

Assessment of Chronic Diarrhea in Early Infancy in Tehran Tertiary Care Center; Tehran-Iran

Farzaneh Motamed¹, *Naheid Kazemi², Raheleh Nabavizadeh²

¹ Associate Professor, Department of Pediatric Gastroenterology, Children's Medical Center, Pediatric Center of Excellence, Tehran University of Medical Science, Tehran, Iran.

² Resident of Pediatrics, Children's Medical Center, Pediatric Center of Excellence, Tehran University of Medical Science, Tehran, Iran.

Abstract

Introduction

Chronic diarrhea of infancy is a heterogeneous syndrome that includes several diseases with different etiologies. The aim of this study was to investigate chronic diarrhea, its etiologies, clinical features and outcomes in infancy.

Materials and Methods

Retrospective study investigating infants hospitalized in the Gastroenterology Department of Tehran Tertiary Care Center. The main demographic data, etiology, characteristics of diarrhea, and outcome were evaluated. Data were analyzed by SPSS software, version 16.

Results

In this study, 63.9% of cases were female and 36.1% were male. 24 cases (66.7%) had osmotic diarrhea and 11 (30.6%) had secretory diarrhea. In this study there was no significant statistical correlation between type of diarrhea and sex, gestational age, severity of dehydration, birth weight and nutrition. The majority of patients with osmotic (58.3%) and secretory diarrhea (63.6%), had weight percentile below 3%, which showed a significant statistical difference ($P < 0.03$). Etiologies found in newborns included: food allergy (41.7%), glucose/ galactose malabsorption (19.4%), post gastroenteritis malabsorption (11.1%), sepsis (8.3%), autoimmune enteropathy (5.6%), galactosemia (2.8%), pseudo membranous colitis (2.8%), cystic fibrosis (2.8%), intestinal malrotation (2.8%), congenital chloride diarrhea (2.8%). A total of 4 out of 36 patients (11.1%) had early onset of diarrhea. Intestinal biopsy was done in 7 (20%) cases.

Conclusion

Chronic diarrhea in infancy has different etiologies and outcomes. According to high prevalence of allergy in this study, more attention needs to be paid to this issue. On the other side, food allergy was more common in nonexclusive breast fed infants, which shows breast feeding has a protective effect against neonatal diarrhea.

Key Words: Allergy, Chronic diarrhea, Etiology, Infancy.

*Corresponding Author:

Naheid Kazemi, MD, Resident of Pediatrics, Children's Medical Center, Pediatric Center of Excellence, Tehran University of Medical Science, Tehran, Iran.

Email: naheidkazemi@yahoo.com

Received date: Feb 8, 2015 ; Accepted date: Feb 22, 2015

Introduction

Diarrhea in infants is defined as the passage of three or more abnormally loose or watery stools per day(1). Diarrhea is culprit for 18% of deaths in children age group which is estimated as 1.5 million deaths per year in the world and 5 million deaths per year in the developing countries. The most common cause of acute diarrhea in all children is Rotaviruses. Chronic diarrhea, defined as diarrhea that lasts for more than two weeks, in developing countries is mostly due to intestinal infection(2). The risk of serious complications from chronic diarrhea depends on the cause of the diarrhea, age and general health status of the patient(3).

The infants have increased susceptibility to complications related to diarrhea due to immaturity of fluid homeostasis and immunologic responses(4). The list of diseases and mechanisms responsible for diarrhea in infants is large and higher compared to older children and different approach is required for evaluating infants and young children with chronic diarrhea. The most common cause of chronic diarrhea in infancy include: inclusion micro villi disease, food allergy, hirschsprung's disease, malrotation, lymphangiectasia, short bowel syndrome (2).

We believe all these steps should be performed as a result of tight collaboration between the neonatologist, pediatric gastroenterologist, immunologist, geneticist, and nutritionist(5). In the vast majority of cases appropriate therapy must be started immediately to prevent dehydration and long term, and sometimes life-threatening, complications(6). We performed this study to investigate chronic diarrhea, its etiologies, clinical features and outcomes in infancy.

Materials and Methods

Retrospective study investigating infants hospitalized in the Gastroenterology Department of Tehran Tertiary Care Center from December 2010 to December 2012. Thirty six(36) infants under 3 months age, admitted to tertiary care center complaining of chronic diarrhea, were entered the study. Inclusion criteria were: 1. Infants below 3 months. 2. Diarrhea, defined on the basis of increased frequency and watery consistency of stools with dehydration according to definition employed in pediatric gastroenterology(7). 3. Chronic diarrhea defined if duration of diarrhea was more than 14 days(1, 2).

