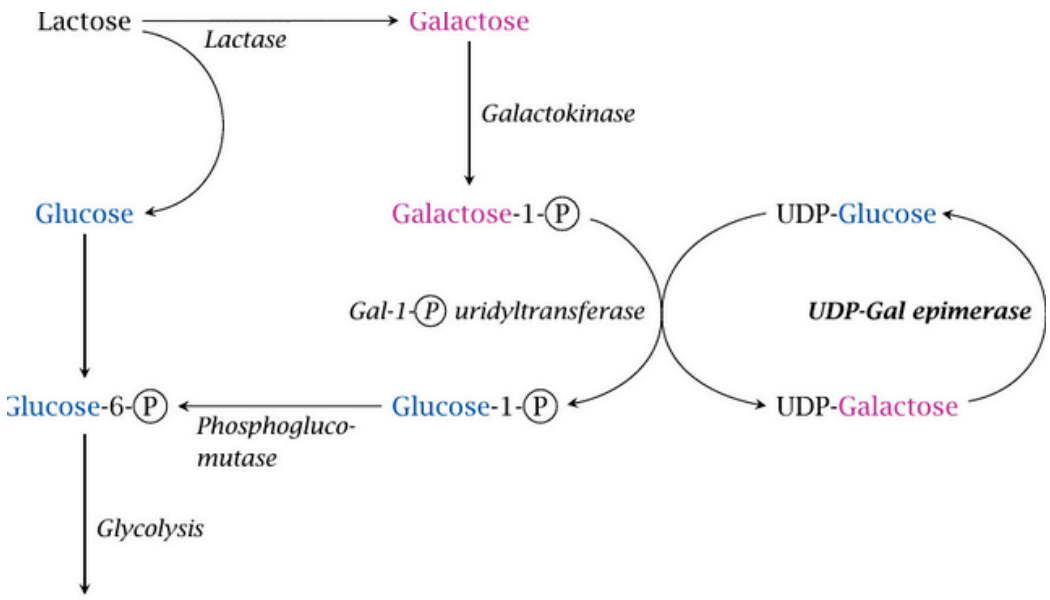

Figure 3 lactose metabolism

Lactose metabolism in hypolactasia

In primary adult type hypolactasia, lactase activity has decreased to about 10 percent of normal levels in infants. The age at which this decline occurs varies between two

years in Thais and 10 to 20 years in Finns.[15] The low enzymatic activity is caused by a reduced amount of lactase protein, not because the enzyme in the mucosa changes into an inactive form.[20] The amount of lactase mRNA appears to correlate with the amounts of lactase enzyme activity, suggesting that the difference in concentrations of human lactase activity can be regulated at the level of gene transcription.[21] It has been shown that lactase is not an adaptive enzyme and therefore feeding lactose cannot inhibit the genetically induced decrease in lactase activity. In hypolactasia, a large part of the lactose in the jejunum does not remain hydrolyzed and is later broken down by intestinal bacteria. The speed and efficiency of lactose metabolism in the intestine is not only determined by lactase activity on a small intestinal mucosa, but also by a number of other factors:

- the amount of lactose in the intestine
- the speed of emptying the stomach and intestinal passage
- the ability of the intestinal microflora to ferment lactose
- the reaction of the large intestine to the osmotic stress

Microbial decomposition of lactose

Micro flora contributes to the absorption of lactose in malabsorbers. Only some of the intestinal microflora, but not all, can ferment lactose.

Tolerance to oxygen	Ability to ferment lactose	
	Fermenters	Non- fermenters
Facultative anaerobes	Escherichia coli Klebsiella oxytoca Klebsiella pneumoniae Enterobacter aerogenes Enterobacter cloacae Streptococcus salioarius Streptococcus intermedius Lactobacillus acidophilus Lactobacillus fermentus	Proteus mirabilis
Anaerobes	Bacteroides melaninogenicus Bacteroides vulgam Bacteroides thetaiotaomikron Bacteroides distasonis Eubacterium aerofaciens Eubacterium rectale Eubacterium siraeum Bifidobacterium adolescentis Bifidobacterium longum Peptostreptococcus productus Clostridium tertium Clostridium paraputrificum	Clostridium innocum

Table 1 lactose fermentation by intestinal bacteria [22]

The composition of the microflora is relatively stable in every human being, but with clear individual differences. Therefore, the degradation cycle in the large intestine takes place at different speeds. In the large intestine, lactose is converted by microbes into short - chain acids and various gases. In vitro, the degradation of glucose leads to the formation of acetic acid, butyric acid, propionic acid, succinic acid, lactic acid and formic acid.[23] In vivo, it is more difficult to track metabolism as most acids are absorbed or metabolized quite quickly. Some acids such as pyruvic acid and succinic acid are only intermediate.

Individual short-chain fatty acids (SCFAs) and diarrhea

Previously, the formation of SCFAs and in particular lactic acid was considered to be the reason for diarrhoea in causing malabsorption of lactose by increasing the osmotic pressure in the large intestine. This causes an increased secretion of water into the lumen or at least prevents the reabsorption of water. However later studies[24, 25] showed that the role of SCFA needs to be reconsidered. SCFAs are very quickly absorbed from the intestines of people who do not differ from other mammals in this respect. SCFAs can be absorbed by both non ionic and ionic diffusion. Their rapid absorption increases the reabsorption of water and sodium from the colon at least at pH 6.4 to 7.4.[26] Therefore, the formation of SCFAs via anaerobic microflora is a special compensation mechanism by which humans can assimilate various substances (including lactose) that are not absorbed in the small intestine.

Lactose Intolerance

Definitions [27]

Lactose intolerance:

Lactose intolerance may be a clinical syndrome of 1 or more than 1 of the following symptoms: abdominal pain, diarrhoea, nausea, flatulence, and/or bloating when lactose or lactose-containing food substances are taken.

Lactose mal-absorption:

Lactose mal-absorption is the physiological problem manifested as lactose intolerance due to an imbalance between the amount of lactose absorbed and the potential of lactase to hydrolyse the disaccharide.

Primary lactase deficiency

It is due to the relative or absolute absence of lactase, developing in different age groups of childhood and in different race groups and is the most common cause of malabsorption and lactose intolerance. Primary lactase deficiency is also referred to as adult type hypolactasia, lactase non-persistence or hereditary lactase deficiency.

Secondary lactase deficiency

Secondary lactase deficiency is a lactase deficiency that results due to small intestine injury, caused by diseases such as acute gastroenteritis, persistent diarrhoea, small intestine overgrowth, cancer chemotherapy or other causes of damage to the small intestine mucosa and may be present at any age, but more is common in infancy.

Congenital lactase deficiency

Congenital lactase deficiency is extremely rare. Before the 20th century, children with congenital lactase deficiency cannot be expected to be able to survive when no easily accessible and nutritionally sufficient lactose - free breast milk substitute was available.

Developmental lactase deficiency

Developmental lactase deficiency is now defined as the relative lactase deficiency observed among pre-term infants of less than 34 weeks' gestation.

History of lactose intolerance

The Western medicine only recently identified the global prevalence and genetic causes of lactose intolerance. Its symptoms were described as early as Hippocrates (460–370 BC)[28], but it was assumed that tolerance was the norm until the 1960s. Intolerance was explained to be caused as a result of a milk allergy, intestinal pathogens or as psychosomatic–it was recognized later that some ethnic cultures did not cultivate dairy and that people from these cultures often reacted badly to milk consumption.[29] One was that the majority of people of European descent have a very low incidence of lactose intolerance and long history of dairy farming. Tolerance was therefore the norm in most societies studied by early medical scientists. Another reason is that lactose intolerance tends to be underreported: people with lactose intolerance can tolerate at least some lactose before showing symptoms and their symptoms differ in severity.

Most people can digest a small amount of milk, e.g. in tea or coffee, without any adverse effects. Fermented dairy products, like cheese, contain considerably less

lactose than plain milk. Therefore, many lactose intolerant people who consume only small amounts of milk or have only mild symptoms especially in societies where tolerance is the norm may not be aware that they cannot digest lactose. Finally, in the 1960s, it was recognized that lactose intolerance was correlated with race in the United States.[30] Subsequent research revealed that lactose intolerance was more prevalent worldwide than tolerance[31] and that the variation was due to genetic differences, and not due to adaptation to cultural practices.[32]

Etio-pathogenesis of lactase deficiency

Lactose intolerance is a consequence of deficiency of lactate. This could be due to genetic or environmental causes. In either case, symptoms are caused by inadequate lactase levels in the duodenum lining. Lactose, which is un-hydrolysed, cannot be directly absorbed into the bloodstream from the small intestinal wall, so it passes intact into the colon in the absence of lactase. Colon bacteria can metabolize lactose and the resulting fermentation produces large amounts of gas (a hydrogen, carbon dioxide and methane mixture) which causes the various abdominal symptoms. Unabsorbed sugars and fermentation products also increase the colon's osmotic pressure and cause more water to flow into the intestines (diarrhoea).

Genetics of lactose intolerance[33,34]

Lactase is coded by LCT gene located on long arm of the chromosome 2 (2q21.3). Any mutations in the LCT gene may lead to lactase deficiency. Mutations that cause congenital variant of the lactose intolerance cause severe impairment in digesting breast milk. Lactose intolerance of adulthood is caused by gradually decreasing expression of the LCT gene with increasing age. This expression is controlled by a

segment of another gene called MCM6. The genes LCT and MCM6 are both in region 21 on the long arm (q) of chromosome 2. The locus can be expressed as 2q21 [34] changes in this MCM6 element can leads to loss less expression of LCT gene and the individuals are "lactose tolerant" throughout life time. Those in whom the MCM6 segment is unchanged turn "lactose intolerant". The deficiency of lactase can also be associated with certain heritages. It is more common among Asian Americans, African Americans, Mexican Americans and Native Americans. DNA analysis of 94 ancient skeletons in Europe and Russia concluded that the lactose tolerance mutation appeared about 4,300 years ago and spread throughout Europe.

Types of lactase deficiency [27]

Lactase deficiency is the cause for lactose intolerance. Based on the pathogenesis lactase deficiency can be classified as;

1. Primary lactase deficiency
2. Secondary lactase deficiency
3. Developmental (neonatal) lactase deficiency
4. Congenital lactase deficiency

1. Primary lactase deficiency

Primary lactase deficiency is also known as adult-type hypolactasia, lactase non persistence, or hereditary lactase deficiency. Primary lactase deficiency is relative or absolute absence of lactase presenting in various ages of childhood leading to manifestations much later in life. It is the most common cause of lactose malabsorption and lactose intolerance.

About 70% of the world's population has a primary deficiency of lactase.[35] The percentage varies with ethnicity (figure 2) and is related to the use of dairy products in the diet, causing the genetic selection of persons with the ability to digest lactose.

