Persistent Diarrhea: 15 Years Experience at a Tertiary Care Hospital

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Objective: *To determine the risk factors, causative enteric pathogens, final diagnosis and treatment outcomes of persistent diarrhea in children.*

Material and Method: *A retrospective study of the patients who had diarrheal symptoms for at least 14 days diagnosed as persistent diarrhea (PD) and admitted at QSNICH during January 1997 and December 2011. Demographic data, risk factors, causative enteric pathogens, management and outcome were reviewed.*

Results: *The review included 79 PD patients. Excluded were patients who were HIV seropositive, had GI anomalies and/or other underlying immune deficiencies. The demographic data showed mean age 11.42 months and male:female 56:23 (2.43:1). Feeding with infant formula before admission was 43% compared to exclusive breastfeeding that was only 10%. Normal nutritional status was found in half of the cases (52.1%) and protein energy malnutrition (PEM) was present in 42.3%. Stool for enteropathogens was positive only in 49.4% and the most common being mixed enteropathogens.*

Secondary lactase deficiency was the cause of PD in half (50%) of the patients. Management consisted of rehydration, intravenous antibiotics 53%, and other adjuvant therapies such as cholestyramine, zinc and probiotics. Along with rehydration, all patients received aggressive nutritional management upon admission. The diarrhea subsided in less than 7 days in about 70% of the patients.

Conclusion: *The present study supports that important risk factors for PD are very young age group (especially under 1 year old), lack of breastfeeding and malnutrition. Enteropathogens were found in only about half of the patients and the most common cause of PD was secondary lactase deficiency. Most of the diarrhea subsided in less than 7 days of admission with proper management and aggressive nutrition upon admission.*

Keywords: *Persistent diarrhea, Malnutrition, Nutritional management*

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Persistent diarrhea is defined as an episode of diarrhea of presumed infectious etiology which starts acutely but lasts for more than 14 days after excluding chronic or recurrent diarrheal disorders such as tropical sprue, gluten sensitive enteropathy or hereditary disorders[1]. Risk factors include very young age, lack of breastfeeding, previous infection, prior usage of antibiotics, prolonged episodes of acute diarrhea and micronutrient deficiencies[2,3]. Malnutrition can act as a risk factor and/or an outcome of persistent diarrhea.

Queen Sirikit National Institute of Child Health (QSNICH) is one of the tertiary care centers for pediatric patients in Thailand. Total diarrheal cases ranged from 3.6 to 5.9% of total outpatient cases. Cases with persistent and chronic diarrhea ranged from 0.35 to 1.24% of total diarrheal admissions.

The impact of persistent diarrhea on physical and mental health including brain growth is generally accepted. The economic burden from PD is also a serious problem in developing and underdeveloped countries. Hospital cost of acute diarrhea in QSNICH is about 1,500-2,500 Thai baht (THB), while that for PD is much higher (10,000-20,000 THB). This is mainly due to longer hospital stay of 1-2 weeks in PD compared to 3 days for those with acute diarrhea. Loss of parental income and/or caretaker salary for taking care of the child in hospital adds to the economic burden. Stepwise nutritional management (both enteral and parenteral) including complications from infection (catheter and

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non-catheter related sepsis) was the most common complication responsible for prolonged hospital stay in this study.

The target of this review was on finding the possible risk factors for PD and looking at the treatment and outcomes in these patients.

Material and Method

This was a retrospective study of the patients who had diarrhea for more than 14 days, diagnosed as PD and were admitted at QSNICH during January 1997 to December 2011. Exclusion criteria were HIV seropositive, GI anomalies and/or underlying immunodeficiency. Demographic data, risk factors, causative enteric pathogens, management and outcome were reviewed.

