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Original Article

Effect of nutritonal therapy on Helicobacter Pylori infections in severely malnourished children

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Abstract

Background Severe malnutrition young children has been a problem in Indonesia for many years. In recent years the condition may be increasing. Besides a lack of nutrition, *H.pylori* infection may contribute to this condition.

Objective To determine if severely malnourished children have high rates of *H. pylori* infection, and to test if improving nutritional deficiency by drinking skimmed milk can reduce the number of *H. pylori* cases.

Methods A total of 83 children aged 6 – 36 months with severe malnutrition (weight-for-age <-3 Z-scores), who were outpatients at the Nutrition Clinic in Bogor served as subjects for this longitudinal study. Out of 83 children, 42 subjects (50%) tested positively for *H. pylori* infection (Group P) and 41 subjects (49.4%) tested negatively (Group NP). All subjects received the same nutritional intervention consisting of medical care, 250 g of skimmed milk, and guidance concerning proper feeding and care of children at every clinic visit, for a duration of 6 months.

Results The study revealed that after 6 months of nutritional intervention, the percentage of children suffering from diarrhea was significantly ($P < 0.05$) reduced in Group P, while no significant change was demonstrated in Group NP. The nutritional intervention also demonstrated a noticeable effect on the incidence of *H. pylori* infection, reducing the number of *H. pylori* infections by 29% in Group P. In Group NP, 100% of the children remained free of *H. pylori* infection after intervention. No new cases of *H. pylori* infection appeared in either group. An improvement in nutritional status was also observed: 23.8% of severely undernourished children in Group P and 34.1% in Group NP improved after intervention.

Conclusion Drinking skimmed milk twice daily, as well as parental counseling on proper feeding and child care, led to improved nutritional status of severely malnourished children. We also observed that skimmed (non-fat) milk may have a role in preventing and treating malnourished children with *H. pylori* infection. **[Paediatr Indones. 2010;50:278-83]**.

Keywords: *H.pylori infection, diarrhea, and nutrition intervention.*

Based on the latest survey carried out by Indonesian National Health Research and Development, the prevalence rate of severely undernourished (weight-for-age <-3 Z-scores) children was 5.4%. Prevalence of undernourished children (weight-for-age <-2 Z-score) was 18.6%, stunted (height-for-age <-2 Z-score) was 36.8%, and wasting (height-for-weight <-2 Z-score) was 13.6%.[1] Besides poor diet as mentioned above, *H. pylori* infection is may be a contributing factor of undernutrition.[2] In the developing world, overcrowding in the home, such as close person-to-person contact and bed-sharing, poor sanitation and socio-economic conditions, can be important factors in the transmission of *H. pylori* and other pathogens. High infection rates of *H. pylori* among newborn and young children in developing nations appear to be a major cause for diarrhea and chronic undernutrition with failure to thrive.[3,4]

Based on these views, our study, carried out at the Nutrition Research and Development Center, Bogor, Indonesia, aimed to determine (1) if severity of protein energy malnutrition correlated to higher rates of *H. pylori* infection, and (2) if nutritional intervention in

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children suffering from severe malnutrition could help prevent and treat *H. pylori* infection.

Methods

The Nutrition Research and Development Center of the Ministry of Health conducts research and provides public services, including rehabilitation of severely malnourished children. Outpatients to the center are children mostly referred from community health centers ("Puskesmas") from the surrounding area. At the clinic the children receive simple treatment for illnesses and their mothers receive nutrition education, particularly on feeding and caring of children.

Initially, 98 children were included in the study, all of whom had weight-for-age <–3 SD based on NCHS standards. However, 15 children dropped out for various reasons: (a) 3 children lived 3 to 4 hours away and could not afford transportation fees to the Clinic; (b) mothers of 3 children had new babies and could not bring their older child to the Clinic; (c) families of 5 children moved outside the Bogor area; (d) parents of 3 children refused because of transportion expense and lack of motivation as they considered their children to not be ill; and (e) 1 child died. Therefore, 83 children with severe malnutrition aged 6 to 36 months, were the subjects in our study.

