Outcome of Moderate to Severe Malnutrition Following Persistent Diarrhoea – A Hospital-Based Retrospective Study

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SUMMARY

We aimed to determine the outcome of nutritional intervention in children with moderate to severe malnutrition following persistent diarrhoea (PD), referred to a tertiary referral unit in Malaysia. Thirty-one (44%) of the 71 children (median age 19 months) with PD had moderate to severe malnutrition on admission. Fifty-three (75%) required dietary modification and 15 (21%) needed parenteral nutrition (PN, median duration 96 days). Of the 70 patients in whom remission of diarrhoea could be ascertained, 64 (91%) achieved remission. Three required home PN. At three months after discharge, there was a significant improvement in the mean weight-for-height z-score as compared to the original score at initial presentation (from -1.83 ± -1.77 to -0.80 ± -1.17; p < 0.001), although 12 (22%) of the 55 patients in whom nutritional status could be ascertained still had moderate to severe malnutrition. In conclusion, moderate to severe malnutrition was a common complication following PD resulting from diverse causes. With appropriate therapy, remission can be achieved in majority of patients, although a small number of patients needed home PN because of persistence of diarrhoea.

KEY WORDS:
Persistent diarrhoea, Malnutrition, Nutritional intervention

INTRODUCTION

Persistent diarrhoea (PD) is generally defined as diarrhoea lasting longer than 14 days' duration[1]. The aetiology of childhood PD is diverse, with multiple consecutive infections of the gastrointestinal tract leading to secondary lactose intolerance, cow milk protein intolerance (CMPI) and postenteritis syndrome as important causes of PD in developing countries[1-3]. In developed countries, however, the role of enteric infections has become less important over the last few decades[4,5]. Primary disorders of the gut, such as autoimmune enteropathy,[6] microvillous inclusion diseases (MvID),[7] and other enteropathies causing protracted diarrhoea, have become important causes of PD in childhood[5, 8, 9].

Irrespective its cause, malnutrition remains a serious complication of PD[10,11]. Recent studies have shown that in certain selected cases, home parenteral nutrition (PN) and intestinal transplant may be necessary and is feasible for children with intractable diarrhoea[6,12]. However, highly specialised clinical skill required for intestinal transplantation, and the resources necessary for home PN is generally unavailable in many developing countries. Enteral nutrition (EN) remains an important mode of nutritional intervention in malnutrition following PD.

We have previously observed that the causes of PD in Malaysian children were varied and the outcome was generally good[13]. The aims of the present study are to ascertain the severity of malnutrition and the outcome of nutritional intervention in children with moderate to severe malnutrition resulting from PD seen at a tertiary referral unit in Malaysia.

MATERIALS AND METHODS

The present study was conducted at the Department of Paediatrics, University of Malaya Medical Centre (UMMC), Kuala Lumpur, from January 1998 to December 2004.

Setting and design

It was a retrospective, hospital-based review, and was approved by the Ethical Committee of UMMC. UMMC is a tertiary referral centre for paediatrics in Malaysia but also serves the local population of Kuala Lumpur. Throughout the study period, experience on home PN was gradually developed in UMMC, but intestinal transplantation was not available in Malaysia.

Inclusion criteria

PD was defined as passage of loose or watery stool of at least three episodes per day for 14 days or more[1]. Patients aged younger than 12 years with PD admitted to the Department of Paediatrics, UMMC, over a 7-year period (January 1998 to December 2004) were included. Patients with diarrhoea due to an underlying malignancy or the effects of chemotherapy and those with incomplete medical records were excluded.

Case Selection

Hospital admission records of Department of Paediatrics, UMMC during the study period were screened for the following key words: PD, CMPI, lactose intolerance, gastrointestinal infection, chronic inflammatory bowel disease (CIBD), chronic liver problems and surgical gastrointestinal problems. In addition, patients with diarrhoeal diseases with hospitalisation ≥ 10 days during the study period were also screened. The clinical records of patients were retrieved from the Department of Medical Records and were reviewed.