Results

The review included 79 patients who had diarrhea for at least 14 days. About 90% of total cases were referred from district and provincial hospitals. Excluded were patients who were HIV seropositive, had GI anomalies and/or other underlying immune deficiencies. The demographic data showed a mean age of 11.42 months (ranged 1 month-9.5 years) (Fig. 1) and male:female 56:23 (2.43:1). Feeding with infant formula before admission was 43% compared to exclusive breast-feeding which was only 10% (Fig. 2). Normal nutritional status was found in half of the cases (52.1%) and protein energy malnutrition (PEM) was present in 42.3% (Fig. 3). Stool for enteropathogens was positive in only 49.4% and the most common finding was mixed enteropathogens (Fig. 4). Rotavirus was detected in 10 out of 79 cases of which 2 cases were also associated with campylobacter jejuni and one with aeromonas.

Secondary lactase deficiency was the major cause (50%) of PD followed by secondary cow's milk protein allergy in 31.3%, post infectious enteritis 11.3%, fat malabsorption 2.5%, bile salt diarrhea 2.5%, and monosaccharide intolerance 1% (Table 1). Management consisted of rehydration, intravenous antibiotics 53%,

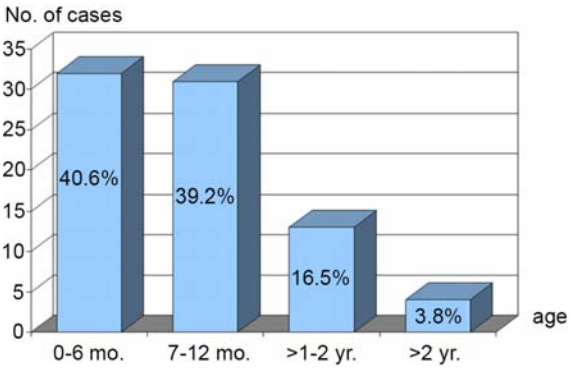

Fig. 1 Age at presentation.

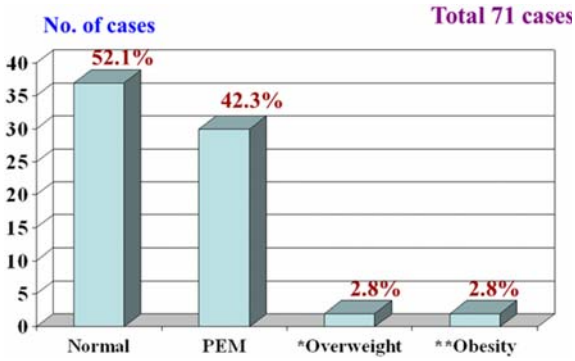

Fig. 3 Nutritional status.

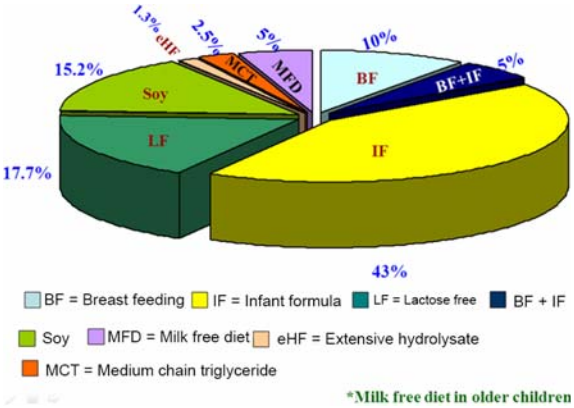

Fig. 2 Formula before admission.

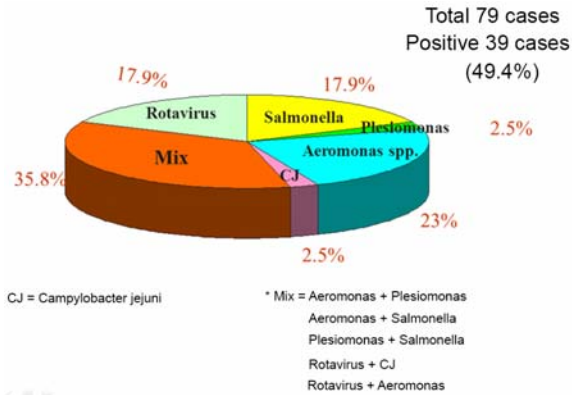

Fig. 4 Enteropathogens.

and other adjuvant therapies such as cholestyramine, zinc and probiotics (Fig. 5). Along with rehydration, all patients received aggressive nutritional management upon admission. Enteral feeding was the preferred route of feeding, so breast milk and many special formulas were required for nutritional management (Fig. 6). For the growing child (over 6 months of age) chicken rice porridge (hospital formula) was used as complementary food. The diarrhea subsided in less than 7 days in about 70% of the patients (Fig. 7). 8.9% had length of stay of >30 days. The reasons for prolonged hospitalization were septicemia (including catheter related sepsis), severe PEM and malabsorption. The longest duration of hospitalization in a single patient was 90 days.