Mothers and their children were asked to visit the clinic at least 12 times during the course of the study: weekly during the first month, bi-weekly in months 2-4, and monthly in months 5-6. At each clinic visit, a pediatrician gave medical care to subjects, and 250 g of skimmed milk. While the child was being treated, mothers were given guidance by a nutritionist concerning feeding and care of their children, and they were encouraged to give them skimmed milk. The mothers were also urged to purchase additional skimmed milk for their children. At subsequent visits, mothers were asked about their child's home feeding, including children's reaction to food and any signs of improvement in their condition.[5]

Home visits were carried out by nutritionist or midwives in the first, sixth, tenth, sixteenth and twentieth weeks of the study. During the visits, dietary information was collected, and nutritional practices at home, including child feeding, child care, sanitation were observed. The skimmed milk drinking was also observed by field workers. At the first visit to the clinic, mothers provided information on socio-economic status, and home dietary and nutritional practices, including feeding, child-care, sanitation, and food hygiene. The child's state of health, particularly frequency, duration and severity of diarrhea was also recorded.

Anthropometric measurements (weight, length, and arm circumference), and blood draws for hemoglobin (Hb) and hematocrit (Ht) were performed at every clinic visit. Examination for *H. pylori* infection was performed at the first and final clinic visits.

Anthropometric measurements were performed by nutritionists using standard procedures.[6] Length was measured using a portable measuring board designed by the Nutrition and Food Research and Development Center in Bogor, calibrated to an error of 0.1 cm. The weight of the naked child was measured using a Baby Scale (Misaki Inc. Japan) with an accuracy of 0.1 kg. Arm circumference was measured to the nearest 0.1 cm, using a fiberglass tape placed gently, but firmly around the middle of the freely hanging, left upper arm.[6]

Blood was drawn from each child via finger prick. Hematology analysis included Hb testing by cyanmethemoglobin procedure, and Ht testing by microcentrifuge method.[6] We evaluated for *H. pylori* infection using the ^{13}C-urea breath test, following the technique adopted by the International Atomic Energy Agency (IAEA), Vienna-Austria.[7] After fasting $\geq$ 3 hours, 50 mg of ^{13}C-urea was administered with 30 ml skimmed milk, followed by another 30 ml skimmed milk to rinse the mouth. Expired air samples were collected pre-procedure (baseline) and 30 as well as 45 minutes after tracer application. Duplicate baseline breath samples were taken, but other test samples were taken singly. Samples were taken using a nasal cannula, and slowly withdrawn using a 50 ml syringe. The sample was pushed into an exetainer tube, capped immediately, and kept at 4 - 8 °C. Samples were analyzed by mass spectrometer at Saint John's Medical College, Bangalore, India. An increase of 3.5 or more over baseline after 30 and 45 minutes of ^{13}C-urea administration was taken as a positive result.

Out of 83 children at the onset of our study, 50% (N = 42) had *H. pylori* infection (Group P) and 49% (N = 41) did not have *H. Pylori* infection (Group NP). We compared these 2 groups by statistical analysis to establish the effectiveness of the nutritional intervention regimen on *H. pylori* infection. The statistical analysis was performed with SPSS windows software and included means, SDs, and association among related variables. We used chi-square analysis to compare nutritional status between groups. An analysis of variance (ANOVA) model was used for all group comparisons before and after treatment. The study was approved by the Ethics Committee of the Ministry of Health, and parents provided informed consent. Personal information collected was kept confidential. The findings were used for scientific purposes and to support nutrition program development, particularly for rehabilitation of children with severe malnutrition.

Results

A.1. Weaning status and morbidities

Table 1 shows the number of breastfed children and weaning status. Thirty-three (40%) children from the total (83 children studied) had been weaned. Other than the oldest age category (≥30 months) the highest percentage of weaned children was in the youngest age group (6–11 months). The most common reasons a child was weaned early were (1) subsequent pregnancy, (2) inadequate breast milk, (3) child's refusal to breastfeed, (4) frequently ill child, and (5) caregiver was the grandmother. Inadequate breast milk was likely related to the poor quality and quantity of food consumed by mothers due to financial constraints. Although the percentage of children > 24 months who were still breastfed was lower (14%) than those who were weaned (20.4%), however breastfeeding is still important for children even > 24 months.

The number of children suffering from one or more diseases was 84%, as shown in **Table 2**. The highest percentage (47.0%) of children were suffering from upper respiratory infections (tonsillitis, tonsilopharyngitis, common cold, and pharyngitis), followed by a combination of upper respiratory infection and gastrointestinal infection (13.3%).