This article was accepted: 11 June 2008
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Data Collections
The following data were collected: basic demography, presenting symptoms, feeding and family histories, pre-existing medical or surgical problems, clinical features on admission, nutritional status - anthropometry, degree of malnutrition (weight-for-height z-score, WHZ-score), signs of malnutrition (pallor, oedema, wasting of gluteal muscles, abdominal distension), and signs of underlying conditions. Relevant results of blood, stools, endoscopy (colonoscopy and upper gastrointestinal endoscopy), histology and imaging studies, where appropriate, were collected. Treatment rendered to patients, including types, route, duration and complications of EN and PN as well as other nutritional supplements given, were noted. Outcome data were obtained from the case notes of the patients and where appropriate, telephone interview of the main care provider.

Outcome measures
The final status of all patients at 1st of July, 2005, six months after the end of the enrollment period, was determined. Primary outcome (alive or death) and secondary outcome (durations of diarrhoea and hospitalization, weight, height and WHZ-score at three months after discharge) measures were noted. Clinical remission was defined as a diarrhoea-free period lasting longer than two days while on feeding entirely through the enteral route.

Diagnostic criteria
Investigations of PD described previously were used consistently throughout the study period[13]. The diagnostic criteria of secondary lactose intolerance,[14] monosaccharide intolerance,[15] and CMPI were similar to the established diagnostic criteria of these conditions, and were described previously[13, 16-18]. Patients who were allergic to cow's milk as well as other protein-containing foods, including eggs, soy and fish was labelled as multiple food proteins intolerance[19]. No enteric pathogens or other specific intestinal diseases were detected in patients with carbohydrate intolerance or CMPI. Post-enteritis syndrome was diagnosed when there was PD following an acute gastroenteritis with no isolated causative organism[2]. Patients with a causative organism isolated from stool were classified as enteric infection. Intractable diarrhoea of infancy was defined as PD despite protracted bowel rest, requiring long-term PN in children without underlying specific diagnosis[20].

Severity of malnutrition and nutritional rehabilitation
Severity of malnutrition was classified by using WHZ-score compared to NCHS/WHO 1978 reference values[21]. Presence of moderate to severe malnutrition was considered as significant malnutrition. The anthropometric measurements were entered into Epi Info™, version 3.3.2 (Centers for Disease Control and Prevention, Atlanta, USA) to calculate the z-score. The following scale was used to classify degree of malnutrition: no malnutrition, WHZ-score >-1; mild malnutrition, WHZ-score -1 to -2; moderate malnutrition, WHZ-score -2 to -3; severe malnutrition, WHZ-score < -3. Oral or enteral routes were used for nutritional rehabilitation whenever feasible and safe. PN was used when there was a contraindication for enteral feeding.

Statistical methods
Data was analyzed using the Statistical Package for the Social Science (SPSS), version 11.5. WHZ-scores were calculated by using nutrition software of Epi InfoTM. Pearson chi-square (χ^2) test was used to detect the association of various factors of malnutrition and PD. Multiple logistic regression test was used to detect the predictors of malnutrition and prolonged diarrhoea. Paired-samples T-test was used to demonstrate the difference between WHZ-score at admission and at follow-up.

RESULTS

Of the 151 case records screened initially, 80 (53%) cases were excluded. Of these, 67 cases did not fulfil the inclusion criteria (duration of diarrhoea < 14 days, n=55; other diagnoses, n=11; underlying malignancy, n=1). Another seven cases had incomplete record. The remaining six patients had a pre-existing diagnosis and were admitted for relapse of the underlying conditions. Thus 71 cases were included for final analysis.