Data was collected from patient's medical files and was recorded in a specific questionnaire form. This study was approved by the Ethics Committee of our institution (Tehran University of Medical Sciences). Demographic data, laboratory findings including: stool exam, and culture, characteristics of diarrhea including severity of dehydration, osmotic or secretory diarrhea and result of small or large biopsy if had done, were elicited. Osmotic or secretory diarrhea is defined by measuring stool osmotic gap that osmotic diarrhea has osmotic gap over 50 and secretory diarrhea has below 50(6).

Possible correlation between variables including: gender, gestational age, birth weight, weight percentile, severity of dehydration with etiology and type of diarrhea, were investigated by statistical analysis. data were analyzed in SPSS-16 and the $P < 0.05$ was considered statistically significant

Results

The medical files of admitted infants with chronic diarrhea during three years, were reviewed and 36 cases were found to be suitable to enter the study. Median age of patients was 75 days (between 39-90 days) and median birth weight of patients was 4,408 grams.

Different variables and frequencies in the study population are shown in (Table.1).

Table1: Different variables and their frequencies in the study population

Variables	Frequency	Percent
Gender	Female	23 63.9
	Male	13 36.1
Type of diarrhea	Osmotic	24 66.7
	Secretory	11 30.6
	No data	1 2.8
Nutrition	Breast milk	9 25
	Formula	14 38.9
	Both	12 33.3
	No data	1 2.8
Weight percentile at admission	<3%	21 58.3
	3-25%	8 22.2
	25-50%	4 11.1
	>50%	3 8.3
Birth weight	<2500 gr	5 13.9
	>2500 gr	29 80.6
	2500 gr	2 5.6
Gestational age	<37w	5 13.9
	>37w	27 75
	No data	4 11.1
Dehydration severity	5 % low	20 55.6
	Medium 10%	13 36.1
	% Severe 15	2 5.6

Diagnosis of food allergy was reported in 15 cases (41.7%) which, diagnosis was confirmed by symptomatic improvement to extensively hydrolyzed formula (Aptamil pepti; Danone, Nutricia, Schiphol, Netherland) or the diet without cow's milk protein in lactating mother. Glucose /galactose malabsorption reported in 7 patients (19.4%) that confirmed by clinical manifestations and laboratory tests: stool low PH, positive stool reducing

substance, serum acidosis and improvement on glucose/galactose free formula (Galactomin 19; SHS company, Germany). Post gastroenteritis malabsorption was found in 4 cases (11.1%) which diagnosed with clinical manifestation and response to lactose free formula(Isomil; Abbott laboratories, Abbott park, USA).

Three cases (8.3%) received diagnosis of sepsis that 2 of them had positive blood culture with pseudomonas spp. Two patients (5.6%) presented with autoimmune enteropathy based on duodenum and colon biopsy and response to corticosteroid treatment. Galactosemia was reported in one case (2.8%), which was diagnosed by serum glucose chromatography, difference of oxidase glucose and Benedict test that confirmed by Galactose-1-Phosphate Uridyltransferase (GALT) test and response to galactose free formula (Isomil formula; Abbott, Abbott laboratories, Abbott park, USA). One case (2.8%) with history of hirschsprung's disease that was admitted with complaint of chronic diarrhea had pseudomembranous colitis in colon Biopsy. For one case (2.8%) with chronic steatorrhea and sweat chloride>60meq/L final diagnosis of cystic fibrosis was achieved.

Intestinal malrotation reported in one case (2.8%).The diagnosis was confirmed with radiography. One case (2.8%) had congenital chloride diarrhea on the base of clinical manifestation, history of ployhydramnios and laboratory results including: secretory diarrhea, stool chloride more than 100 meq/lit and hypochloremic metabolic alkalosis.

Four patients (11.11%) had early onset of diarrhea: one with congenital chloride diarrhea, one with glucose/galactose malabsorption and one with cystic fibrosis presented in first day after birth and the other, autoimmune enteropathy that presented second day after birth.

In this study, food allergy was the most common etiology (41/7%) and cystic fibrosis, chloride diarrhea, pseudomembranous colitis, malrotation and galactosemia had the lowest prevalence(2.8%).