Table 1. Breastfed and weaned children by age

Age	Breast Feeding			
	Breastfed		Weaned	
(mo)	(n)	(%)	(n)	(%)
6-11	7	8	10	12.0
12-17	23	28	4	5
18-23	8	10	2	2
24-29	8	10	7	8
≥ 30	4	5	10	12.0
Total	50	61	33	39

A.2. Results of nutritional intervention

At the beginning of the study, all subjects suffered from severe malnutrition (Weight-for-Age < -3 Z score). After 6 months of nutritional intervention, the percentage of children who remained severely malnourished was 76% (N = 32) in Group P, and 65.9% (N= 27) in Group NP, as illustrated in Figure 1. The percentage of children who improved in nutritional status was significantly ($P < 0.05$) higher in Group NP than in Group P. An improvement in nutritional status was observed: 24% of children in Group P and 34% in Group NP after intervention. These findings indicate that both groups responded positively to nutritional intervention. *H. pylori* infection may have influenced the rate of response to intervention.

Table 3 shows the mean weight, height, arm circumference, and hemoglobin (Hb) values of the two groups measured at baseline and 6 months later. After intervention, the mean weight increased 1.1 kg in Group P and 1.5 kg in Group NP; the mean height increased 4.5 cm in Group P and 5.3 cm in Group NP; the mean arm circumference increased 0.7 cm in Group P and 1.0 cm in Group NP; the mean Hb decreased 0.3g/dl in Group P while mean Hb in Group NP increased 0.4 g/dl. After correction for the initial values as a covariant, the main effect of the treatment was significantly higher for weight ($P <0.05$) and length ($P <0.05$) in Group NP than Group P. However, the test showed no significant difference arm circumference between the two groups. Also, the mean Hb values, which increased in Group NP but decreased in Group P after intervention, showed no significant difference. As expected, children in Group NP experienced a greater improvement for all indicators than those in Group P.

Table 2. Illnesses observed in subjects

Illness	Number of Children	
	(n)	(%)
Upper respiratory infection (URI): tonsillitis, tonsilo- pharyngitis, common cold, pharyngitis	39	47
Lower respiratory infection (LRI): TB and bronchitis	5	6
Gastrointestinal infection (GI)	5	6
Skin infection	2	2
Ventricular Septal Defect, Tetralogy of Fallot	1	1
Combined URI + LRI	5	6
Combined URI + GI	11	13
Other combinations of 2 or 3 illnesses	2	2
Appeared healthy	13	16
Total	83	100.0

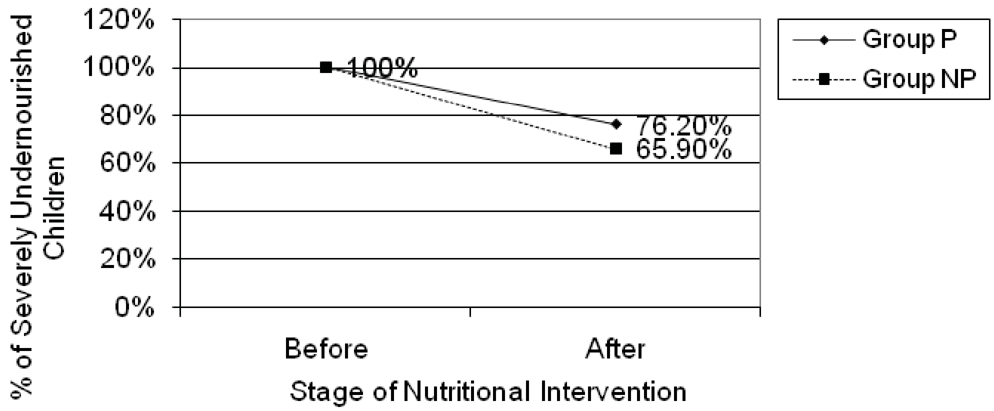

Figure 1. Changes in nutritional status before and after nutritional intervention.

Table 3. Mean and changes in weight, height, arm circumference and Hb values before and after treatment.