Basic demographic features
There were 35 males and 36 females (male: female ratio = 1:1). Forty-four percent (n=31) of the patients were infants aged less than one year old, 32% (n=23) were toddlers between 1 to 5 years, while 24% (n=17) were older than five years of age. The median age at admission was 19 months (mean age: 36 months, range 0.5 to 144 months).

Underlying cause of chronic diarrhoea (Table I)
Causes of PD were diverse and can be divided into five main groups. In group 1 (enteric infections, n=20, 28%), non-typhoidal Salmonella (n = 8) was the commonest pathogen implicated. Other bacterial, protozoal, viral and intestinal helminthiasis were noted as well. Patients in group 2 (food intolerance, n=19, 27%), lactose intolerance and CMPI were equally common. In group 4 (CIBD, n=15, 21%), Crohn disease (n=4) was the commonest form of CIBD diagnosed.

The last group consisted of miscellaneous causes of PD. One patient had human immunodeficiency virus (HIV) enteropathy. The diagnosis was established on a positive HIV antibody and HIV DNA polymerase test in the serum. The diagnosis of MvID in a patient was confirmed by electron microscopic examination of the small bowel biopsy. Another patient had onset of PD at the age of six months. The facial features were similar to those described by Girault *et al*[27], with prominent forehead, flat nose, hypertelorism and sparse and unmanageable hair. However, the histological and electron microscopic examination of the small bowel biopsy were normal. The two patients with cystic fibrosis and another two patients who were subsequently diagnosed as primary sclerosing cholangitis, presented with chronic steatorrhea.

There were two siblings from healthy, non-consanguineous parents who had intractable diarrhoea in association of proximal tubular acidosis, hypophosphatemia, phosphaturia, and severe rickets not responding to high doses of oral and parenteral vitamin D. Both siblings had the onset of diarrhoea within the first month of life and required prolonged PN.

Clinical features at presentation (Tables II)
Not all patients had prolonged diarrhoea on first admission, some developed PD during the course of illness after admission. The median duration of diarrhoea at presentation was 45 days (ranged 2 days to 8 years; mean = 259 days). More than half of patients had watery stools (n=43, 61%). Most of the patients (n = 45, 63%) had a frequency of diarrhoea between 5 to 10 episodes per day. Dehydration was noted in 17 patients (24%).

Degree of malnutrition
Twenty-seven patients (38%) had evidence of muscle wasting and three patients (4%) had significant pitting edema on admission. Using WHZ-score at admission, malnutrition was common at presentation (n=52, 73%). Of these, 22 patients (31%) had mild, 21 (30%) had moderate, and 9 (13%) had severe malnutrition. Generally patients with postenteritis syndrome (all of the four patients) and food intolerance (14 of 19, 74%) had no or only mild malnutrition. Significant malnutrition (defined as moderate and severe malnutrition) was commonly seen in those with CIBD (5 of 15, 33%), enteric infections (11 of 20, 55%), and the miscellaneous group (10 of 15, 67%).

Predictors of moderate to severe malnutrition on first presentation (Tables III & IV)
Several demographic, socio-economic and clinical factors were analyzed as potential predictors of moderate to severe malnutrition resulting from PD. On multiple logistic regression analysis, two variables remained statistically significant in predicting moderate to severe malnutrition: presence of pallor (p = 0.02) and perianal excoriation (p = 0.02) on admission.

Nutritional intervention
Enteral nutrition: Fifty-three (75%) patients required dietary modification. Continuous enteral feeding was given to 14 patients (20%, mean duration = 35 days), majority were in transition from PN to oral feeding. It was successfully discontinued in all patients except in two cases before discharge from the hospital. One of these had short gut syndrome and was transferred back to the referring hospital for continuing care. The second was the patient with protracted diarrhoea and phenotypic abnormalities who was discharged on home PN and EN.