In this study it was no statistical difference between type of diarrhea and gender, gestational age, severity of dehydration, birth weight and nutrition. Results showed 58.3% of cases with osmotic diarrhea and 63.6% with secretory diarrhea had weight percentile at admission below 3% and there was statistical difference between type of diarrhea and weight percentile at admission ($p < 0.03$). In infants with food allergy, 33.3% had more than 5 White Blood Cell (WBC), 13.9% had less than 5 WBC and 50% no WBC in stool exam and in this group 13.9% of infants had more than 5 Red Blood Cell (RBC), 19.4% had less than 5 RBC and 63.9% no RBC in stool exam. Prevalence of food allergy in non-exclusive breastfed infants was 3.5 times greater than exclusive breast fed infants, but the difference was not statistically significant ($P = 0.243$).

Risk of allergy and sepsis were higher in preterm infants compared with term infants, but the difference was not statistically significant ($P = 0.4$). 60% of infants with gestational age below 37 weeks, had 10% dehydration but 62.96% of infants with gestational age over 37 weeks had 5% dehydration, which was a significant statistical difference between gestational age and severity of dehydration ($P = 0.044$).

Intestinal biopsy was done in 7 (20%) of patients. One case had diagnosis of glucose/ galactose malabsorption with normal biopsy results. One case had sepsis in which biopsy had done to rule out other diagnoses, one had changes suggestive of auto immune enteropathy in biopsy and four cases had pathological changes, suggesting allergy. Positive stool culture was found in none of the cases. A total

Four (11.1%) deaths were reported among 36 patients: one due to cystic fibrosis, two due to sepsis and one in glucose/ galactose malabsorption patient.

Discussion

The results of study showed that in this particular age group; diarrhea is a relatively uncommon but critical condition underlying broad spectrum of diseases. Several diseases responsible for infantile diarrhea and number of etiologies are higher compared to older patients. The most common etiology in this study was food allergy (41.7%).

In a retrospective study by Passariello et al. evaluating infants hospitalized in Neonatal Intensive Care Unit (NICU) in Italy, from 5801 infants in NICU, 39 cases had diarrhea, which was acute in 92.3% and chronic in 7.7% of cases. The most common cause of diarrhea in these infants was food allergy (20.5%) and hirschsprung's disease, hospital diarrhea, metabolic errors, and cystic fibrosis had the lowest incidence. (2.5%)(5). This implies the variation in different studies are.

Recently, international study of Asthma and Allergy in childhood reported an increase in allergic disease prevalence in the younger pediatric age group (8). In this study, food allergy was the most common cause of diarrhea in non exclusive breastfed infants. It is presumed that breast feeding has an allergy preventive effect compared with cows' milk formula feeding, but the extent of the preventive effect remains controversial (9).

In a recent finnish study of non-selected newborns followed up to 17 years of age, breast feeding was associated with lower rates of eczema and food allergy at 1 and 3 years, as well as a lower score of respiratory allergy up to 17 years of age, compared with cows' milk formula fed individuals (10). It is presumed that exclusive breast feeding or combination

with avoidance of supplementary foods, in high risk infants with atopic disease in at least one first degree relative, has preventive effect on allergy in infants less than 4 months (3).

in the study by Victora in Brazil, infants who received powdered milk or cow's milk in addition to breast milk, were at 4.2 times higher risk of death from diarrhea compared with infants who did not receive artificial milk; while the risk for infants who didn't receive any breast milk was 14.2 times higher (11); but in this study there was no correlation between nutrition and mortality rate. In this study 60% of infants with chronic diarrhea has weight percentile under 3% that demonstrates that malnutrition prolongs the duration of diarrhea and Increases its mortality rate.

The interaction between malnutrition and diarrheal disease is bi-directional. Increases in immunization coverage, better health care access, improvements in water and electrolyte replacement, and other socioeconomic changes affect both mortality from diarrhea, and childhood nutrition status (12). The majority of patients with osmotic (58.3%) and secretory diarrhea (63.6%), had weight percentile below 3%; which shows malnutrition as a risk factor for both types of diarrhea. In a study done by Nichols et al. on infants with chronic diarrhea and malnutrition, maltase and lactase enzyme wasn't found in intestinal villi, which caused osmotic diarrhea (13). Our study demonstrates that infants with gestational age below 37 weeks had more severe dehydration than infants over 37 weeks of gestation (20% vs. 3/8%, $p < 0.04$); which can be explained by prematurity of hemodynamic regulatory systems in preterm infants.