Time	Weight		Height		Arm circumference		Hb values	
	Group P (kg)	Group NP (kg)	Group P (cm)	Group NP (cm)	Group P (cm)	Group NP (cm)	Group P (g/dl)	Group NP (g/dl)
Before	6.6 (+1,24)	7.0 (+1,38)	70.1 (+5,97)	71.6 (+8,02)	11.6 (+1,19)	11.8 (+1,29)	11.0 (+1,70)	10.4 (+1,24)
After	7.8 (+1,28)	8.6 (+1,42)	74.6 (+5,83)	77.0 (+7,44)	12.4 (+1,02)	12.8 (+0,99)	10.7 (+1,95)	10.8 (+1,28)
Change	1.1 (+0,53)	1.5 (+0,89)	4.5 (+1,48)	5.3 (+2,05)	0.7 (+1,18)	1.0 (+1,25)	-0.3 (+2,02)	0.4 (+1,64)
t	13.93	16.97	19.71	23.05	3.97	5.75	0.74	1.25
P	P<0.001	P<0.001	P<0.001	P<0.001	P<0.01	P<0.01	NS	NS

Note: Anova (Bonferroni test): Significant differences ($P < 0.05$) were found between Group P and Group NP in weight and height.

Table 4 reports the changes in clinical status of children suffering from anemia, diarrhea and *H. pylori* infection. Although one child from Group P was no longer anemic after intervention, there were no significant differences in anemia for either group. We observed a significant decrease in the incidence of diarrhea in Group P ($P < 0.05$), but not in Group NP. Children with diarrhea may have

Tabel 4. Status of anemia, diarrhea, and *H. pylori* infection before and after intervention

Status	Time	Group P (N=42)				Group NP (N=41)			
		Positive		Negative		Positive		Negative	
		(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Anemia	Before	26	61.9	16	38.1	23	56.1	18	43.9
	After	25	59.5	17	40.5	23	56.1	18	43.9
Diarrhea	Before	14	33.3	28	66.7	7	17.1	34	82.9
	After	6	14.3	36	85.7	6	14.6	35	85.4
H. Pylori	Before	42	100	0	0	0	0	41	100
	After	30	71.4	12	28.5	0	0	41	100

responded more slowly to intervention. As shown in **Table 4**, the intervention also demonstrated a noticeable effect on the incidence of *H. pylori* infection, reducing the number of *H. pylori* infections by 29% in Group P. In Group NP, 100% of the children remained free of *H. pylori* infection after intervention. No new cases of *H. pylori* infection appeared in either group.

Discussion

A consensus, issued by the European *H. pylori* Study Group and the *H. pylori* Working Groups of the European Society for Pediatric Gastroenterology,[2] agreed that the prevalence of *H. pylori* infection in developing countries is very high and may represent a long-life condition, which makes the gastrointestinal tract very vulnerable to pathological bacterial invaders. It results in promotion of colonization of pathogens in the small intestinal tract, which come into competition for nutrition of the host. Under-nourishment and failure to drive are signs of this pathological condition. In a cross sectional study of *H. pylori* infection (has not been published yet) carried out in 275 children aged 6 – 36 months from low socio-economic status in rural and suburb areas in Bogor, West Java – Indonesia, we found that the prevalence of *H. pylori* infection in the community was 46.9% (N=129). Stunted, a deficit of length-for-age is the one among the three indicators of malnutrition (underweight, wasted, stunted) is significantly ($P<0.05$) associated with *H. pylori* infection, although the other two of indicators following the same pattern. These findings demonstrate that *H. Pylori* infection has an effect on malabsorption leading to a negative impact on the ability of children to thrive.

The clinical study reported here demonstrates that nutritional intervention in severely undernourished children results in an improvement of the incidence of diarrhea and leads to an improvement of nutritional status. The percentage of children suffering from diarrhea was significantly ($P < 0.05$) reduced in Group P (children infected with *H. pylori*), but not in Group NP (children not infected with *H. pylori*). The combination of *H pylori* infection and diarrhea may have slowed the rate of the response to the intervention. The group with higher incidence of diarrhea, group P, showed greater improvement in diarrheal status after intervention.

In Group P, we observed that 28.6% of subjects were cured of *H. pylori* infection after intervention. In Group NP, 100% children remained negative for *H. pylori* infection after intervention. There were no new cases of *H. pylori* infection in either group. These findings indicate that nutritional intervention yielded a significant decrease in *H. pylori* infection, and may have prevented other children from being infected with *H. pylori.* In addition, we found that both groups improved their nutritional status in response to the intervention, though a higher response was seen in Group NP than in Group P.

Based on the above findings, skimmed milk, drunk twice daily, probably played an important role in decreasing *H. pylori* infections and maintaining an uninfected state in Group NP during the 6 month study. Of importance is that the incidence of *H. pylori* infection dropped by about one-third after intervention. Similarly, severe malnourishment dropped by 24% in Group P and 34% in Group NP after intervention. The prospect of using skimmed milk to reduce severe malnutrition is promising.

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