Various formulae were used for feeding. Casein hydrolysate (Pregestemil®, Mead Johnson, Nijmegen, The Netherlands) was used in patients with enteric infection (n=7), food protein intolerance (n=4), and carbohydrate intolerance (n=3). Medium-chain triglyceride enriched peptide-chain formula (Portagen®, Mead Johnson, Nijmegen, The Netherlands) (n=7), amino-acid-based elemental formula (Neocate®, Scientific Hospital Supply, International, Liverpool, UK) (n=7), lactose-free cow's milk-based formula (n=4) and soy formulae (n=3) were also used. One patient with CMPI was advised to return to breastfeeding. Another ten patients were given calorie-enriched formula as supplement to improve the total calorie intake.

Parenteral nutrition (Table V): A total of 15 patients (21%) required PN (mean duration 96 days). Of these, one had normal nutritional status, eight had moderate malnutrition, and six had severe malnutrition. Twelve patients required PN for more than 14 days (range 8 to 730 days). Fourteen patients had PN via a central venous catheter. Five patients had at least one documented episode of catheter-related sepsis. One patient developed cholestatic jaundice which subsided with conservative treatment. Three patients were discharged with home PN (MvID, intractable diarrhoea with proximal renal tubular acidosis, and intractable diarrhoea with phenotypic abnormalities).

Outcome
Primary outcome: Four deaths were noted, two of which were not related to PD or malnutrition. The first was a 3 month-old boy with severe multiple food protein intolerance with onset of diarrhoea at day 3 of life. The diarrhoea was in remission and the patient was gaining weight satisfactorily with PN and elemental formula while in the hospital. He was diagnosed to have severe tracheobronchial malacia and died of postoperative complication following a tracheotomy. The second was the child with HIV enteropathy. The acquired immune deficiency syndrome (AIDS) and persistent diarrhoea were in remission after appropriate therapy. The child died at three years of age of non-Hodgkin lymphoma complicating AIDS.

Of the remaining two patients, the first was a 19 month-old girl with abdominal tuberculosis, who had progressive abdominal distension, intermittent fever, loss of weight and protein-losing enteropathy. Despite anti-tuberculous and nutritional therapies, she died of severe bacterial sepsis. The second was the patient with MvID who was on home PN. Gradually there was loss of central venous access. The patients died at $4^{1}/_{4}$ years of age, two years after discontinuation of home PN.

Clinical remission: One patient with CMPI was lost to follow-up and the remission status was unknown. Two patients died without achieving remission (see above). Of the 70 patients in whom remission status could be ascertained, clinical remission was achieved in 64 patients (91%). In addition to the two patients who died while not in remission, another four patients were not in remission on review: (a) MvID, (b) the patient with intractable diarrhoea and phenotypic abnormalities, (c) two siblings with proximal renal tubular acidosis and intractable diarrhoea. Three patients were discharged on home PN.

Duration of hospitalization (Table II): Generally early discharge was possible with more than half (n=39, 55%) of patients discharged within 14 days of admission. The median duration of hospitalization was 12 days (mean = 29 days, range 2 – 271 days). Another 20 (28%) patients stayed between 15 to 30 days, 8 (11%) between 31 to 90 days, 3 (4%) between 91 to 180 days, and 3 longer than 181 days after admission. Not surprisingly, the three patients who were eventually discharged on home PN had the longest duration of hospitalization. Patients with significant malnutrition had a longer hospital stay than those with no or mild malnutrition (47 days vs. 16 days; P = 0.007).

Table I: Underlying causes of chronic diarrhoea in 71 patients admitted to Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur from 1998 to 2004