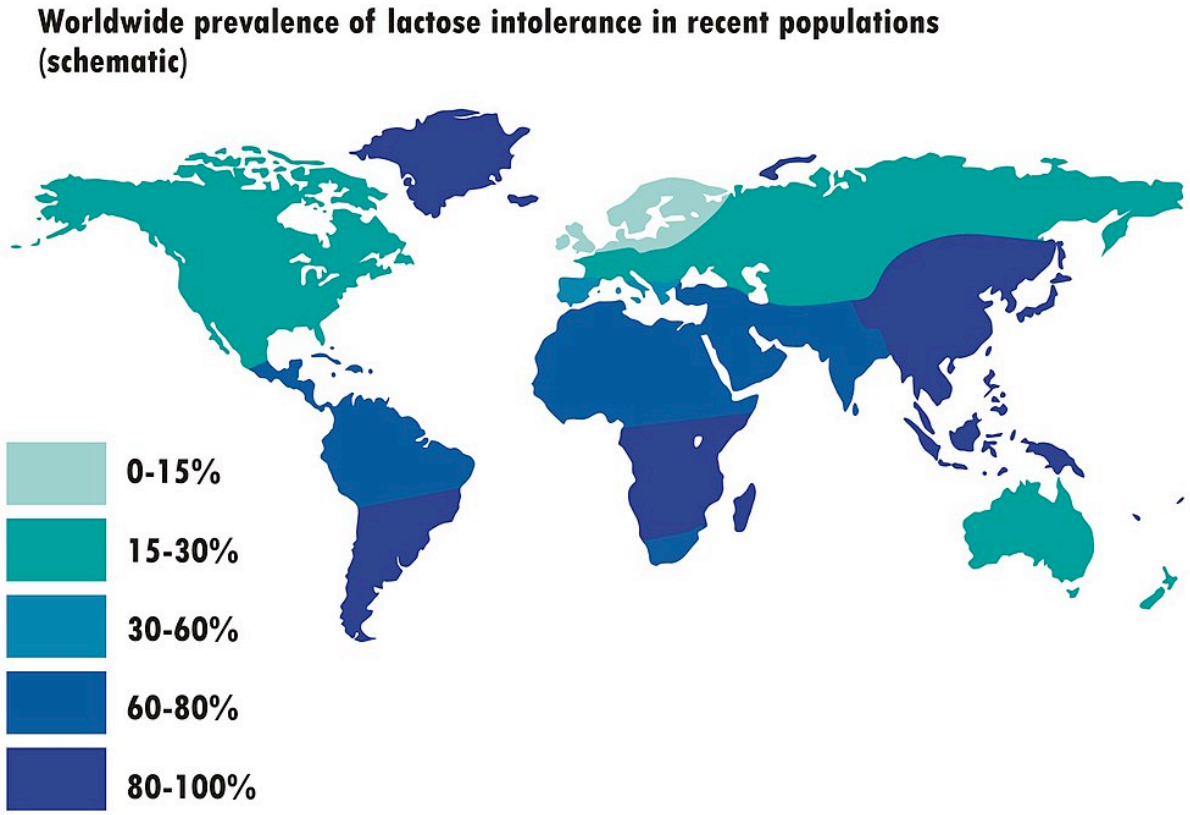

Figure 4 prevalence of lactose intolerance worldwide [36]

In populations with dominance of milky foods in the diet, the mostly northern European population has a primary lactase deficiency of only 2 percent of the population. Contrast to this, the prevalence of primary lactase deficiency in Hispanic people is between 50% and 80%, in black and Ashkenazi Jews 60% to 80% and in Asian and American Indians nearly 100%.[37]

Ethnicity	*% of population having primary lactate deficiency*

European	2
Hispanic	50-80
Black and Ashkenazi jews	60-80
Asians	Nearly 100

Table 2 primary lactate deficiency in various ethnic groups

The age and prevalence of the onset differentiate between different populations. Approximately 20 percent of Hispanic, Asian and black children under 5 years of age have lactase deficiency and lactose malabsorption, while white children do not typically develop lactose intolerance symptoms until after 4 or 5 years of age. However, most of the individuals show clinical symptoms in late adolescence or adulthood.[13]

2. Secondary lactase deficiency

Lactase deficiency secondary to another underlying pathophysiologic condition is called as secondary lactase deficiency. Acute GI tract infection (eg: rotavirus) is one of the most common causes of secondary lactase deficiency. These infections injure the small intestinal villi, causing loss of lactase containing epithelial cells. These cells (often lactase deficient) are replaced by immature epithelial cells which lack lactase and consequently cause lactose intolerance, although the symptoms are not so significant.[38] Recent studies found that children with rotaviral diarrhoea categorised as having no or only mild dehydration can continue on breast feeds without any changes in clinical outcome. However, in infants <3 months or are malnourished or exhibiting other risk factors, the lactose intolerance can alter the clinical outcome.[39]

Secondary lactase deficiency is also found in celiac disease, crohns disease and other enteropathies. Severe malnutrition can lead to intestinal atrophy subsequently lactose intolerance. The majority of infants and babies with malnutrition related malabsorption can continue to tolerate dietary carbohydrates, including lactose.[40] However, the World Health Organization recommends that milk containing lactose should be avoided in children with persistent post-infectious diarrhoea (diarrhoea lasting more than 14 days) when a dietary milk or yogurt trial fails.[41]

Causes of secondary lactate deficiency
• Acute gastroenteritis • Celiac disease • Intestinal irradiation • Antimetabolite therapy • Malnutrition • Intestinal resection • Immunodeficiency • Giardiasis • Inflammatory bowel disease • Neomycin • Cow's milk allergy

Table 3 causes of secondary lactase deficiency [42]

3. Developmental (neonatal) lactase deficiency

By definition it is the relative lactase deficiency observed among pre-term infants of less than 34 weeks' gestation. Although some studies noted that feeding preterm infants with lactase supplemented or lactose free feeds may be beneficial,[43] no long-

term deleterious effects were documented in those fed with lactose containing feeds or breast milk.[44] Bacterial lactose metabolism reduces fecal pH, and now has a beneficial effect, favoring certain organisms (e.g. Bifidobacterium and Lactobacillus species) in young infants instead of potential pathogens (Proteus species, Escherichia coli and Klebsiella species).[13]

4. Congenital lactase deficiency

Congenital lactase deficiency is a rare disease that has been rarely reported.[45,46] Affected newborn infants present with severe diarrhea following introduction of human milk or lactose-containing formula. Small intestinal biopsies show normal histological characteristics, but low or completely absent concentration of lactase.[47] Unless quickly detected and treated, the condition is life - threatening due to dehydration and loss of electrolytes. Removal of lactose from the diet and switching to either lactase supplemented or lactose free diets forms the main stay of treatment.

Signs and symptoms of lactose intolerance

Symptoms of lactose intolerance, including abdominal distention, flatulence, abdominal cramping and diarrhea, are directly related to the amount of lactose ingested. These symptoms need not be correlated to the degree of deficiency of intestinal lactase. Mal-absorbed lactose produces an osmotic load that draws fluid and electrolytes into the intestinal lumen and causes loose stools. The onset of diarrhea and other symptoms is related to the level of non-absorbed lactose. Within 12 g of lactose or nearly 280 ml of milk, children can present with chronic abdominal pain.[48] Unabsorbed lactose is also a substratum for intestinal bacteria, particularly in colon. Bacteria metabolize lactose, which produces volatile fatty acids and gasses (methane,

carbon dioxide and hydrogen) which cause flatulence. The fatty acids lower fecal pH and make the fecal pH test an unspecific but sometimes useful marker for malabsorption of lactose (or other carbohydrates). When the bacterial metabolic processes produce enough intestinal gas to stimulate the intestinal nervous system through intestinal distention, visceral (abdominal) cramping results.

Symptom	*Pathophysiology*
Loose stools	Mal-absorbed lactose is highly osmotic → draws fluid into lumen → loose stools
Flatulence	Bacteria metabolize unabsorbed lactose→produce gasses like methane, carbon dioxide and hydrogen→ flatulence
Cramps	Accumulate intestinal gases→Intestinal lumen over distended→ nerves stimulated→cramps

Table 4 pathophysiology of symptoms

Diagnosis of lactose intolerance

To assess the intolerance to lactose, intestinal function is challenged by the ingestion of more milk products than can easily be digested. Clinical symptoms usually occur within 30 minutes, but can take up to 2 hours depending on other foods and activities. The response could be as one or more of the symptoms of nausea, diarrhea, bloating, cramping, and flatulence depending upon the degree of lactose intolerance. After confirming the diagnosis evaluation type of lactase deficiency (primary or secondary) need to be followed.

Due to the variability in presentation, diagnosing lactose intolerance only on basis of clinical symptoms is although easy is less scientific. Some of the important tests designed to evaluate lactose intolerance are;

1. **Breath tests;**

   a. Hydrogen breath test:

      Although this is more reliable than history, least invasive diagnostic test it can only be used in older age groups.

      Method:

      Standard amount of lactose (2gm/ kg to a maximum of 25 gm of lactose or 60-230 ml of milk lactose) after fasting overnight and measuring the amount of hydrogen in the expired air over a period of 2 to 3 hours. The increase in hydrogen (20 ppm) expired after approximately 60 minutes is consistent with the malabsorption of lactose.

      Factors affecting the test results:

      - conditions affecting the intestinal flora (e.g., recent use of antimicrobial agents)
      - lack of hydrogen-producing bacteria
      - ingestion of high fiber diets prior to testing
      - small intestinal bacterial over-growth
      - intestinal motility disorder

   b. [^{13} C] lactose breath test [49]

A 13CO2 breath test is performed using naturally enriched 13C-lactose as a substratum in patients with chronic abdominal pain or chronic diarrhea. The cumulative excretion of 13CO2 4 hours after 13C-lactose was compared to the excretion of the H2 breath and the activity of jejunal lactase. A relationship between cumulative 13CO2 excretion (4 hours) and lactase activity was found to be physiologically significant, with 14.5 percent 13CO2 excretion being the best cut-off point for differentiating between patients with low and normal lactase activities. The 13CO2 breath test was found to be more sensitive (0.84 vs. 0.68) and more specific (0.96 vs. 0.89) than the H2 breath test when low lactase activity was detected. The results of the two simultaneous breath tests provide a reliable picture of the patient's lactose absorption status. If not explained by history, the differences in the results of 13CO2 and H2 lactose breath tests indicate in which patients a jejunal biopsy should be performed. If lactase activity and biopsy morphology are normal, other causes of discordance should be examined.

2. Lactose tolerance test (blood test)[13]:

This test is less sensitive than the hydrogen breath test.

Method:

At the time of onset of symptoms after ingestion of the standard lactose dose (2 g / kg body weight or 50 g/m ^{2} body surface area; maximum 50g of 20% water solution) blood glucose levels are measured. If the maximum increase in blood glucose concentration after a lactose tolerance test dose is less than 26 mg/dL, malabsorption of lactose is diagnosed.

Factor affecting the test results:

- Insulin released in response to carbohydrate load lowers the glucose levels.

3. Stool tests;

a. Stool acidity test: [50]

This test is particularly useful to diagnose lactose intolerance in infants. The infant is given lactose for drinking. The lactose is digested and absorbed in the small intestine when the individual is tolerant; otherwise it is not digested and absorbed and reaches the colon. Mixed with lactose, the bacteria in the colon cause acidity in the stool. Stools passed after lactose intake are tested for the acidity level. The infant is intolerant of lactose if the stools are acidic. The stool pH in lactose intolerance is less than 5.5.

b. Stool for Reducing Substances[13]:

Reducing substances in the stool indicate that carbohydrates are not being absorbed. Hence presence of reducing substances indicates lactose intolerance. Benedict's reagent 5ml is taken and mixed with 8 drops of liquid part of stool sample and heated and colour change is observed

c. Stool test for parasites[13]:

To detect parasites like Giardia lamblia and Cryptospiridia species in the stool.

4. Lactose quick test or quick test on intestinal biopsy: [51]

This test is more useful in diagnosing adult type hypolactasia. UG endoscopy is performed and duodenal biopsies obtained. Biopsies have also been taken from the stomach and duodenum for histological examination to detect the presence of other disorders that cause malabsorption symptoms. The biopsy specimens were immediately examined. This test is based on a colorimetric test that evaluates the lactase activity: the color development in the test liquid after 20 minutes indicates whether the lactase enzyme is present in the specimen or not. In case of normal result, the color develops when the biopsy specimen's lactase enzyme breaks down the milk sugar added to the test buffer. However, if the activity of lactase is lacking or reduced no reaction or slight color reaction occurs, and the test is positive.

5. **Genetic analysis** [52]

This test enables a definitive non - invasive diagnostic test. The persistence of lactase activity in adults is associated with two polymorphisms:

a. C / T 13910

b. G / A 22018

Both of these are seen in the MCM6 gene. These polymorphisms can be detected using DNA molecular biology techniques extracted from blood or saliva samples. The procedure is to extract and amplify DNA from the sample using a strip hybridization protocol. Depending on the different combinations obtained in the Colored bands it is possible to determine whether the patient is lactose intolerant.

MANAGEMENT

Lactose avoidance:

Limiting the lactose to a level that is tolerated is the main strategy of management and is tailored to each individual because lactase deficient individuals vary in the amount of lactose that is tolerated.[53] However, those having primary lactase deficiency and no small intestine injury can consume at least 12 grams of lactose per sitting without symptoms, or with only mild symptoms. It is tolerated even better if consumed throughout day in divided portion.[54,53]

Patients must be educated about the lactose content in different dairy products to enable them to make better choices.

