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Shafiqul Alam Sarker
Abdul Majid Molla
A. K. M. M. Karim
M. Mujibur Rahaman

INTERNATIONAL CENTRE FOR
DIARRHOEAL DISEASE RESEARCH, BANGLADESH
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July 1982

Scientific Report No. 57

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Shafiqul Alam Sarker[1]
Abdul Majid Molla[2]
A.K.M.M. Karim[3]
M. Mujibur Rahaman[4]

INTERNATIONAL CENTRE FOR
DIARRHOEAL DISEASE RESEARCH, BANGLADESH
G.P.O. Box 128, Dacca 2
Bangladesh

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1 Medical Officer (former Research Fellow)

2 Scientist

3 Medical Officer

4 Deputy Director & Senior Scientist

PREFACE

The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) is an autonomous, international, philanthropic and non-profit centre for research, education and training as well as clinical service. The Centre is derived from the Cholera Research Laboratory (CRL). The activities of the institution are to undertake and promote study, research and dissemination of knowledge in diarrhoeal diseases and directly related subjects of nutrition and fertility with a view to develop improved methods of health care and for the prevention and control of diarrhoeal diseases and improvement of public health programmes with special relevance to developing countries. ICDDR,B issues annual report, working paper, scientific report, special publication, monograph, thesis and dissertation, and newsletter which demonstrate the type of research activity currently in progress at ICDDR,B. The views expressed in these papers are those of authors and do not necessarily represent views of International Centre for Diarrhoeal Disease Research, Bangladesh. They should not be quoted without the permission of the authors.

ABSTRACT

Intake of calories during acute diarrhoea and after recovery was studied longitudinally. Thirty-six children aged between 1 and 4 years and hospitalized with diarrhoea were selected for the study, 12 had cholera, 12 had entero-toxigenic *E.coli* and 12 had rotavirus. In the acute stage, the mean calorie intake was 71 Kcal/kg/day for the cholera patients, 80 Kcal/kg/day for *E.coli* and 63 Kcal/kg/day for the rotavirus patients. After stoppage of diarrhoea (early convalescent stage) the intake improved to 128 Kcal/kg/day for cholera patients, to 126 Kcal/kg/day for those with *E.coli* and the intake in late convalescent stage (2 weeks after discharge from the hospital) was 115 and 114 Kcal/kg/day respectively. Rotavirus patients showed a slower rate of improvement in comparison to the patients with cholera and *E.coli*. The calorie intake in rotavirus was 84 Kcal/kg/day and 100 Kcal/kg/day in early and late convalescent stages respectively. These results suggest that anorexia may be an important factor in reducing food intake during the acute stage of diarrhoea. Low intake of calorie during the acute stage could be compensated by providing higher intake during the convalescent period both in cholera and *E.coli* patients. Rotavirus patients seem to have a prolonged period of low intake of food followin diarrhoea.

INTRODUCTION

Diarrhoea is recognized as a major health problem in children throughout the developing world (1). The role of diarrhoea in the development of malnutrition is also well recognized (2). Among several mechanisms by which diarrhoea may produce and exacerbate protein energy malnutrition, reduction of intake of food, impaired digestion and absorption, and increased catabolism are thought to be of major importance (3). Restriction of food intake in acute diarrhoea is often related to cultural practices, beliefs and taboos, but frequently reduced intake is the direct result of poor appetite, vomiting and fever which often accompany the infectious process (4,5). Mata *et al.*, concluded that frequent infection rather than lack of food is largely responsible for low dietary intake in children from the developing countries (6). Repeated attacks of diarrhoea with accompanying anorexia influencing dietary intake is considered to be an important factor in the diarrhoea-malnutrition cycle which could be effectively interrupted by early rehydration and rapid refeeding (7). While it is a well established fact that rehydration is of crucial importance in the treatment of diarrhoea, little is known on dietary management in diarrhoeal children. Besides, there is very little information available on the extent of anorexia during and after diarrhoea due to different etiologies. This study reports the quantitative reduction of calorie intake during acute diarrhoeal episodes in patients with three different and principal causes of diarrhoea throughout the world i.e. *Vibrio cholerae*, enterotoxigenic *E.coli* and rotavirus. Efforts have also been made to test early refeeding and document changes of intake during post-diarrhoeal period as well.