Causes	n
Enteric Infection (n=20, 28%)	
Bacterial	
Non-typhoidal Salmonella	8
Others (a)	4
Abdominal tuberculosis	2
Intestinal helminths (b)	4
Giardiasis	1
Rotavirus	1
Food intolerance (n=19, 27%)	
Carbohydrate intolerance	
Secondary lactose intolerance	6
Monosaccharide intolerance	1
Protein intolerance	
Cow's milk protein intolerance (CMPI)	7
Multiple food protein intolerance	4
Mixed CMPI & secondary lactose intolerance	1
Post-enteritis syndrome (n=4, 6%)	
Chronic inflammatory bowel diseases (n=15, 21%)	
Crohn's disease	4
Ulcerative colitis	2
Indeterminate colitis	7
Eosinophilic enteropathy	2
Miscellaneous (n=13, 18%)	
Cystic fibrosis	3
Intractable diarrhea with proximal renal tubular acidosis	2
Primary sclerosing cholangitis	2
Short bowel syndrome	1
Intestinal pseudo-obstruction	1
Intestinal lymphangiectasia	1
Acquired immunodeficiency syndrome (AIDS) enteropathy	1
Microvillus inclusion disease	1
Intractable diarrhea of infancy with phenotypic abnormalities	1
Total	**71 (100%)**

(a) 1 each for Shigellosis, Klebsiella; enteropathogenic Escherichia. coli and Aeromonas.
(b) Mixed Ascaris lumbricoides & Trichuris . trichura 2; mixed Entameba histolytica & Trichuris trichura 2

Table II: Clinical features of 71 children with persistent diarrhoea on first presentation

	All (N=71)	Enteric infections (n=20)	Food intolerance (n=19)	Post-enteritis syndrome (n=4)	CIBD (n=15)	Miscellaneous (n=13)
At first presentation						
Mean age (months ± SD)	35 ± 41	42 ± 44	12 ± 23	18 ± 19	69 ± 45	25 ± 30
Mean duration of diarrhoea before first admission (days ± SD)	259 ± 653	52 ± 73	80 ± 153	17 ± 4	703 ± 111	381 ± 746
Signs of malnutrition at presentation						
Pallor	17	7	2	0	7	3
Gluteal muscle wasting	27	8	4	0	4	9
Pedal edema	3	2	0	0	0	1
Severity of malnutrition a (n, %)						
None or mild	40 (56)	9 (45)	14 (74)	4 (100)	10 (67)	3 (23)
Moderate or severe	31 (44)	11 (55)	5 (26)	0 (0)	5 (33)	10 (77)
Mean WHZ-score	-1.83 ± -1.77					
Duration of hospitalization (days ± SD)	29 ± 50	34 ± 49	23 ± 25	5 ± 3.6	15 ± 14	52 ± 85
Number required PN (%)	15 (21)	3 (15)	5 (26)	0 (0)	2 (13)	5 (38)
Outcome						
Remission (n, %)	64 (91)	19 (95)	18 (95)	4 (100)	15 (100)	8 (62)
Home PN	3	0	0	0	0	3
At 3 months follow-up after discharge (n=55) [b]						
Severity of malnutrition * (n, %)						
None or mild	43 (78)	8 (67)	9 (75)	4 (100)	14 (93)	8 (67)
Moderate or severe	12 (22)	4 (33)	3 (25)	0 (0)	1 (7)	4 (33)
Mean WHZ-score	-0.80 ± -1.17					

a. See text for definition of and degree of malnutrition
b. Information on nutritional status was available on 55 patients at 3 months after discharge
WHZ-score: weight-for-height Z-score, PN: parenteral nutrition

Table III: Predicting factors of moderate to severe malnutrition on first presentation