Food	***Serving size***	***Lactose (gms)***
Milk – regular	1cup/ 250ml	12
Milk- reduced fat	1cup/ 250ml	13
Yoghurt- regular	200gm	9
Yoghurt- low fat	200gm	12
Cheese- cheddar	30gm	0.02
Cheese-creamed cottage	30	0.1
Butter	1tsp	0.03
Ice- cream	2 scoops (50gm)	3

Table 5 lactose content in different dairy products [55]

Hidden sources of lactose

Bread and other baked foods
Processed breakfast cereals
Readymade cake biscuit and cake mixes
Margarine
Salad dressings
Cadies
Snacks

Table 6 hidden sources of lactose [56]

Milk	***% of lactose***
Cow's milk	4.7
Goat's milk	4.7
Sheep's milk	4.7
Buffalo milk	4.86
Yak milk	4.93

Table 7 % of lactose in different milks [57]

Lactase supplements: [58]

In geographic locations where total lactose avoidance is not possible or in patients who wish to consume lactose laden products, lactase supplements might come handy. Lactase enzymes similar to those produced in human's small intestines are produced industrially by Aspergillus genus fungi. The enzyme β-galactosidase is an over the counter tablet in many countries.

Limitations:

- It only works well in high acid environments.
- It is denatured in highly acidic environment, so an empty stomach pH environment denatures it.
- Is ineffective if it does not reach the small intestine before the food. So timing the dose is difficult and varies from individual to individual.

Lactose and dietary calcium

Studies show that absorption of calcium increases with the increasing dietary lactose[59] therefore it is often theorized that lactose intolerance can predispose to calcium deficiency owing to the decreased lactose intake.[60] The effects of childhood lactose - free diets on the long - term bone mineral content and the risk of fractures and aging osteoporosis remain unclear.Long - term studies are warranted to study the relation between calcium, vit D and lactose intolerance to eliminate the risks to bone health. Recent studies suggest that genetic testing may be useful in the future to identify individuals with a higher risk of lactase deficiency and consequently reduced bone mineral density,[61] potentially allowing early interaction with dietary manipulation or nutrient supplement.

Materials and methods

The study entitled "Study on lactose intolerance in children with acute diarrhea" was conducted in the Department of pediatrics at a tertiary care center from June 2017 to November 2018.

Study group consisted of 150 subjects who had acute diarrhoea. 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.

Study design: Hospital based prospective observational study

Study duration: June 2017 to November 2018

Place of study: Pediatric Department of RL Jalappa Hospital

Sample size: 150

Sample size was calculated by using the formula

$$“\ n=4Pq/L^2\ “$$

- P(prevalence) = 40.6
- Q (100-P) = 59.4
- L (allowable error) = 8

Prevalence is considered from the study conducted by Chandrasekaran R, Kumar V, Walia BNS etal., [62]

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

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 Department of Pediatrics, R L Jalappa 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.

Colour	***Amount of sugar in the sample***	***Grading***
Green Precipitate	0.1-0.5gm %	(+1)
Yellow Precipitate	0.5-1gm%	(+2)
Orange Precipitate	1-2 gm%	(+3)
Red Precipitate	>2 gm %	(+4)

Table 8 Benedict's test interpretation

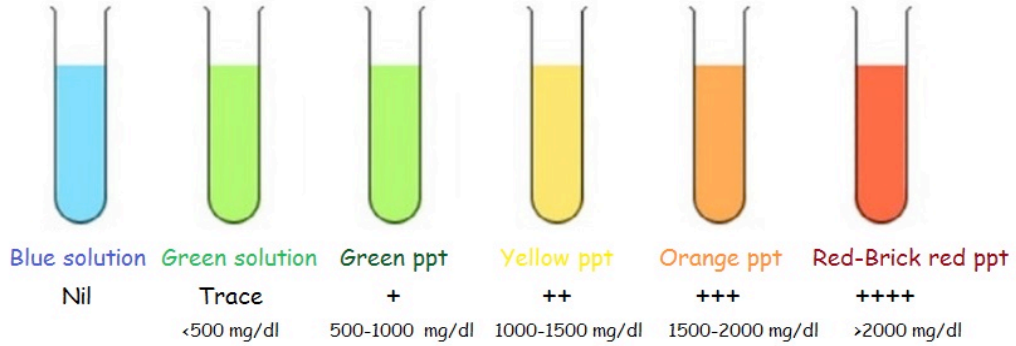

Figure 5 Benedict's test interpretation

Patients with diarrhoea, vomiting, abdominal distension, having pH $\leq$5.5 and reducing sugar $\geq$ 0.5 -1 gm % (+2) 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 affect of Lactose free diet on the duration of Illness.

Data was collected in structured data collection forms.

All the findings and observations were entered in Microsoft excel master sheet.

Statistical analysis

Continuous data was represented as mean ± standard deviation. Categorical data was expressed as numbers in percentage, fishers exact test was used to determine significant differences between two groups. Significance for the statistical tests was pre determined at a probability value of 0.05 or less. ($p< 0.05$). All the data was analysed using SPSS, EPI INFO 7, windows Excel, Windows Word software and results were published.

Observations and results

The study entitled “Study on lactose intolerance in children with acute diarrhea” 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

Age distribution

	Number of children	% (n=150)
1m to 1yr	91	60.7
1yr to 5 yr	59	39.3

Table 9 Age distribution

Table 10 shows distribution of study subjects according to age. Out of the total 150 children 91 belonged to age group, 1 month to less than 1 year and 59 belonged to age group 1 to 5 yrs.

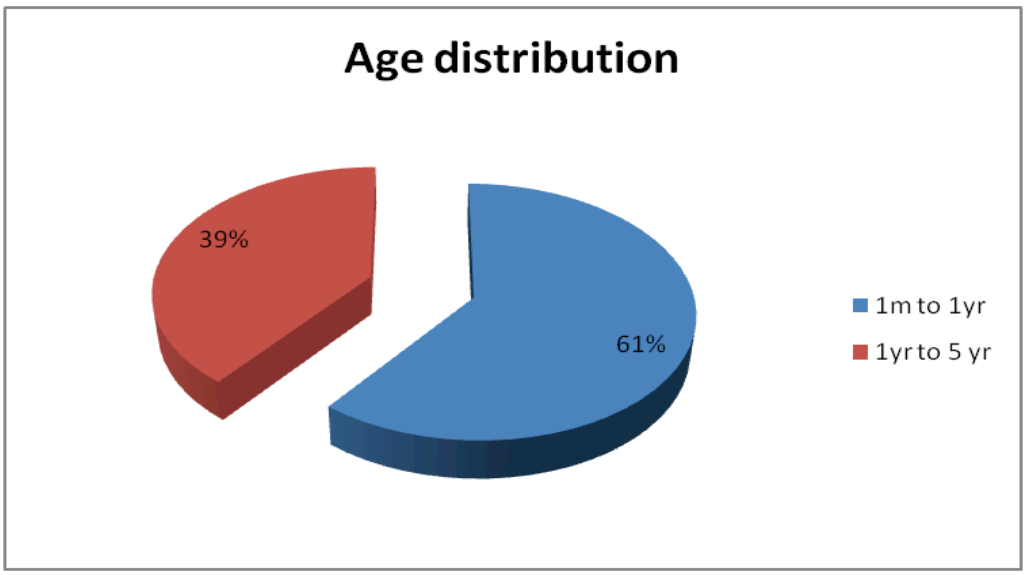

Figure 6 Age distribution

Gender distribution

Sex	Number of children	% (n=150)
Male	81	54.0
Female	69	46.0

Table 10 Gender distribution

Table 11 shows distribution of study subjects according to sex. The present study had a total number of 81 males and 69 females and the male: female ratio was 1.17:1.

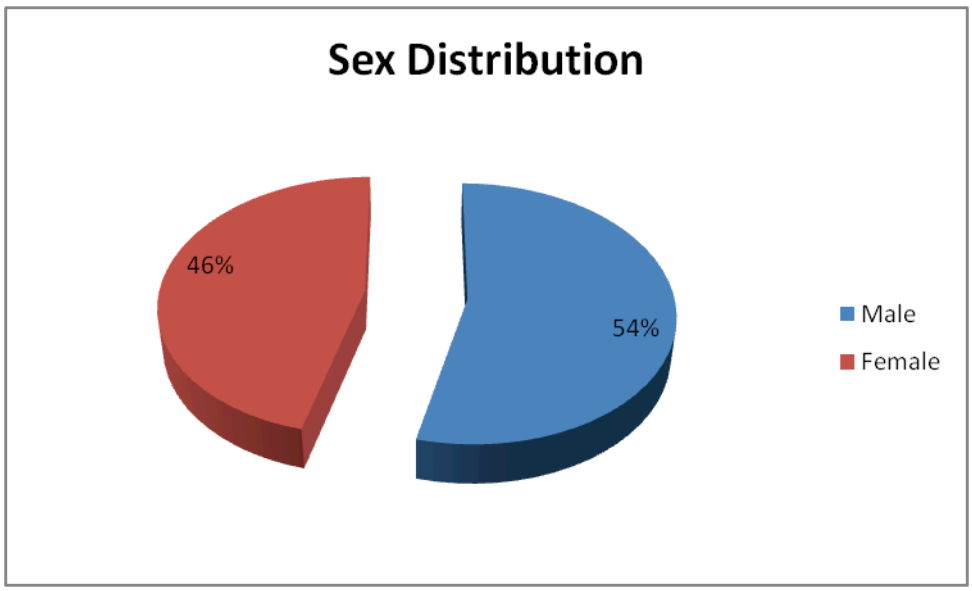

Figure 7 Gender distribution

Stool pH distribution

Stool pH	Number of children	% (n=150)
<5.5	54	36.0
>5.5	96	64.0

Table 11 Stool pH distribution

Table 12 shows distribution of study subjects according to pH. 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.

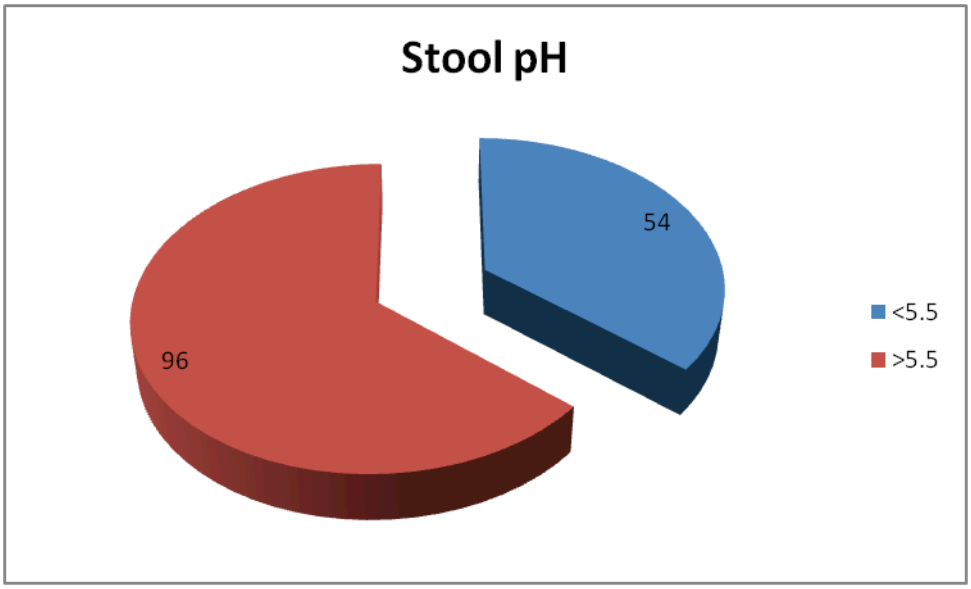

Figure 8 Stool pH distribution

Reducing substances in stool

Reducing substances	number of cases	% (n=150)
present	61	40.7
absent	89	59.3

Table 12 Reducing substances in stool

Table 13 shows distribution of study subjects according to presence or absence of reducing substances in stool. Stool was sent to test for reducing substances. Of the total 150 samples sent reducing substances were present in 61 (41%) cases and absent in 89(59%) cases.