PATIENTS AND METHODS

The study was conducted at the metabolic unit of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). During May to December, 1980, 45 children aged 1-4 years presenting with history of diarrhoea and mild to moderate dehydration (8) were selected for the study. Rehydration was completed and maintained as needed using intravenous fluid (Na^+ 133 mEq/l, K^+13 mEq/l, Cl^-98 mEq/l, HCO_3^-48 mEq/l). No antibiotic was administered during the study period. Refeeding started after initial rehydration under close observation by personnel well trained in metabolic balance studies. A semi-solid cooked meal containing rice, boneless minced chicken, lentils and vegetable oil was offered for lunch and supper. Semolina (suzi), sugar, egg and oil cooked together and a piece of bread was given for breakfast. A banana was served as a mid-afternoon snack. Fresh cow's milk with sugar was given twice, once between breakfast and lunch and again at bedtime. Except for milk, banana and bread, all food offered were cooked once-a-month and kept at -40°C. Samples of cooked food were homogenised and analysed for nutrient contents. The study diet was found to be acceptable when pretested on 10 healthy children aged 1-4 years. The composition of the diet is shown in Table I. The children

TABLE I--NUTRIENT COMPOSITION OF STUDY DIET

	Wt. (gm) Supplied	Cal/gm	Protein (gm%)	Fat (gm%)
Boiled rice	250	1.20	2.125	0
Meat-vegetable curry*	75	1.34	7.56	5.27
Banana	65-100	1.24	1.812	0.20
Full strength milk	500	.77	2.37	2.8
Khichuri**	200	.94	2.575	1.75
Dessert/Halua***	150	1.47	2.7	3.58
Bread	35	3.01	8.06	2.55

* Potato, oil, chicken, pumpkin and onion cooked as curry with condiment.

** Rice, pulses, oil, chicken and potato cooked together with salt and condiment.

*** Milk, egg, semolina, oil and sugar cooked together.

were offered food after rehydration which took approximately four hours. They were encouraged to eat but were not forced. The exact amount consumed was measured by substracting the leftover from the amount offered. A scale (OHAUS Company, USA) with sensitivity of 0.1 gm was used for dietary weighing.

To determine the actual caloric intake, duplicate samples of each item of food were sent to the laboratory which were dried in an oven to a constant weight and its value was determined in an adiabetic bomb calorimeter. Children were allowed to breast-fed *ad libitum*. The quantity consumed was determined by test-weighing and making corrections for urine and faecal losses.

Laboratory studies included measurement of serum electrolytes and total solids before rehydration. Darkfield examination of stool for vibrios and routine stool culture for the detection of pathogenic bacteria including enterotoxigenic *E.coli, Vibrio cholerae, salmonellae* and *shigellae* were done. *E.coli* colonies were tested for heat labile enterotoxin using Y_1-adrenal cell assay (9) and for heat-stable enterotoxin using the infant-mouse assay (10). Rotavirus antigen were detected from stool by enzyme linked immunosorbent assay (ELISA) method (11). Study patients were hospitalized for seven to nine days (average 8 days). During this period patients were observed for the end of diarrhoea, indicated by stoppage of liquid stool or passing of formed stool. The period when liquid stool was passed was termed as the acute stage. The period between the first formed stool or after stoppage of diarrhoea until discharge from hospital was termed as the early convalescent stage. Patients were brought back to the hospital 14 days after discharge for another three

day stay, and this period was called late convalescent stage. The procedure for measurement of food intake during the late convalescent stage was the same as described for the acute and early convalescent stages. Patients with mixed infections or patients not yielding any enteropathogen or those who failed to return for the follow-up study were excluded from the analysis.