Factors	Total	No or mild malnutrition (n=40)	Moderate to severe severe malnutrition (n=31)	P-value	Odds Ratio (95% CI)
Ethnic group, Chinese	30	18	12	0.521[a]	0.7 (0.3 – 1.9)
Gender, Male	35	21	14	0.922[b]	1.0 (0.4 – 2.4)
Feeding history (breastfeeding > 6 months)	9	4	5	0.397	0.5 (0.1 – 2.2)
Characteristics of diarrhoea					
Age of onset < 12 months	31	18	13	0.213	1.8 (0.7 – 4.7)
Duration before admission > 45 days	36	14	24	0.028	2.9 (1.1 – 7.7)
Diarrhoea frequency > 10 times / day	16	12	4	0.807	1.2 (0.4 – 3.5)
Presenting symptoms and signs					
Fever	34	20	14	0.624	1.3 (0.5 – 3.2)
Vomiting	31	16	15	0.375	1.5 (0.6 – 3.9)
Abdominal distension	14	3	11	<0.001	13.7(2.8 – 67.4)
Dehydration				0.739	1.2 (0.4 – 3.5)
Pallor	19	7	12	0.005	4.7 (1.5 – 14.5)
Obvious muscle wasting	27	7	20	<0.001	7.6 (2.6 – 22.0)
Pitting edema	3	1	2	0.358	3.0 (0.3 – 34.7)
Perianal excoriation	6	7	9	0.049	3.0 (1.0 – 9.7)

a. Chinese vs. non-Chinese
b. Males vs. females

Table IV: Predictors of moderate to severe malnutrition – a multivariate analysis

Factors	β	S.E. (β)	Significance	Odds ratio (95% CI)
Diarrhoea before admission > 45 days	1.05	1.01	0.296	2.86 (0.40 – 20.56)
Abdominal distension	1.49	1.47	0.309	4.44 (0.25 – 78.40)
Pallor	3.02	1.30	0.020	20.58 (1.62 – 261.47)
Muscle wasting	1.23	0.92	0.181	3.44 (0.56 – 20.96)
Perianal excoriation	3.23	1.42	0.023	25.28 (1.55 – 411.57)

Table V: Duration of parenteral nutrition in persistent diarrhoea

Diagnosis	Duration of PN (days)
Enteric infection	
Abdominal tuberculosis (n=1)	60
Salmonella gastroenteritis (n=1)	17
Food intolerance	
CMPI (n=1)	21
Lactose intolerance (n=2)	9, 17
Multiple food protein intolerance (n=2)	38, 67
Chronic inflammatory bowel diseases	
Crohn's disease (n=1)	16
Eosinophilic enteritis (n=1)	13
Miscellaneous	
Renal tubular acidosis (n=2)	17, 145
Microvillus inclusion disease (n=1)	730
Intractable diarrhea of infancy (n=1)	122
Intestinal pseudo-obstruction (n=1)	8
Short bowel syndrome (n=1)	161

CPMI: Cow's milk protein intolerance
PN: Parenteral nutrition

Table VI: Comparison between degree of malnutrition on admission and at 3 months follow-up after discharge

Degree of malnutrition	Admission n (%)	3 months' follow-up n (%)
No (WHZ-score > -1)	19 (27)	34 (49)
Mild (WHZ-score -1 to -2)	22 (31)	9 (13)
Moderate (WHZ-score -2 to -3)	21 (30)	9 (13)
Severe (WHZ-score < -3)	9 (13)	3 (4)
Unknown	0 (0)	14 (20)
Total	71 (100)	69 (100) *

* Two patients died before 3 months' follow up.

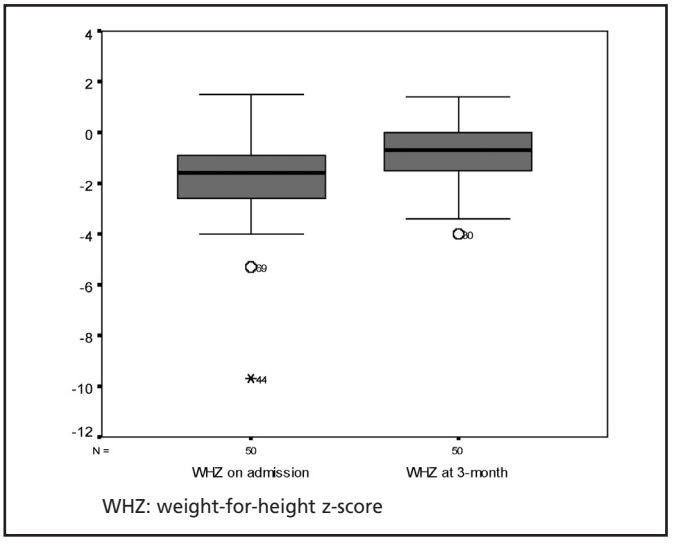

Fig. 1: Comparison of weight-for-height z-score on admission and 3 months after discharge in patients with persistent diarrhea.