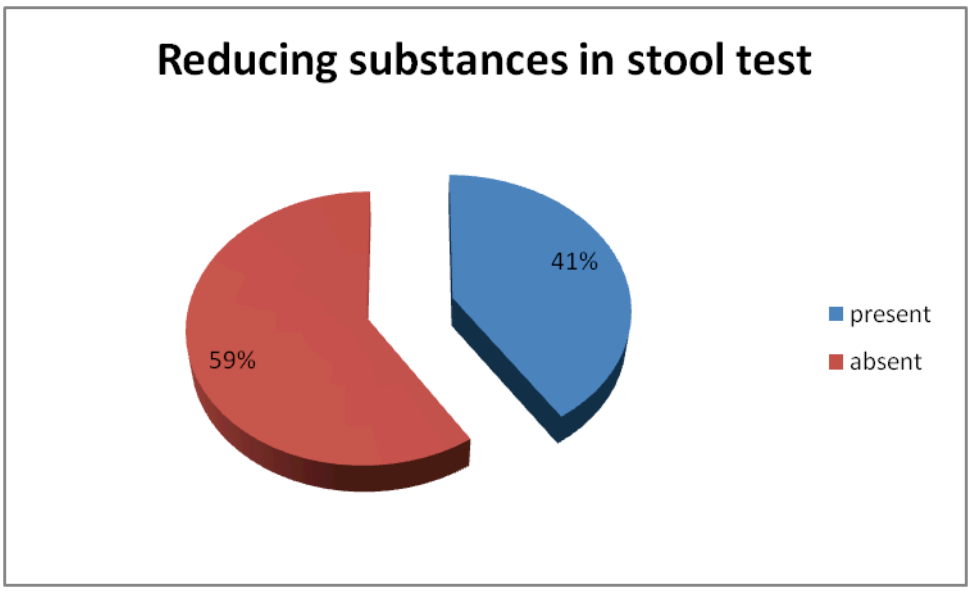

Figure 9 Reducing substances in stool

Incidence of lactose intolerance

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

Table 13 Incidence of lactose intolerance

Table 14 shows incidence of lactose intolerance. Among the 150 cases of acute diarrhoea, 54 were diagnosed as having lactose intolerance and 96 cases were lactose tolerant.

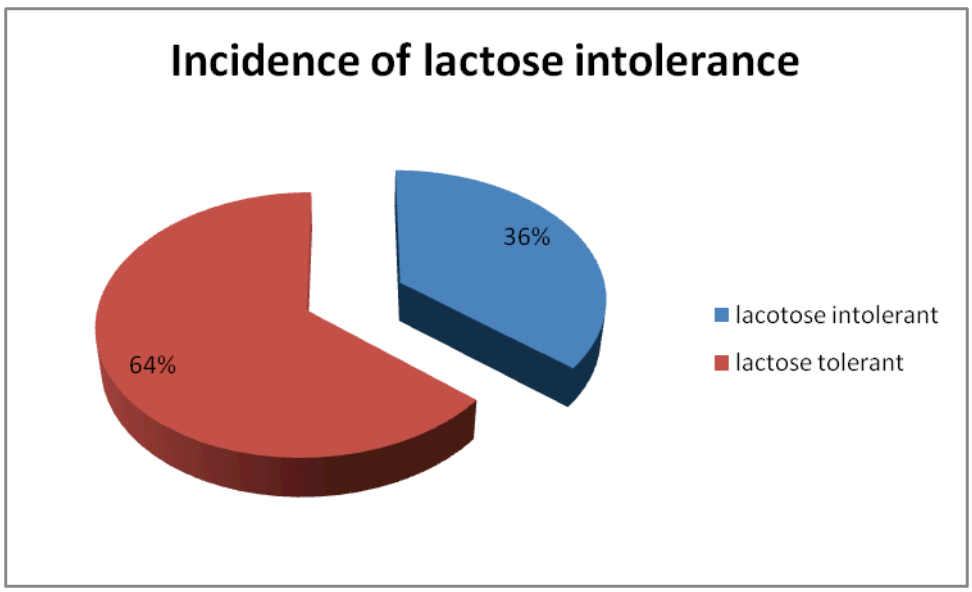

Figure 10 Incidence of lactose intolerance

Gender distribution between lactose intolerant and lactose tolerant

	male	female	p Value
Lactose intolerant	33	21	0.23
Non-lactose intolerant	48	48	

Table 14 Gender distribution

Table 15 shows gender distribution between lactose intolerant and lactose tolerant. There 19 males and 13 females in the age group of 1m to 12m and 14 males and 8 females in the age group of 13 m to 5 yrs.

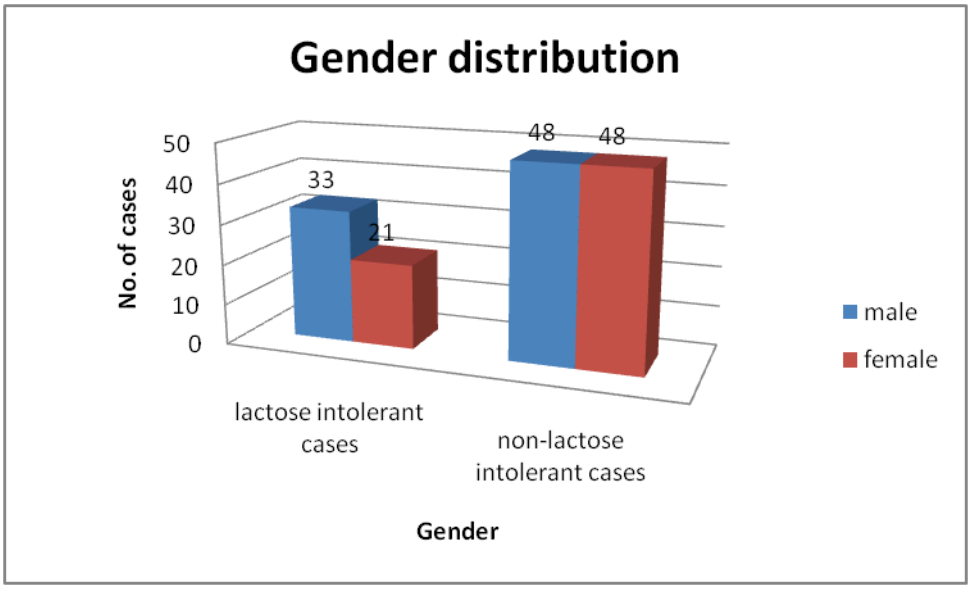

Figure 11 lactose intolerant vs lactose tolerant cases

Age vs gender distribution in cases with lactose intolerance

	male	female
1m to 12m	19	13
13m to 5yrs	14	8

Table 15 Age vs gender distribution in cases with lactose intolerance

Table 16 shows age vs gender distribution in cases with lactose intolerance. Out of 54 subjects who were lactose intolerant 32 were in the age group of 1month to 12 months and 22 were in the age group of 13 months to 5 years.

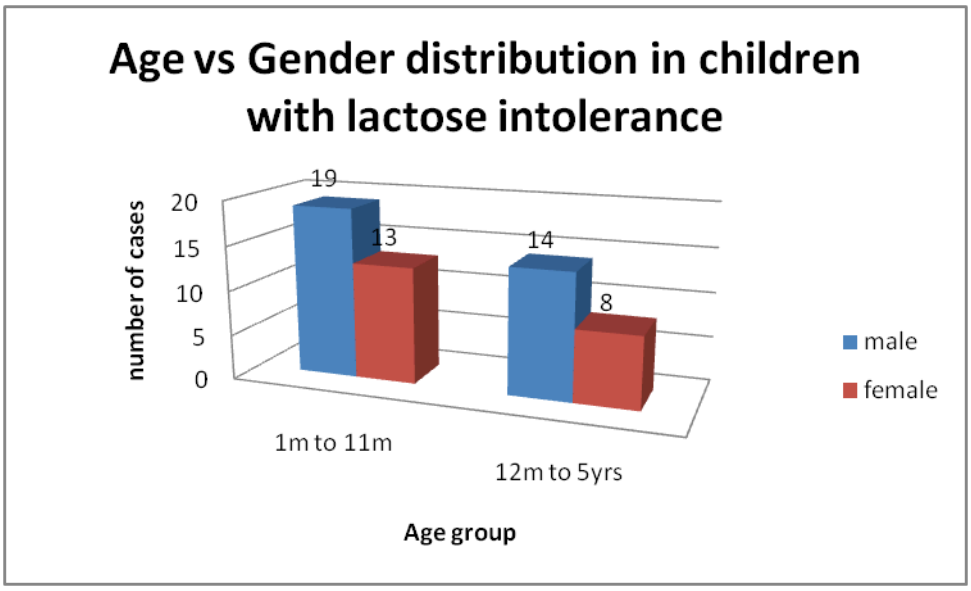

Figure 12 Age vs gender distribution in cases with lactose intolerance

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	

Table 16 Correlation between lactose intolerance and degree of dehydration

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.

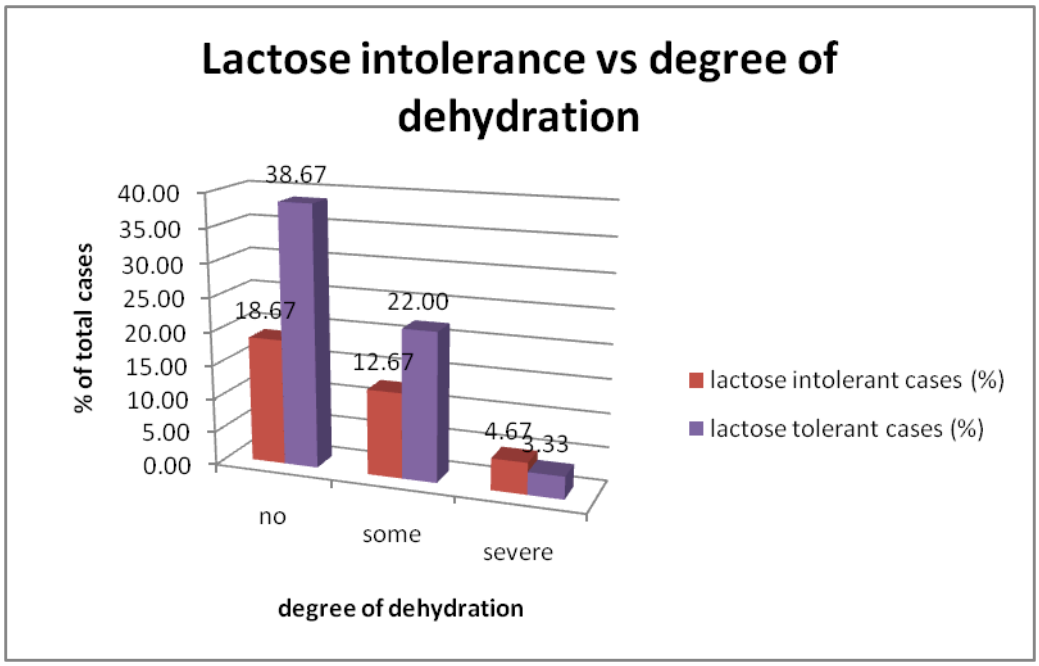

Figure 13 Correlation between lactose intolerance and degree of dehydration

Correlation between malnutrition and lactose intolerance

	Number of cases with lactose intolerance	% of cases with lactose intolerance (n=54)	Number of cases without lactose intolerance	% of cases without lactose intolerance (n=96)	Chi-square & p-value
normal	19	35.71	61	63.41	13.01 & p= 0.011 (significant)
grade 1	13	23.81	19	19.51	
grade 2	14	26.19	11	10.98	
grade 3	4	7.14	4	3.66	
grade 4	4	7.14	2	2.44	

Table 17 Correlation between malnutrition and lactose intolerance

All the cases were evaluated for signs of protein energy malnutrition and were graded as normal or graded from 1 to 4. While 19(35.7%) lactose intolerant were normal 61(63.4%) of the lactose tolerant 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.