Discussion

Most of the acute diarrheal episodes subside within 7 days. Prolonged diarrhea for more than 7 days is considered one of the risk factors for PD[2]. Infants with prolonged diarrhea were twice as likely to develop PD in later childhood compared with infants with acute diarrhea[3]. According to WHO 1985 data, 3-20% of episodes of acute diarrhea become persistent[4] and 90% of PD occurs in infants below 1 year of age[5]. International study from India, Bangladesh, Brazil & Senegal showed diarrhea related mortality from acute diarrhea ranged 25-46% while that from persistent diarrhea ranged from 23-62%[6]. In this study, 80% of PD were under 1 year old which implies that the younger age group is more prone to PD compared to the older age group. Malnutrition was found in nearly half of the PD patients in this study (42.3%) supporting the importance of underlying nutritional status in these patients. Protein energy malnutrition leads to impairment of body immunity by decreasing T-lymphocyte number, serum complement, specific antibody production and impairment of delayed hypersensitivity[7]. Exclusive breastfeeding was found in only 10% of total patients. The low percentage of breastfeeding in PD patients may indicate the lack of its protective benefit against antimicrobial agents causing PD such as lactoferrin, lysozyme, secretory IgA, which are usually present in human milk[8,9].

Prior antibiotics use has been significantly associated with PD, which implies that unnecessary antibiotics prescribed for acute diarrhea may prolong the episode making it "persistent"[10]. Most of our PD cases had received prior intravenous antibiotics from

Table 1. Diagnosis

Condition	Cases (79)	%
2ry lactase deficiency	40	50
Cow's protein senitive enteropathy	25	31.3
Post infectious enteritis	9	11.3
Monosaccharide intolcrance	1	1.3
Bile salt diarrhea	2	2.5
Fat malabsorption	2	2.5

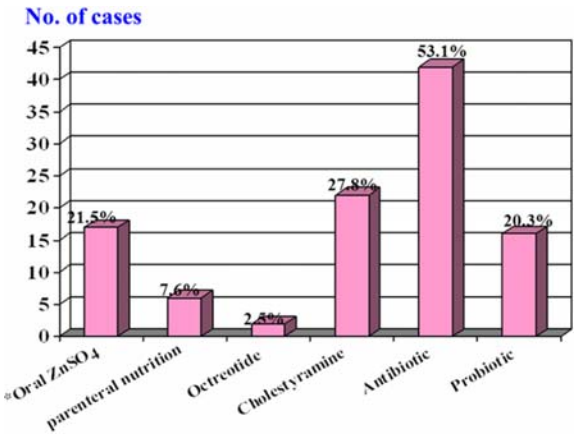

Fig. 5 Treatment.

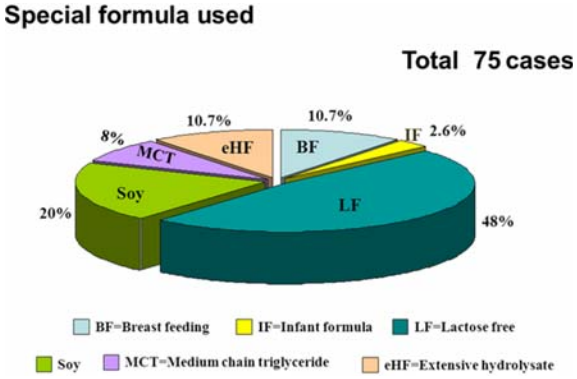

Fig. 6 Treatment.