Nutritional outcome of patients with malnutrition (Table VI, Figure 1)
The median duration of follow-up was 90 days (mean = 380 days). Information on WHZ-score at three months after discharge were available in 55 patients (82% of 67 survivors). Overall, the nutritional status at review three month after discharge showed a significant improvement as compared to on first admission (mean WHZ-score from -1.83 ± -1.77 improved to -0.80 ± -1.17; $p < 0.001$; Figure 1).

At three months follow-up, majority (62%, n = 34/55) of patients had normal nutritional status (no malnutrition, WHZ-score > -1.0), although 9 (16%) patients still had persistent mild malnutrition, 9 (16%) had moderate malnutrition, and 3 (5%) had severe malnutrition. Generally patients with no or mild malnutrition on admission had a better nutritional outcome at three months after discharge as compared to those with moderate-to-severe malnutrition on admission. Of the 25 patients who had initially had moderate to severe malnutrition on admission and in whom the nutritional status at three months after discharge was available, ten patients (40%) still had significant malnutrition.

The WHZ-score of two patients deteriorated at three months follow-up. One of these was a patient with cystic fibrosis who has very frequent chest infections requiring multiple hospital admissions for parenteral antibiotics. The family was not receptive to feeding through percutaneous gastrostomy. The second patient was a one month old female infant with CMPI. There were severe social concerns about the family.

DISCUSSION

The present study confirmed our previous observation that aetiologies of PD in children referred to a tertiary center in Malaysia was diverse, and the primary outcome was generally a favorable one. However, malnutrition complicating PD remained a concern, even after clinical remission was achieved in most of the cases.

In assessing the nutritional status following PD, the authors used the WHZ-score, derived from Epi Info 2002, which is an index of wasting[10]. This has the advantage of simplicity and is more sensitive than just the detection of physical signs for malnutrition, such as presence of gluteal muscle wasting. In the present study, only 37% of patients had gluteal muscle wasting, but 42% of patients had a WHZ-score of less than -2, indicating moderate malnutrition. But computing WHZ-score also requires computer software and may not be available to smaller hospitals and nutrition centers in many developing countries[10]. Thorough physical examination, looking for signs of malnutrition, and computing of WHZ-score at first presentation, if available, are both important in helping to determine nutritional complications following PD[23].

The degree of malnutrition in the present study follows the World Health Organization (WHO) integrated management of childhood illness (IMCI) guidelines,[29] where a WHZ-score less than -3 indicates severe malnutrition. However, there are some concerns about the accuracy of using Epi Info 2002, where both WHO 1978 and Center for Disease Control (CDC) 2000 reference standards are available[10]. The CDC 2000 standard markedly overestimates the degree of wasting compared with the earlier 1978 standard, because of the increase in obesity in American children over the 22 years[25]. The 1978 reference was used in the present study, thus eliminating the potential of over-estimation of severity of malnutrition[10].

As compared to studies on severe and PD in children from developed countries,[4, 5] it is obvious that enteric infections played a more important role in the present study, even after considering the difference in the inclusion criteria between the Italian studies and the present study[4, 5]. Irrespective of the underlying cause, malnutrition remains an important concern after PD[10, 11]. Enteric infections accounted for 27% of all cases of PD. Arguably, cases classified under food intolerance such as carbohydrate intolerance and CMPI, as well as post-enteritis syndrome, could also be triggered by an episode of gastrointestinal infection leading to PD[2]. Thus the total cases of enteric infection could actually be higher.