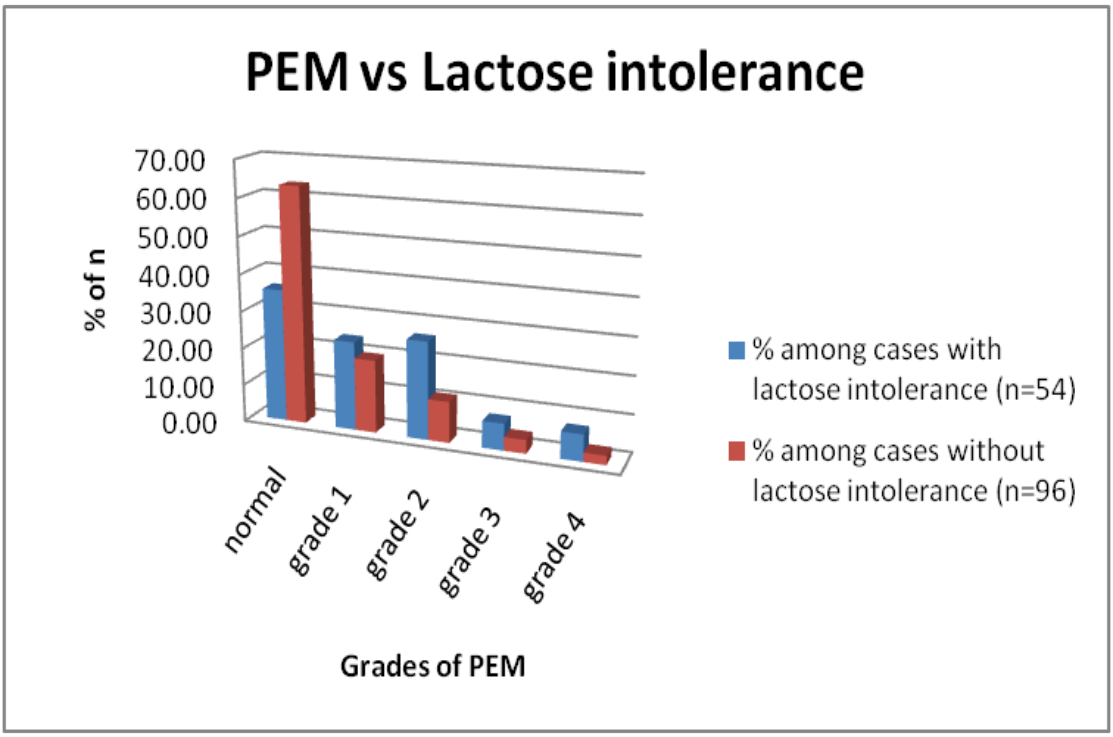

Figure 14 Correlation between malnutrition and lactose intolerance

Correlation between duration of illness and lactose intolerance

	Mean duration of diarrhea (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	

Table 18 Correlation between duration of illness and lactose intolerance

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.

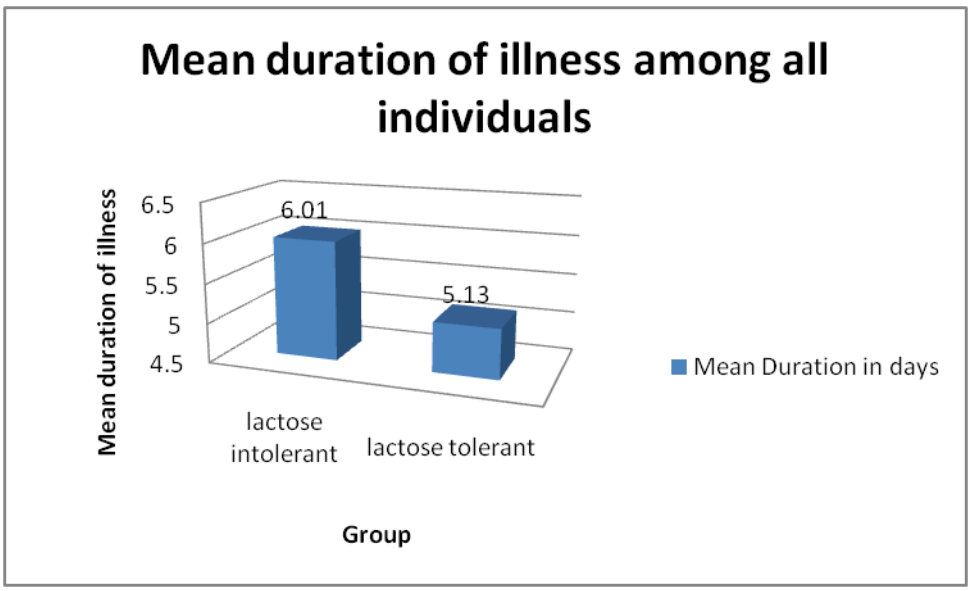

Figure 15 Correlation between duration of illness and lactose intolerance

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	

Table 19 Correlation between duration of illness and low lactose 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 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.

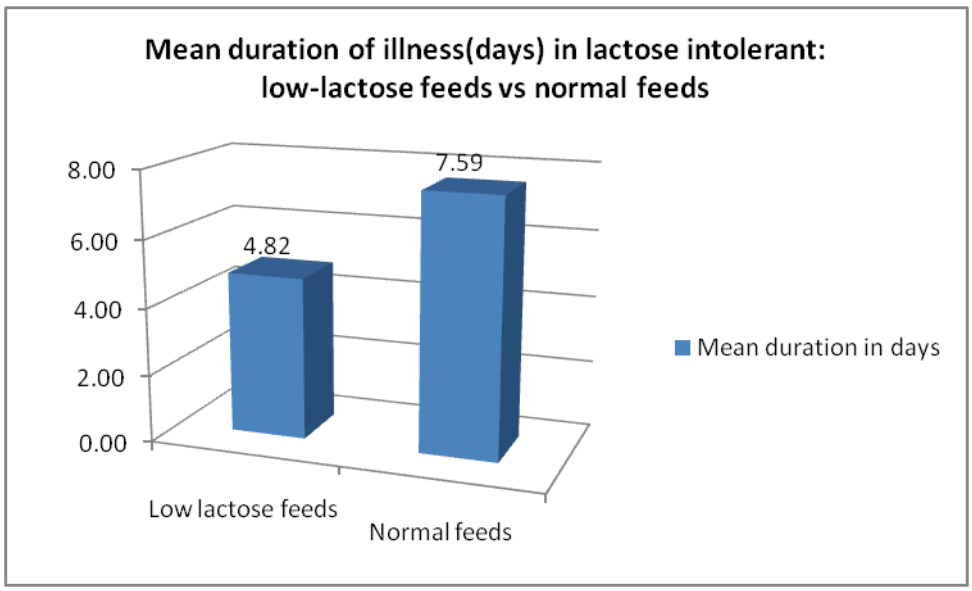

Figure 16 Correlation between duration of illness and low lactose feeds

Correlation between duration of illness and malnutrition

	Mean	Stdev
Malnutririon	6.00	1.50
Normal	5.35	1.45

Table 20 malnutrition vs duration of illness

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.

	mean	stdev
Anemia	6.00	1.49
No Anemia	5.42	1.48

Table 21 Anemia vs duration of illness

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

Socio economic factor and effect on lactose intolerance

Social class	*No of children*		*Total*	*Chi-square and pvalue*
	Lactose intolerant	*Lactose tolerant*		
1(upper class)	0	1	1	27.1
2(upper middle class)	5	4	9	P<0.0001
3(middle class)	8	26	34	
4(lower middle class)	23	61	84	
5(lower class)	18	4	22	

Table 22 socioeconomic class vs lactose intolerance

In the present study cases were classified into various socioeconomic classes using BG Prasad socioeconomic scale. A total of 84 cases were in lower middle class among which 23 cases were lactose intolerant and 61 cases were lactose tolerant. While there was only one case from upper class maximum number of cases were from lower middle class. There was a statistically significant correlation between socioeconomic class and lactose intolerance with pvalue <0.0001.

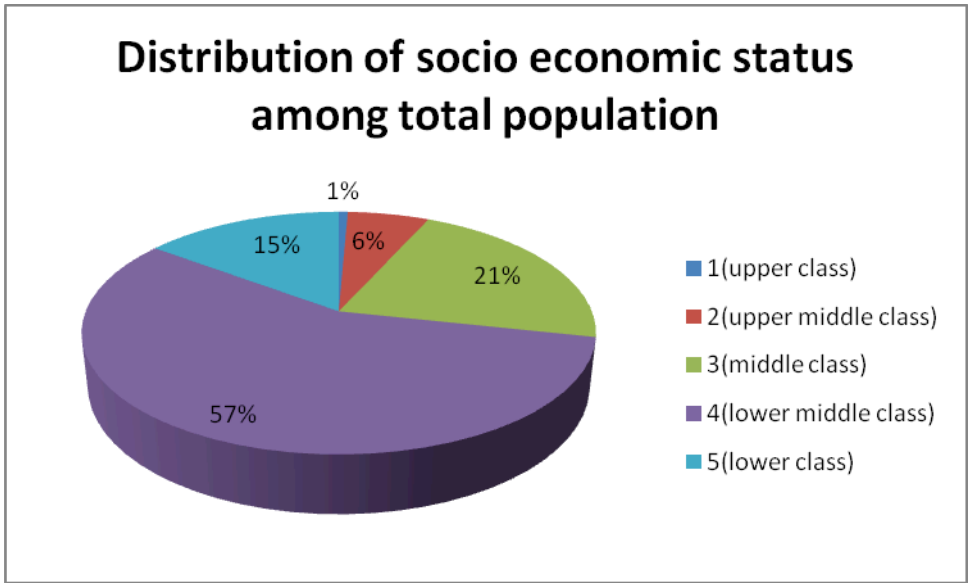

Figure 17 distribution of socio economic class among the total population

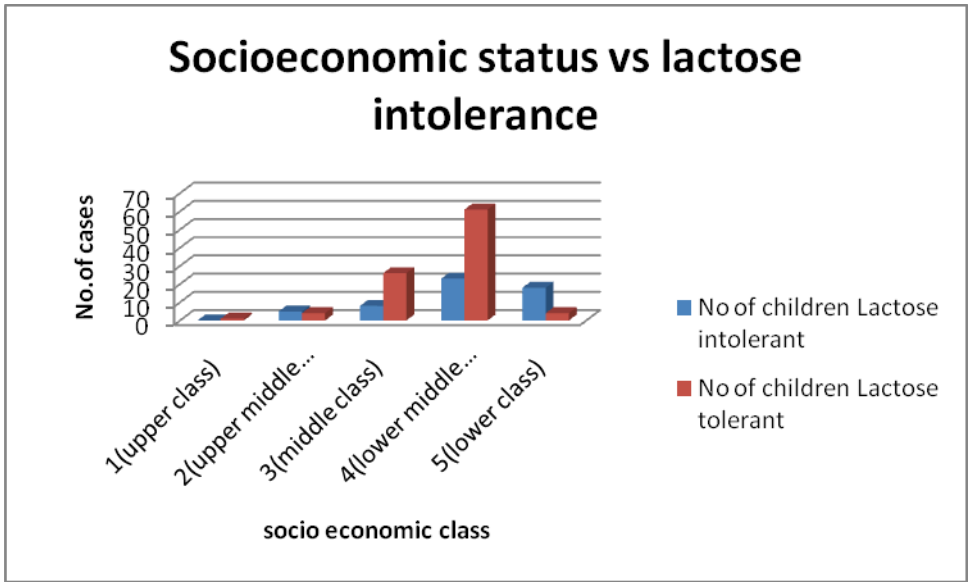

Figure 18 socioeconomic class vs lactose intolerance

Discussion

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

Of the children attending RL *Jalappa Hospital a* total of 150 children satisfied the inclusion criteria and were involved in the study. More number of children (91-60.7%) belonged to younger age group of 1m to 1 year compared to the 59(39.3%) in the 1year to 5 year age group. In a study done by Prabakar Durairaj et al [63] 26% of children belonged to age group below 6m, 40% were between 6m to 1 year and 12.5 % were between 1 to 2 yrs of age.

The present study had a total number of 81 males and 69 females and the male : female ratio was 1.17:1. The ratio is inconsistent with the Karnataka state male : female ratio of 1:1.06.[64] Many of the international studies like the one done by Hossein Sanein et al [65] depict an inverse relationship where females are more than males. This could be attributed to the similar trends of male to female ratio in general population in those communities.

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 [66] a total of 245 cases of acute diarrhoea were evaluated using faecal pH and presence of reducing substances as diagnostic tools. They found that 11.4 % 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.

Stool was sent to test for reducing substances. If the reducing substances were more than 0.25% 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,[67] were comparable. In this study a total of 3,427 samples were sent to test for reducing substances. Among them, 57.2% of the lactose intolerant samples and 17.4% of the total samples had >2.5 % of reducing substances.

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 >0.25% 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 [68] 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 rotoviral enteritis was 67.03%. In a study done in Mexico by Lifshitz F et al [67] 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 6.75 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 [62] 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.

Of the total 54 cases of lactose intolerance in the present study 33 were males and 21 were females with a male female ratio of 1:0.64. The result was statistically insignificant with a p-value of 0.23. Although similar data for secondary lactose intolerance was scanty in literature, a study done by Baadkar et al.[69], revealed a female preponderance in lactose intolerance. This trend is not comparable to the present study as the study included only adult cases with lactose non lactase persistence.