In this study the most common cause of death 2(50%) was sepsis that both of them had positive blood culture. In a study by Chisti on infants hospitalized due to diarrhea in Bangladesh, the case-fatality

rate was significantly higher among bacteremic infants compared with those without bacteremia. (33% vs. 6%, $p < .01$) (14). Bacteremia appears to be an important link between diarrheal illness and death. In children with diarrhea who are suspected of being septic, early implementation of anti-microbial therapy against the broad spectrum of pathogens appears to be indicate(15) .

Conclusion

This study demonstrates that chronic diarrhea of infancy, includes several diseases with different etiologies. Early diagnosis and timely treatment are both crucial in prognosis of infantile diarrhea. This study demonstrated that food allergy is the most common etiology that the suspicion importance of food allergy in infants presenting with diarrhea has highlighted. The further clinical and epidemiologic studies, are needed for improving diagnostic approach for infantile diarrhea.

Acknowledgments

We thank of colleagues Department of Pediatric Gastroenterology of Children Medical Center (Tehran University of Medical Sciences) for clinical data collection.

Conflict of interests: None.

References

1. Farthing M, Salam MA, Lindberg G, Dite P, Khalif I, Salazar-Lindo E, et al. Acute diarrhea in adults and children: a global perspective J Clin Gastroenterol 2013;47(1):12-20.
2. Kliegman MR, Stanton BF, Schor NF, Geme III J, Behrman RE. Chronic Diarrhea:Nelson text book of pediatrics. 19thed, editor. Pennsylvania: Saunders; 2011. 1339-46 p.
3. Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated

- from studies published between 1992 and 2000. *Bull World Health Organ* 2003;81(3):197-204.
4. Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, et al. Trends in neonatal morbidity and mortality for very low birthweight infants. *Am J Obstet Gynecol* 2007;196(2):147.
 5. Passariello A, Terrin G, Elisabetta M Mario De Curtis B, Paludetto R, Berni Canani R. Diarrhea in neonatal intensive care unit. *World J Gastroenterol* 2010 June 7; 16(21): 2664-68.
 6. Terrin G, Tomaiuolo R, Passariello A, Elce A, Amato F, Di Costanzo M, et al. Congenital diarrheal disorders: an updated diagnostic approach. *Int J Mol Sci* 2012;13(4):4168-85.
 7. Baqui AH, Black RE, Yunus M, Hoque AR, Chowdhury HR, Sack RB et al. Methodological issues in diarrhoeal diseases epidemiology: definition of diarrhoeal episodes. *Int J Epidemiol* 1991;20(4):1057-63.
 8. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;368(9537):733-43.
 9. Kerner JA Jr. Use of infant formulas in preventing or postponing atopic manifestations. *J Pediatr Gastroenterol Nutr* 1997;24(4):442-6.
 10. Saarinen VM, Kajosaari M. Breast feeding as prophylaxis against atopic disease: prospective follow-up until 17 years old. *Lancet* 1995; 346(8982):1065-9.
 11. Victora CG, Smith PG, Vaughan JP, Nobre LC, Lombardi C, Teixeira AM, et al. Infant feeding and deaths due to diarrhea. A case-control study. *Am J Epidemiol* 1989;129(5):1032-41.
 12. Høst A, Koletzko B, Dreborg S, Muraro A, Wahn U, Aggett P, et al. Dietary products used in infants for treatment and prevention of food allergy. *Arch Dis Child* 1999;81(1):80-4.
 13. Nichols BL, Carrazza F, Nichols VN, Putman M, Johnston P, Rodrigues M, et al. Mosaic expression of brush-border enzymes in infants with chronic diarrhea and malnutrition. *J Pediatr Gastroenterol Nutr* 1992;14(4):371-9.
 14. Chisti MJ, Saha S, Roy CN, Salam MA. Predictors of bacteremia in infants with diarrhea and systemic inflammatory response syndrome attending an urban diarrheal treatment center in a developing country. *Pediatr Crit Care Med* 2010;11(1):92-7.
 15. Struelens MJ, Bennish ML, Mondal G, Wojtyniak BJ. Bacteremia during diarrhea: incidence, etiology, risk factors, and outcome. *Am J Epidemiol* 1991;133(5):451-9.