Certain causes of PD may be associated a more severe degree of malnutrition than others. In the present study, degree of malnutrition at first presentation was more severe in patients with enteric infections and the miscellaneous causes, but less severe in those with CIBD, food intolerance or post-enteritis syndrome. We noted that the presence of pallor and perianal excoriation were significant indicators for significant malnutrition (Tables III & IV). Although pallor may indicate the chronicity of PD and hence more severe degree of malnutrition, the duration of PD before admission was not an independent risk factor for significant malnutrition. Perianal excoriation was seen in various causes of PD, including carbohydrate intolerance and Crohn's disease. The presence of both pallor and perianal excoriation in a patient with PD should indicate the presence of significant malnutrition.

With appropriate therapy, cessation of diarrhoea and remission was achieved in a majority of patients (94%). Four deaths were observed, two of which were not related to PD or

its complication, reflecting the complexity and multi-system involvement of certain causes of PD. Remission was not achieved in four patients; three of these patients were discharged on home PN. All the patients who failed to attain remission had onset of diarrhoea in the neonatal or early infancy period, belonging to the neonatal enteropathies described by Sherman *et al.*[9]. However, the two siblings with intractable diarrhea, proximal renal tubular acidosis and rickets could not easily be classified into any known neonatal enteropathies[9, 22].

Not surprisingly, some of the patients with malnutrition, especially those with a more severe degree of malnutrition, the nutritional status improved slowly even after remission. Unfortunately, anthropometry data beyond three months after discharge were not available for the present study to show the medium to long term nutritional outcome of these children with PD. Some studies showed that in children with severe malnutrition who were followed over three years, the final catch-up growth were not significantly different between those who had higher initial velocity of growth and those who didn't[26].

Three patients with PD in the present study required home PN,[27] which has been regarded in developed countries as an accepted form of therapy for children with intestinal failure[28]. However, there are quite a few notable complications with home PN[29]. In UMMC, Kuala Lumpur, home PN is a relatively new mode of therapy offered to children with intestinal failure. The patient with MvID was the first patient given home PN. He was doing fairly well for the first two years after starting home PN. There was a gradual loss of central venous access, resulting in a premature stop of home PN. Some authors have regarded intestinal transplantation as the preferred therapy for MvID over home PN[12]. However, intestinal transplantation was not available in Malaysia.

There are some limitations to the present study. Firstly, it was a hospital-based study from a tertiary referral hospital in Malaysia, therefore the spectrum of the PD described in the present study and the degree of malnutrition may just represent the more severe of cases that need expert care. In addition, being a retrospective study, some data, especially nutritional status on follow-up were lacking for analysis. There was also no appropriate control for risk factor for significant malnutrition following PD. Finally, the present study did not address the issue of micronutrients deficiency following PD[11].

Nevertheless, the present study showed that with appropriate therapy, remission could be achieved in a majority (91%) of patients with PD. However, in a small group of patients, especially those with onset of diarrhoea within the first few months of life, the prognosis were poor and remission will never be attained. Such patients will certainly benefit from home PN and intestinal transplant, the latter mode of treatment is currently not available in Malaysia. Significant malnutrition is a common complication following PD. With EN and PN, nutritional status improved in a majority of patients, although not surprisingly, improvement is somewhat slower in those who moderate to severe malnutrition at first presentation, even though they stayed longer in the hospital. Continuing follow-up of these patients is therefore imperative.

ACKNOWLEDGMENT

The authors wish to acknowledge Professor CCM Boey for reading the manuscript, and the assistance of Professor IW Booth, Institute of Child Health, Birmingham Children's Hospital, Birmingham, United Kingdom, for helping to arrange electron microscopic examination of some of the small bowel biopsy in arriving the diagnosis, particularly cases of microvillous inclusion disease and persistent diarrhoea with phenotypic abnormalities.

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