All the cases included in the study were evaluated for signs of dehydration and were classified as no dehydration, some dehydration or severe dehydration. The

results showed no correlation between lactose intolerance and degree of dehydration. 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. Similar correlation was not found in literature for comparison.

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.,[70] 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,.[45] 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,[71] 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).

Correlation between socioeconomic status and lactose intolerance was studied. While maximum number of cases belonged to lower middle class there was only 1 case belonging to upper class. There was a statistically significant correlation between socioeconomic status and lactose intolerance (p<0.0001). However, as the study was done in a hospital which is in rural area, most of the patients belong to lower socio

economic status. No studies were found comparing the socio economic status and lactose intolerance. However, a study done by Abhik Roy etal found increased incidence of malabsorption syndromes in lower socioeconomic classes.[72]

In the present study data regarding the specific pre illness diet of the patient was not captured. However, we have collected the data regarding the calorie and protein intake of the children and expected calorie and protein required. When compared the children who are malnourished were having a significant calorie deficit.

Summary & Conclusion

This is a prospective study of lactose intolerance in 150 cases with acute diarrhoea. The cases were admitted to paediatric ward of the Department of Paediatrics, Sri Devaraj Urs Academy Of Higher Education And Research, Tamaka , Kolar.

The most affected children belonged to the age group of 1m to 1 yr and males outweighed females with male to female ratio of 1.17:1.

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.

In cases with lactose intolerance there was a male sex predilection with a male : female ratio of 1:0.64.

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.

To Conclude

- Acute diarrhoea is one of most common cause of admission in children with varied causations and outcomes.
- 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.
- 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.

BIBLIOGRAPHY

1. Lakshminarayanan S, Jayalakshmy R. Diarrheal diseases among children in India: Current scenario and future perspectives. J Nat Sci Biol Med. 2015;6(1):24–8.

2. Misselwitz B, Pohl D, Frühauf H, Fried M, Vavricka SR, Fox M. Lactose malabsorption and intolerance: pathogenesis, diagnosis and treatment. United Eur Gastroenterol J. 2013 Jun;1(3):151–9.

3. Thapar N, Sanderson IR. Diarrhoea in children: an interface between developing and developed countries. The Lancet. 2004 Feb 21;363(9409):641–53.

4. WHO | Clinical management of acute diarrhoea [Internet]. WHO. [cited 2018 Dec 1]. Available from: http://www.who.int/maternal_child_ adolescent/ documents/who_fch_cah_04_7/en/

5. Practice parameter: the management of acute gastroenteritis in young children. American Academy of Pediatrics, Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis. Pediatrics. 1996 Mar;97(3):424–35.

6. King CK, Glass R, Bresee JS, Duggan C, Centers for Disease Control and Prevention. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep. 2003 Nov 21;52(RR-16):1–16.

7. Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. Cochrane Database Syst Rev. 2010 Nov 10;(11):CD003048.

8. Johnston BC, Shamseer L, da Costa BR, Tsuyuki RT, Vohra S. Measurement issues in trials of pediatric acute diarrheal diseases: a systematic review. Pediatrics. 2010 Jul;126(1):e222-231.

9. Cook GC, N G Asp, A Dahlqvist Activities of brush border lactase, acid β-galactosidase, and hetero-β-galactosidase in the jejunum of the zambian african. Gastroenterology. 1973 Mar;64(3):405-10

10. Brüssow H. Nutrition, population growth and disease: a short history of lactose. Environ Microbiol. 2013 Aug 1;15(8):2154–61.

11. Campbell AK, Matthews SB. Darwin diagnosed? Biol J Linn Soc. 2015 Dec;116(4):964–84.

12. Pubchem. alpha-Lactose [Internet]. [cited 2018 Nov 24]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/84571

13. Heyman M. Lactose Intolerance in Infants, Children, and Adolescents. PEDIATRICS. 2006 Sep 1;118(3):1279–86.

14. Newcomer AD, McGill DB. Lactose tolerance tests in adults with normal lactase activity. Gastroenterology. 1966 Mar;50(3):340–6.

15. Sahi T, Isokoski M, Jussila J, Launiala K, Pyörälä K. Recessive inheritance of adult-type lactose malabsorption. Lancet Lond Engl. 1973 Oct 13;2(7833):823–6.

16. Kruse TA, Bolund L, Grzeschik K-H, Ropers HH, Sjöström H, Norén O, et al. The human lactase-phlorizin hydrolase gene is located on chromosome 2. FEBS Lett. 1988 Nov 21;240(1–2):123–6.

17. Leloir LF. The enzymatic transformation of uridine diphosphate glucose into a galactose derivative. Arch Biochem Biophys. 1951 Sep;33(2):186–90.

18. Assessment of Liver Metabolic Function - [PDF Document] [Internet]. [cited 2018 Nov 24]. Available from: https://vdocuments.mx/assessment-of-liver-metabolic-function.html

19. Tengström B. Renal excretion of galactose in man, with determination of the maximal tubular reabsorption for galactose. Scand J Clin Lab Invest. 1968;21(4):321–6.

20. Potter J, Ho MW, Bolton H, Furth AJ, Swallow DM, Griffiths B. Human lactase and the molecular basis of lactase persistence. Biochem Genet. 1985 Jun;23(5–6):423–39.

21. Groen J. The absorption of Hexoses from the upper part of the Small Intestine in man. J Clin Invest. 1937 Mar 1;16(2):245–55.

22. Gorbach SL. Microbiology of the Gastrointestinal Tract. In: Baron S, editor. Medical Microbiology [Internet]. 4th ed. Galveston (TX): University of Texas Medical Branch at Galveston; 1996 [cited 2018 Nov 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK7670/

23. Montalto M, Curigliano V, Santoro L, Vastola M, Cammarota G, Manna R, et al. Management and treatment of lactose malabsorption. World J Gastroenterol WJG. 2006 Jan 14;12(2):187–91.

24. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism [Internet]. [cited 2018 Nov 24]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3735932/

25. Cuatrecasas P, Lockwood DH, Caldwell JR. Lactase deficiency in the adult. A common occurrence. Lancet Lond Engl. 1965 Jan 2;1(7375):14–8.

26. Cummings JH, Pomare EW, Branch WJ, Naylor CP, Macfarlane GT. Short chain fatty acids in human large intestine, portal, hepatic and venous blood. Gut. 1987 Oct;28(10):1221–7.

27. Lactose Intolerance in Infants, Children, and Adolescents | FROM THE AMERICAN ACADEMY OF PEDIATRICS | Pediatrics [Internet]. [cited 2018 Nov 24]. Available from: http://pediatrics.aappublications.org/content/118/3/1279

28. Wilson J. Milk Intolerance: Lactose Intolerance and Cow's Milk Protein Allergy. Newborn Infant Nurs Rev. 2005 Dec 1;5:203–7.

29. Isolated Intestinal Lactase Deficiency in the Adult. - PubMed - NCBI [Internet]. [cited 2018 Nov 23]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/14044269

30. Bayless TM, Rosensweig NS. A racial difference in incidence of lactase deficiency. A survey of milk intolerance and lactase deficiency in healthy adult males. JAMA. 1966 Sep 19;197(12):968–72.

31. Flatz G, Saengudom C, Sanguanbhokhai T. Lactose intolerance in Thailand. Nature. 1969 Feb 22;221(5182):758–9.

32. Primary adult lactose intolerance and the milking habit: a problem in biological and cultural interrelations. I. Review of the medical research - Abstract - Europe PMC [Internet]. [cited 2018 Nov 23].Available from: https://europepmc.org/abstract/med/4902756

33. Labrie V, Buske OJ, Oh E, Jeremian R, Ptak C, Gasiūnas G, et al. Lactase nonpersistence is directed by DNA-variation-dependent epigenetic aging. Nat Struct Mol Biol. 2016 May 9;23(6):566–73.

34. Mattar R, de Campos Mazo DF, Carrilho FJ. Lactose intolerance: diagnosis, genetic, and clinical factors. Clin Exp Gastroenterol. 2012 Jul 5;5:113–21.

35. Kretchmer N. Lactose and lactase--a historical perspective. Gastroenterology. 1971 Dec;61(6):805–13.

36. Worldwide_prevalence_of_lactose_intolerance_in_recent_populations.jpg (JPEG Image, 1722 × 1187 pixels) - Scaled (55%) [Internet]. [cited 2018 Nov 24]. Available from: https://upload.wikimedia.org/wikipedia/commons/2/27/ Worldwide_ prevalence_of_lactose_intolerance_in_recent_populations.jpg

37. Sahi T. Genetics and epidemiology of adult-type hypolactasia. Scand J Gastroenterol Suppl. 1994;202:7–20.

38. Murphy MS. Guidelines for managing acute gastroenteritis based on a systematic review of published research. Arch Dis Child. 1998 Sep 1;79(3):279–84.

39. Bhatnagar S, Bhan MK, Singh KD, Saxena SK, Shariff M. Efficacy of milk-based diets in persistent diarrhea: a randomized, controlled trial. Pediatrics. 1996 Dec;98(6 Pt 1):1122–6.

40. Habte D, Hyvarinen A, Sterky G. Carbohydrate malabsorption in kwashiorkor. Ethiop Med J. 1973 Jan;11(1):33–40.

41. Evaluation of an algorithm for the treatment of persistent diarrhoea: a multicentre study. International Working Group on Persistent Diarrhoea. Bull World Health Organ. 1996;74(5):479–89.

42. Angelides AG, Davidson M. Lactose Intolerance and Diarrhea: Are They Related? Pediatr Ann. 1985 Jan 1;14(1):62–75.

43. Erasmus HD, Ludwig-Auser HM, Paterson PG, Sun D, Sankaran K. Enhanced weight gain in preterm infants receiving lactase-treated feeds: A randomized, double-blind, controlled trial. J Pediatr. 2002 Oct;141(4):532–7.

44. Shulman RJ, Feste A, Ou C. Absorption of lactose, glucose polymers, or combination in premature infants. J Pediatr. 1995 Oct;127(4):626–31.

45. Lifshitz F. Congenital lactase deficiency. J Pediatr. 1966 Aug 1;69(2):229–37.

46. Savilahti E, Launiala K, Kuitunen P. Congenital lactase deficiency. A clinical study on 16 patients. Arch Dis Child. 1983 Apr;58(4):246–52.

47. Asp N-G, Dahlqvist A, Kuitunen P, Launiala K, Visakorpi JK. Complete Deficiency of Brush-Border Lactase in Congenital Lactose Malabsorption. The Lancet. 1973 Aug;302(7824):329–30.

48. Gremse DA, Greer AS, Vacik J, DiPalma JA. Abdominal pain associated with lactose ingestion in children with lactose intolerance. Clin Pediatr (Phila). 2003 May;42(4):341–5.

49. Hiele M, Ghoos Y, Rutgeerts P, Vantrappen G, Carchon H, Eggermont E. 13CO2 breath test using naturally 13C-enriched lactose for detection of lactase deficiency in patients with gastrointestinal symptoms. J Lab Clin Med. 1988 Aug;112(2):193–200.

50. How to Test for Lactose Intolerance: Stool Acidity Test [Internet]. [cited 2018 Nov 26]. Available from: https://www.medicinenet.com/stool_acidity_ test/article. htm#what_is_a_stool_acidity_test

51. Kuokkanen M, Myllyniemi M, Vauhkonen M, Helske T, Kääriäinen I, Karesvuori S, et al. A biopsy-based quick test in the diagnosis of duodenal hypolactasia in upper gastrointestinal endoscopy. Endoscopy. 2006 Jul;38(7):708–12.

52. Enattah NS, Sahi T, Savilahti E, Terwilliger JD, Peltonen L, Järvelä I. Identification of a variant associated with adult-type hypolactasia. Nat Genet. 2002 Feb;30(2):233–7.

53. Szilagyi A. Adaptation to Lactose in Lactase Non Persistent People: Effects on Intolerance and the Relationship between Dairy Food Consumption and Evalution of Diseases. Nutrients. 2015 Aug 13;7(8):6751–79.

54. Silanikove N, Leitner G, Merin U. The Interrelationships between Lactose Intolerance and the Modern Dairy Industry: Global Perspectives in Evolutional and Historical Backgrounds. Nutrients. 2015 Aug 31;7(9):7312–31.