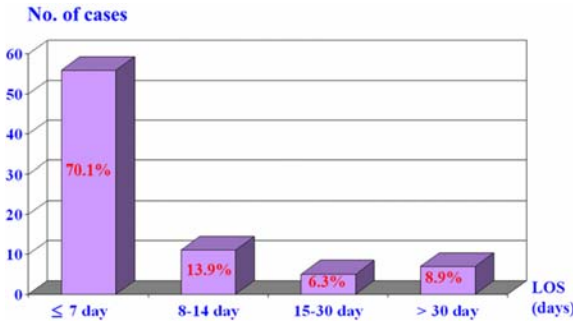

Fig. 7 Length of stay.

the referral hospital for treatment of PD for various reasons. Therefore, we could not clearly demonstrate this risk factor as the cause of PD in this study. Micronutrient deficiency can cause transient immune deficiency, which could be a risk factor for PD[2]. Zinc deficiency may result in prolongation of mucosal injury and delayed intestinal repair mechanisms[11]. The importance of zinc deficiency in protein energy malnutrition (PEM) can be demonstrated in several studies[9]. In the present study, oral zinc was given in 21.5% and added in parenteral nutrition in 7.6% of PD patients. However, zinc level were not studied in the present study.

Stool for enteropathogens was positive in only 49.4% in this study and most of them were mixed enteropathogens. There is no evidence that any specific pathogen is associated with PD in children under the age of six years in low and middle income countries[12]. In the present study intravenous antibiotics were prescribed in 53.7% of total cases, mainly in those patients with severe diarrhea and septicemia (catheter and non-catheter related sepsis) and severe PEM. Secondary lactase deficiency was the most common cause of PD in this study (50%). Aggressive nutritional management is the most important treatment for PD especially in the form of enteral feeding when it is tolerated[13]. Encouraging breastfeeding was the first option for enteral feeding. However, since 90% of PD cases referred from other hospital had been stopped from breastfeeding, a relactation trial was met with limited success only. Special formulas were prescribed for most of the patients including lactose-free, soy, medium chain triglyceride (MCT) or extensive hydrolysate formula (eHF) depending on the type of problems they had. The unpalatable taste and expensive costs of eHF formula are beyond the reach of health resources in developing countries[14]. The challenge is to make inexpensive, home-available and culturally acceptable ingredients in community settings[15]. In the present study, a lactose-free formula was used with success for treatment of PD patients in nearly half of the cases (48%) going along with the diagnosis of secondary lactase deficiency. About one-third of PD patients in the present study required changing formula to soy protein (20%) and eHF (10.7%). Nasogastric drip feedings is preferred to bottle feeding in order to avoid volume load and giving better absorption from slow and constant rate of feeding[16]. This method of feeding was used in the present study for some patients, who were severely malnourished and/or had voluminous watery diarrhea. Parenteral nutrition is essential for severe PEM and/or oral feeding intolerance. In the present study, parenteral nutrition was given to 7.6% of the cases and cholestyramine was used in 27.8% for the treatment of bile salt diarrhea. Probiotics was used as adjunctive therapy in 13.9% of the cases. Although it seems to give some benefit for PD patients, the results were inconclusive. Cochrane's review concluded that there is insufficient evidence to recommend the use of probiotics as adjunctive therapy for PD at this time[17]. Short hospital stays (less than 7 days) in this study were observed in 70% of PD patients and may have been the result of proper and stepwise nutritional management.

Conclusion

The present study included 79 PD patients in a 15-year period. Although PD is presumed to be infectious etiology, the result of this review could not specify any enteropathogen as the cause of PD. No routine antimicrobial use is recommended for treatment of PD. Aggressive, stepwise nutritional management is the most important treatment for PD.

Acknowledgement

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Potential conflicts of interest

None.