55. Diet for Lactose Intolerance | GastroNet [Internet]. [cited 2018 Nov 27]. Available from: http://www.gastro.net.au/diets/lactose.html

56. Eating, Diet, & Nutrition for Lactose Intolerance | NIDDK [Internet]. National Institute of Diabetes and Digestive and Kidney Diseases. [cited 2018 Nov 27]. Available from: https://www.niddk.nih.gov/health-information/digestive-diseases/lactose-intolerance/eating-diet-nutrition

57. Tables of lactose content [Internet]. [cited 2018 Nov 27]. Available from: https://www.food-intolerance-network.com/food-intolerances/lactose-intolerance/tables-of-lactose-content.html

58. O'Connell S, Walsh G. Physicochemical characteristics of commercial lactases relevant to their application in the alleviation of lactose intolerance. Appl Biochem Biotechnol. 2006 Aug;134(2):179–91.

59. Abrams SA, Griffin IJ, Davila PM. Calcium and zinc absorption from lactose-containing and lactose-free infant formulas. Am J Clin Nutr. 2002 Aug 1;76(2):442–6.

60. Di Stefano M, Veneto G, Malservisi S, Cecchetti L, Minguzzi L, Strocchi A, et al. Lactose malabsorption and intolerance and peak bone mass. Gastroenterology. 2002 Jun;122(7):1793–9.

61. Obermayer-Pietsch BM, Bonelli CM, Walter DE, Kuhn RJ, Fahrleitner-Pammer A, Berghold A, et al. Genetic Predisposition for Adult Lactose Intolerance and Relation to Diet, Bone Density, and Bone Fractures. J Bone Miner Res. 2003 Dec 15;19(1):42–7.

62. Kumar V, Chandrasekaran R, Bhaskar R. Carbohydrate Intolerance Associated with Acute Gastroenteritis: A Prospective Study of 90 Well-Nourished Indian Infants. Clin Pediatr (Phila). 1977 Dec;16(12):1123–7.

63. Durairaj P, Raju S, Thirumalaikumarasamy S. Clinical profile and risk factors for persistent diarrhoea in children under five years of age in an urban referral centre. Int J Contemp Pediatr. 2017 Oct 24;4(6):1986–94.

64. Sex Ratio (Females/ 1000 Males) | NITI Aayog, (National Institution for Transforming India), Government of India [Internet]. [cited 2018 Dec 12]. Available from: https://niti.gov.in/content/sex-ratio-females-1000-males

65. Saneian H, Yaghini O, Modaresi M, Razmkhah N. Lactose-Free Compared with Lactose-Containing Formula in Dietary Management of Acute Childhood Diarrhea. Iran J Pediatr. 2012 Mar;22(1):82–6.

66. Karabocuoglu M, Sokucu S, Gokcay G, Ucsel R, Neyzi O. Carbohydrate malabsorption in acute diarrhea. Indian Pediatrics. 1994;31(9):1071-4.

67. Lifshitz F, Coello-Ramirez P, Gutierrez-Topete G, Cornado-Cornet MC. Carbohydrate intolerance in infants with diarrhea. J Pediatr. 1971 Nov;79(5):760–7.

68. Hu Y, Gui L, Chang J, Liu J, Xu S, Deng C, et al. The incidence of infants with rotavirus enteritis combined with lactose intolerance. Pak J Pharm Sci. 2016 Jan;29(1 Suppl):321–3.

69. Baadkar SV, Mukherjee MS, Lele SS. Study on influence of age, gender and genetic variants on lactose intolerance and its impact on milk intake in adult Asian Indians. Ann Hum Biol. 2014 Nov;41(6):548–53.

70. Kvissberg MA, Dalvi PS, Kerac M, Voskuijl W, Berkley JA, Priebe MG, et al. Carbohydrate malabsorption in acutely malnourished children and infants: a systematic review. Nutr Rev. 2016 Jan;74(1):48–58.

71. MacGillivray S, Fahey T, McGuire W. Lactose avoidance for young children with acute diarrhoea. Cochrane Database Syst Rev. 2013 Oct 31;(10):CD005433.

72. Roy A, Mehra S, Kelly C, Tariq S, Pallav K, Dennis M et al. The association between socioeconomic status and the symptoms at diagnosis of celiac disease: a retrospective cohort study. Therapeutic Advances in Gastroenterology. 2016;9(4):495-502.

ANNEXURE

PATIENT INFORMATION SHEET

Title of the study: Study on Lactose Intolerance in Children with Acute Diarrhoea

Purpose of the Research: Lactose intolerance can occur in infants and young children suffering from acute diarrhoeal illness, but its clinical importance is restricted to children with severe diarrhoea. The prevalence of lactose intolerance is greater than 50% in South America and Africa, whereas in some Asian countries, the prevalence reaches almost 100%. A study showed that among 54 hospitalised children with acute diarrhoea aged between 6 and 36 months, about 26% of them were found to have sugar intolerance. There are no explicit criteria or guidelines on lactose intolerance secondary to Acute Diarrhea, the factors effecting the outcome such as duration or severity of the disease.

This study aims at identifying the incidence and the factors affecting the outcome of the disease

Procedures and Protocols: The study includes 150 children below 5 years of age suffering with Acute Diarrhoea. The patients will be selected from those admitted in the Department of Pediatrics, R L Jalappa Hospital. After selection, detailed history and physical examination will be 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 will be measured. Examination for abdominal distension will be done. Stool (3ml) will be collected in a clean container. At first physical character of stool and then pH of stool by pH meter will be noted. Reducing sugar will be determined in watery portion of stool with Benedict's reagent

Reimbursements: You will not be given money or gifts to take part in this research.

Confidentiality: We will not be sharing the identity of the participant. The information we collect from you will be kept confidential and only the researches involved in this project will have access to it.

Right to Refuse or Withdraw: You do not have to take part in this research if you do not wish to do so and you can refuse to participate.

Who to Contact: If you have any questions you may ask us now or later, even after the study has started you may contact the following persons.

For more Information:

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INFORMED CONSENT FORM

I, Mr./Mrs. _____ have been explained in a language that I can understand, that my child _____ be included in a study which is Study on Lactose Intolerance in Children with Acute Diarrhea.

I have been explained that my child's clinical finding, investigations, lab values will be assessed and documented for the study purpose.

I have been explained that my child's participation in this study is entirely voluntary and I can withdraw from the study anytime and this will not affect my relation with my doctor or the treatment for his ailment.

I have understood that all the details found during the study are kept confidential and while publishing or sharing of the findings, my child details will be masked.

I, in my sound mind give full consent to add my child in the part of this study.

Signature of the Parent or Guardian:

Name:

Signature of the witness:

Name:

Date: Place:

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿ ಪತ್ರ

ನಾನು Mr./Mrs. _____ ನನ್ನ ಮಗು _____ ಇದು ತೀವ್ರ ಅತಿಸಾರ ಮಕ್ಕಳು ಲ್ಯಾಕ್ಟೋಸ್ ಅಸಹಿಷ್ಣುತೆ ಮೇಲೆ ಸ್ಟಡಿ ಒಂದು ಅಧ್ಯಯನದಲ್ಲಿ ಒಳಗೊಂಡಿದೆ ಎಂದು, ನಾನು ಅರ್ಥವಾಗುವಂತಹ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ನನ್ನ ಮಗುವಿನ ವೈದ್ಯಕೀಯ ಸಂಶೋಧನೆಗೆ ತನಿಖೆಗಳು, ಲ್ಯಾಬ್ ಮೌಲ್ಯಗಳು ಮೌಲ್ಯಮಾಪನ ನಡೆಯಲಿದೆ ಮತ್ತು ಅಧ್ಯಯನ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗಿದೆ ಎಂದು ವಿವರಿಸಲಾಗಿದೆ.

ನಾನು ವಿವರಿಸಲಾಗಿದೆ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಮಗುವಿನ ಭಾಗವಹಿಸುವಿಕೆಯು ಸಂಪೂರ್ಣವಾಗಿ ವೈಯಕ್ತಿಕವಾಗಿದ್ದು ಮತ್ತು ನಾನು ಯಾವುದೇ ಅಧ್ಯಯನ ಹಿಂದೆಗೆದುಕೊಳ್ಳಲು ಮತ್ತು ಈ ನನ್ನ ವೈದ್ಯರು ಅಥವಾ ಅವನಿಗೆ ಬಂದಿದ್ದ ರೋಗ ಚಿಕಿತ್ಸೆ ನನ್ನ ಸಂಬಂಧಿಸಿದಂತೆ ಪರಿಣಾಮ ಸಾಧ್ಯವಿಲ್ಲ.

ನಾನು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಕಂಡುಬರುವ ಎಲ್ಲಾ ವಿವರಗಳು ಖಾಸಗಿ ಇರಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಪ್ರಕಾಶನ ಅಥವಾ ಸಂಶೋಧನೆಗಳ ಹಂಚಿಕೆ ಮಾಡುವಾಗ, ನನ್ನ ಮಗು ವಿವರಗಳು ತಡೆಯುತ್ತವೆ ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ನನ್ನ ಧ್ವನಿ ಮನಸ್ಸಿನಲ್ಲಿ ಈ ಅಧ್ಯಯನದ ಭಾಗವಾಗಿ ನನ್ನ ಮಗು ಸೇರಿಸಲು ಪೂರ್ಣ ಒಪ್ಪಿಗೆ ನೀಡಿ.

ಪೋಷಕರು ಅಥವಾ ಪೋಷಕರ ಸಹಿ:
ಹೆಸರು:

ಸಾಕ್ಷಿಯ ಸಹಿ:
ಹೆಸರು:

ದಿನಾಂಕ:
ಸ್ಥಳ:

PROFORMA

NAME: AGE: SEX:

UHID: INFORMANT:

HISTORY

- Duration of Diarrhea:
- Blood or Mucus in Stool:
- Relation to intake of Milk:
- Abdominal Pain:
- Bloating:
- Flatulence:
- Vomiting:
- Fever:

OTHER ILLNESS:

PAST HISTORY:

FAMILY HISTORY:

ANTHROPOMETRY:

- Weight:
- Height/Length:
- Mid Arm Circumference:
- Head Circumference:
- Body Mass Index:
- Weight for Height/Length:

SOCIO-ECONOMIC STATUS: According to BG Prasad Classification.

DIETARY HISTORY:

VITALS:

Heart Rate: Respiratory Rate:

Blood Pressure: Temperature:

GENERAL EXAMINATION:

- Anemia:
- Abdominal Distension:
- Signs of Dehydration:

1. Thirst:
2. Skin Turgor:
3. Sunken Eyes:
4. Mental Status:
5. Mucus Membranes
6. Pulse Rate:
7. Capillary Refill time:
8. Blood Pressure:
9. Urine Output:

SYSTEMIC EXAMINATION:

- CVS:

- RS:

- P/A:

- CNS:

INVESTIGATION:

- Stool Routine: Ph: Reducing Substances:
- Hemoglobin:

TREATMENT:

NAN Lactose Free Formula:

Antibiotics:

DURATION OF ILLNESS:

IAP CLASSIFICATION OF MALNUTRITION

Grade of malnutrition	Weight for age of the standard (%)
Normal	>80
Grade I	71-80 (mild malnutrition)
Grade II	61-70 (moderate malnutrition)
Grade III	51-60 (severe malnutrition)
Grade IV	<50 (very severe malnutrition)

Age Specific Blood Cell Indices

Age	Normal Hemoglobin	-2 Standard Deviation
1 mon	13.9	10.7
2- 5 mon	11.2	9.4
6 mon	12.6	11.1
6 mon – 2 yr	12.0	10.5
2 - 6 yr	12.5	11.5

	No dehydration	Some dehydration	Severe dehydration
Mental status	Normal	Irritable	Lethargic to comatose
Thirst	Normal	Increased	Unable to drink
Skin Turgor	Normal	Mild delay in turgor	Tenting
Sunken Eyes	Normal	Sunken	Very sunken
Mucous Membranes	Normal	Dry	Very dry
Pulse rate	Normal	Slightly increased	Tachycardia
Capillary refill	2-3 sec	3-4 sec	>4 sec
Blood Pressure	Normal	Normal	Normal or Low
Urine output	Slightly decreased	Decreased	Oliguria, Anuria

Sl No	UHID No	Sex	Age (m)	Hemoglobin	Anemia	Dehydration	Stool pH	Reducing Substance	PEM grading	Duration of illness	Feeds	SES Class
1	329436	F	18	10.1	P	severe	5	yes	N	6	low lactose	5
2	351472	F	8	11.2	N	no	6.5	no	n	5	normal	4
3	363832	M	12	6.5	P	severe	6	no	n	5	normal	1
4	408928	M	10	9.8	P	no	6.5	yes	N	1	low lactose	4
5	413670	F	15.6	7.7	P	no	6	no	g1	4	normal	2
6	435286	M	60	11.7	N	no	6.5	no	n	4	normal	4
7	440997	F	3	9	P	no	6	no	g4	6	low lactose	2
8	441306	M	12	5.8	P	no	6	no	g1	3	normal	2
9	442237	M	48	11.9	N	no	5	yes	N	7	normal	3
10	443222	F	36	11.9	N	no	6	no	n	5	normal	2
11	445007	M	14.4	8.5	P	no	6.5	no	g2	5	normal	4
12	445477	M	9	10.4	P	no	5	yes	N	7	normal	3
13	446751	M	24	11.3	N	some	4.5	yes	N	10	normal	4
14	447118	M	60	12.5	N	some	6	no	n	5	normal	3
15	447368	F	9	9.7	P	no	7	no	g2	4	normal	5
16	447768	F	11	8.7	P	no	6.5	no	g2	6	normal	4
17	447804	F	1	10.6	P	some	5	yes	n	4	normal	3
18	449313	M	36	12.6	N	severe	6	no	g2	6	normal	3
126	449323	F	9	11.1	N	some	4.5	yes	g4	5	low lactose	4
19	450342	M	48	9.4	P	some	6.5	no	n	4	low lactose	4
20	450731	M	11	13.4	N	no	6.5	no	n	6	low lactose	3
21	451216	M	12	7.4	P	no	6	no	g2	6	normal	3
22	451304	F	4	9	P	no	6	no	g1	7	normal	5
23	452120	M	9	8	P	no	4.5	yes	g1	9	normal	3
24	453832	F	3	9.1	P	no	6	no	n	7	normal	4
25	454476	M	1	12.5	N	no	5	yes	g2	9	normal	3
26	456315	M	30	13.4	N	severe	6	no	n	4	normal	4
27	457228	F	18	11.1	N	no	6.5	yes	g2	3	normal	3
28	460483	F	3	9	P	some	6	no	g1	6	normal	5
29	460623	M	6	10.3	P	no	4	yes	g1	8	normal	5
30	461778	F	10	10.3	P	no	4.5	yes	g1	4	low lactose	3
31	464044	M	21.6	8.4	P	no	4.5	yes	N	8	normal	3
32	466604	F	36	11.9	N	some	6	no	g2	4	low lactose	3
33	467919	F	18	9.7	P	no	5	yes	N	3	low lactose	4
34	473183	F	1	7.8	P	no	6.5	no	n	5	normal	3
35	473454	M	30	8.6	P	some	5	yes	N	6	low lactose	3
36	473756	F	12	8.2	P	no	6	no	n	8	normal	3

Sl No	UHID No	Sex	Age (m)	Hemoglobin	Anemia	Dehydration	Stool pH	Reducing Substance	PEM grading	Duration of illness	Feeds	SES Class
37	476240	M	18	8.3	P	no	5	yes	N	7	normal	2
38	476634	M	7	9.4	P	some	5	yes	N	4	low lactose	4
39	480420	M	12	7.9	P	no	5	yes	g2	9	normal	4
40	482873	M	5	9.5	P	some	5	yes	g2	5	low lactose	4
41	485153	F	3.5	11	N	no	6.5	yes	g3	6	normal	5
42	485302	M	1.3	10.6	P	some	7	no	n	5	normal	3
43	487216	F	5	11.3	N	some	6	no	n	6	normal	2
44	487331	M	11	9.2	P	severe	5	yes	N	7	normal	4
45	492705	F	1	11.2	N	some	6.5	no	n	6	normal	5
46	495746	M	14.4	8.9	P	no	5	yes	g1	6	low lactose	3
47	497280	M	2.2	11.4	N	no	6	no	n	3	normal	4
48	499033	M	3	8.4	P	some	5	yes	g2	9	normal	4
49	499093	F	43.2	10.4	P	no	6.5	no	g3	5	normal	5
50	499258	F	8	10.5	P	no	4	yes	g2	8	normal	3
51	500634	M	1.5	11.7	N	some	6	no	n	4	low lactose	4
52	503791	M	24	10.8	P	no	6.5	no	g3	4	normal	2
53	505394	F	24	11.5	N	some	5	yes	N	7	normal	3
54	505617	M	18	10.2	P	some	6	yes	g1	4	normal	3
55	505941	F	12	7.3	P	no	6	no	g1	6	low lactose	5
56	506438	F	15.6	6.9	P	some	7	no	n	3	normal	4
57	506449	F	2	8.9	P	severe	5	yes	g4	8	normal	4
58	506459	F	2	8.9	P	no	4.5	yes	g2	6	normal	5
59	507454	M	12	11.4	N	no	4.5	yes	g1	4	low lactose	3
60	509824	M	10	9.3	P	some	6	no	n	4	normal	4
61	511377	M	11	9.1	P	no	5	yes	g3	6	normal	5
62	512701	M	33.6	11.9	N	no	5	yes	g1	6	normal	3
63	514270	F	14.4	9.5	P	no	6	no	n	6	normal	4
64	514306	M	24	7	P	no	6.5	no	n	4	normal	4
65	514629	M	24	9.3	P	some	5	yes	g2	4	low lactose	4
66	514662	F	12	8.6	P	some	5	yes	g2	10	normal	3
67	514703	M	12	7.9	P	no	6	no	n	6	normal	3
68	515330	F	7	8.4	P	no	6	no	n	5	normal	4
69	515754	F	6	11.6	N	no	6.5	no	n	6	low lactose	4
70	518393	M	11	7	P	no	6.5	no	g2	5	low lactose	4
71	519150	M	12	7.6	P	no	4	yes	N	8	normal	2
72	519213	M	12	6.7	P	some	5	yes	N	6	low lactose	3
73	521285	M	18	8.9	P	no	6	no	g4	6	low lactose	4

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74	522465	M	36	17.6	N	some	6.5	yes	g2	6	low lactose	4
75	523404	M	13	9.5	P	no	6.5	no	n	4	normal	4
76	524609	M	4	8.2	P	no	5	yes	g2	5	low lactose	4
77	525990	M	60	11.6	N	some	6.5	no	g2	3	normal	5
78	526000	F	27.6	10.9	P	no	4.5	yes	g1	4	low lactose	3
79	528318	F	12	9.8	P	some	6	no	n	6	normal	5
80	528501	F	12	7.6	P	some	7	no	n	6	low lactose	4
81	528853	F	1	7.9	P	some	6.5	no	n	8	normal	4
82	529319	F	9	9.3	P	no	6.5	no	n	7	normal	5
83	531403	F	8	9.4	P	no	4	yes	g2	6	low lactose	4
84	535223	M	8	8.9	P	some	6.5	no	n	4	normal	4
85	535841	M	9	7	P	no	6.5	no	n	5	normal	5
86	537537	F	18	11.1	N	no	4	yes	g1	7	normal	3
87	537578	M	15	10.4	P	some	4.5	yes	N	8	normal	3
88	538201	F	15.6	9.8	P	no	6	no	n	5	normal	5
89	538605	M	15.6	9.6	P	no	4.5	yes	g1	6	low lactose	3
90	539336	M	10	11.1	N	no	6	no	g1	4	low lactose	3
91	539826	M	19.2	8.3	P	no	6	no	n	3	normal	4
92	540305	M	10	8.5	P	no	6.5	no	g1	5	normal	4
93	540367	M	9	5.1	P	some	4.5	yes	g2	6	low lactose	4
94	540864	F	19.2	12	N	some	6.5	no	g1	7	normal	4
95	541266	M	10	9.1	P	no	6.5	no	g2	6	normal	4
96	541583	M	12	7.7	P	some	6.5	no	n	6	low lactose	3
97	541704	F	12	11.8	N	some	6	no	n	4	normal	4
98	542228	M	24	12.2	N	some	4.5	yes	g4	5	low lactose	4
99	543569	M	8	8.4	P	some	6.5	no	n	5	normal	4
100	545247	F	36	11.7	N	no	6.5	no	g2	6	normal	4
101	545265	F	16	8.8	P	severe	6.5	no	n	6	low lactose	4
102	545267	F	10	10	P	no	6.5	no	n	6	low lactose	4
103	547490	F	16.8	7.8	P	no	6.5	no	g1	6	low lactose	4
104	547949	M	10	12.1	N	some	4	yes	N	5	low lactose	3
105	548345	M	22	9.9	P	no	6	no	n	4	normal	3
106	548354	M	5	11.2	N	no	6	no	n	4	normal	4
107	548398	M	11	6.4	P	no	4	yes	N	4	low lactose	4
108	550418	F	3	11.6	N	some	6.5	no	n	4	normal	2
109	550864	M	11	7.6	P	some	5	yes	n	5	normal	5
110	551835	F	11	7	P	some	4	yes	g1	4	low lactose	4

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111	552561	M	14.4	6.9	P	no	6	no	n	6	normal	4
112	552636	F	12	10	P	no	4	yes	g3	6	normal	4
125	552926	M	8	9.6	P	no	6.5	no	n	6	normal	4
129	553929	M	7	9.3	P	some	6.5	no	g1	5	normal	4
134	554639	F	36	11.7	N	no	6.5	no	g3	4	normal	4
135	555399	M	48	11.6	N	some	6.5	no	n	6	normal	4
136	556768	M	18	9	P	no	6	no	g1	7	normal	4
127	558595	F	6	11.2	N	some	6.5	no	n	5	normal	4
130	561534	M	19	6.5	P	severe	5	yes	g1	6	normal	4
138	564492	M	48	12.3	N	some	6	no	n	6	low lactose	5
137	565278	M	8	11.6	N	no	4	yes	g3	4	low lactose	5
139	569678	F	10	9.5	P	some	6.5	no	n	7	low lactose	4
131	574477	M	24	6.7	P	severe	5	yes	g2	7	normal	4
140	577457	F	7	10.8	N	some	4	yes	N	5	low lactose	4
132	579436	F	36	9.7	P	severe	5	yes	g3	4	low lactose	4
133	582126	F	12	9	P	no	6.5	no	n	6	low lactose	4
128	584673	F	19	9.9	P	some	4	yes	g1	6	low lactose	5
113	588132	F	3.5	8.3	P	no	6.5	no	g1	5	normal	4
142	594747	F	2	11.8	N	no	4.5	yes	g4	5	low lactose	5
114	600694	M	8	11	N	no	6	no	g1	5	low lactose	4
115	601126	M	14.4	9.9	P	no	6.5	no	g1	4	normal	4
141	602500	F	4	13.4	N	no	6.5	no	n	5	normal	4
116	602501	F	60	12.7	N	some	6	yes	g1	5	normal	4
117	602509	F	36	8.4	P	no	6.5	no	n	3	normal	4
118	604194	F	6	9.1	P	some	6	no	n	6	normal	4
119	605471	F	6	11	N	some	6.5	no	n	5	normal	4
120	608959	M	51.6	9.4	P	some	6	no	n	5	normal	4
121	610700	F	24	10.2	P	severe	5	yes	g1	6	low lactose	4
122	612420	F	7	10.4	P	no	4	yes	g2	6	low lactose	4
123	612752	M	13.2	7.8	P	no	6	no	n	5	normal	4
124	619544	M	12	9.4	P	no	6	no	n	6	normal	4
143	630907	F	7	10.6	N	no	6.5	no	g1	7	low lactose	4
144	636435	F	5	11.2	N	no	6.5	no	g1	5	normal	4
145	638288	M	12	7.8	P	some	6.5	no	n	7	normal	4
146	640465	M	11	7.2	P	no	6.5	yes	n	4	normal	4
147	640997	F	7	11.6	N	some	5	yes	N	7	normal	2
148	643158	M	3	9.2	P	no	6	no	g1	7	low lactose	4

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149	645524	F	4	7.9	P	severe	6	no	n	6	normal	4
150	647251	M	18	10.4	P	no	6	no	n	5	normal	4