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โรคอุจจาระร่วงยืดเยื้อ: ประสบการณ์ 15 ปี ที่ โรงพยาบาลตติยภูมิ

นิยะดา วิทยาศัย, ศิริลักษณ์ เจนนุวัตร

วัตถุประสงค์: *เพื่อศึกษาปัจจัยเสี่ยงเชื้อก่อโรคในลำไส้ การวินิจฉัยสรุปสาเหตุและผลการรักษาในเด็กที่มีปัญหาอุจจาระร่วงยืดเยื้อ*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังในผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่าเป็นโรคอุจจาระร่วงยืดเยื้อตั้งแต่ เดือนมกราคม พ.ศ. 2539 ถึง เดือนธันวาคม พ.ศ. 2554 ได้ทำการศึกษาเก็บข้อมูลผู้ป่วย ปัจจัยเสี่ยง เชื้อก่อโรคในลำไส้ การรักษาและผลการรักษา*

ผลการศึกษา: *จำนวนผู้ป่วยที่มีอาการอุจจาระร่วงอย่างน้อย 14 วันมีจำนวนทั้งสิ้น 79 ราย การศึกษานี้ไม่รวมผู้ป่วย ที่มีผลเลือด HIV เป็นบวกหรือมีความผิดปกติทางกายวิภาคของระบบทางเดินอาหารและ/หรือมีปัญหาภูมิต้านทาน บกพร่อง ข้อมูลผู้ป่วยพบว่าอายุเฉลี่ย 11.42 เดือน อัตราส่วน ชาย:หญิง เท่ากับ 56:23 (2.43:1) ผู้ป่วยได้รับนมผสมสูตรทารกก่อนเข้ารับการรักษาในโรงพยาบาลร้อยละ 43 เมื่อเทียบกับผู้ป่วยที่ได้รับนมแม่อย่างเดียวมีเพียงร้อยละ 10 ผู้ป่วยมีภาวะโภชนาการปกติประมาณครึ่งหนึ่ง (ร้อยละ 52.1) และภาวะทุโภชนาการ (PEM) ร้อยละ 42.3 เชื้อก่อโรคในลำไส้จากอุจจาระพบเพียงร้อยละ 49.4 และส่วนใหญ่พบเป็นเชื้อก่อโรคในลำไส้หลายตัวรวมกัน*

ปัญหาการขาดน้ำย่อยแลคเตสทุติยภูมิเป็นสาเหตุของโรคอุจจาระร่วงยืดเยื้อประมาณครึ่งหนึ่งของจำนวนผู้ป่วยทั้งหมด (ร้อยละ 50) การรักษาประกอบด้วยการแก้ไขภาวะขาดน้ำ ยาปฏิชีวนะ (ฉีดเข้าหลอดเลือดดำ) ร้อยละ 53 และยาที่ช่วยให้อาการหรือลักษณะอุจจาระดีขึ้นเช่น โคเลสไทรามีน, สังกะสีและโพรไบโอติค นอกเหนือจากการแก้ไขภาวะขาดน้ำ ผู้ป่วยทั้งหมดจะได้รับการดูแลโภชนบำบัดเป็นพิเศษตั้งแต่รับไว้ในโรงพยาบาล ผู้ป่วยประมาณร้อยละ 70 หายจากภาวะอุจจาระร่วงในเวลาไม่เกิน 7 วัน

สรุป: *ข้อมูลจากการศึกษานี้สนับสนุนว่าปัจจัยเสี่ยงที่สำคัญของโรคอุจจาระร่วงยืดเยื้อคือ กลุ่มเด็กเล็กโดยเฉพาะ อายุน้อยกว่า 1 ปี ทารกที่ไม่ได้รับนมแม่และภาวะทุโภชนาการ เชื้อก่อโรคจากลำไส้พบเพียงครึ่งหนึ่งของผู้ป่วยทั้งหมด สาเหตุของโรคอุจจาระร่วงยืดเยื้อที่พบมากที่สุดคือ ภาวะขาดน้ำย่อยแลคเตสทุติยภูมิ ผู้ป่วยอุจจาระร่วงยืดเยื้อส่วนใหญ่หายภายใน 7 วันหลังจากรับไว้รักษาในโรงพยาบาลซึ่งน่าจะเป็นผลจากการให้การรักษาและโภชนบำบัดที่เหมาะสมแก่ผู้ป่วยตั้งแต่เริ่มรับไว้ในโรงพยาบาล*