RESULTS

Of the 45 children originally selected, 36 children with a single pathogen and available during the late convalescent stage were studied. The general characteristics, admission picture and laboratory findings of the study children are presented in Table II. The nutritional status as determined by the weight for

TABLE II--GENERAL CHARACTERISTICS, PREADMISSION SYMPTOMS AND LABORATORY FINDINGS OF THE STUDY CHILDREN (MEAN ± SEM)

	Cholera	*E.coli*	Rotavirus
Number of patients	12	12	12
Male	6	8	8
Female	6	4	4
Age (months)	35.7 ± 3.4	32 ± 5.2	17.3 ± 1.2
Weight (kg)	10.2 ± 0.01	9.95 ± 0.4	8.2 ± 0.3
Height (cm)	82.2 ± 0.2	83.3 ± 0.2	73.1 ± 0.1
Weight for age ratio*	71 ± 3.0	74.4 ± 2.0	74 ± 1.7
Weight for height ratio*	91 ± 3.0	89 ± 1.6	92 ± 2.0
Duration of illness before admission (days)	0.9 ± 0.2	2.0 ± 0.1	2.5 ± 0.2
Haematocrit (%)	35.2 ± 1.4	32.3 ± 0.9	32.6 ± 1.2
Serum Protein gm/dl	69 ± 1.8	71 ± 2.2	69 ± 2.8
Serum specific gravity	1.028± .001	1.026 ± .001	1.0261± .001

* National Child Health Statistics (NCHS) Standard.

height and weight for age of the National Child Health Statistics (NCHS) Standard were comparable in all the three groups. In comparison to *E.coli* and rotavirus, the children in the cholera group attended the hospital earlier and were significantly more dehydrated ($P<.05$) as assessed by haematocrit and serum total solid on admission.

On an average the calorie intake of the cholera and *E.coli* groups reached the recommended level of 100 Kcal/kg/day (12) by the end of the 4th day of illness which coincided with the stoppage of diarrhoea. At this point the calorie intake of the rotavirus group was 80 ± 4 Kcal/kg/day and this trend continued for the period of hospitalization after the stoppage of diarrhoea. The maximum intake of calorie in the rotavirus group of children was 88 ± 4 Kcal/kg/day and those of cholera and *E.coli* were 139 ± 5 and 138 ± 5 Kcal/kg/day respectively (Figure 1). During the early convalescent stage, marked improvement in intake was seen in cholera and *E.coli* patients but not among the children with rotavirus (Table III). Interestingly enough, during the late convalescent stage the intake of cholera and *E.coli* group of children dropped. The difference of intake between late convalescent and early convalescent stage was statistically significant ($P<.05$). The intake in the rotavirus group of children showed further improvement in the late convalescent stage to 100 Kcal/kg/day; the difference between the two stages was also significant ($P<.05$). Taking the intake in the late convalescent stage, a reduction of 38% in cholera, 30% in *E.coli* and 37% in rotavirus was noted.

In patients with cholera and *E.coli*, a significant inverse relationship between the intake of food and output of stool was seen during acute diarrhoea ($r = -.63$ and $-.49$ respectively). This however was not observed in rotavirus infection ($r = -.14$) (Figure 2).

Although on an average there was a drop in body weight of the cholera patients, on the second day, a progressive and consistent weight gain was noticed in all other group irrespective of consistency of stool (Figure 3).

DISCUSSION

The results presented here indicate that although dietary intake is reduced during the early phase of hospitalization in diarrhoea due to all etiologies, there was significant increase in intake during the early convalescent stage ($P<.05$). Since cholera and *E.coli* toxins produce diarrhoea by stimulating adenyl cyclase activity in the gut, the low intake during early phases of cholera and *E.coli* diarrhoea may be due to anorexia brought about by the adenosine, the metabolic product of AMP and cyclic AMP, which was found to cause marked suppression of appetite in rats when administered subcutaneously or intravenously (13). Cholera and *E.coli* patients seemed to recover appetite soon after diarrhoea stopped. They also showed a super-normal appetite during the early convalescent stage. This above normal appetite may be a compensatory mechanism for recovering the nutritional loss during the acute stage. Toxin mediated diarrhoea due to cholera and *E.coli* does not have a lasting effect on the gut or the body. Although the calorie intake of rotavirus patients improved in the early and late convalescent stages, their overall intake was still less in comparison to the other two etiologic groups. Rotavirus patients perhaps did not fully recover from the effect of infection interfering with food intake by two weeks time. This finding can be correlated with the presence of variable degrees of malabsorption of nutrients in rotavirus patients (14,15). Since villous epithelial cells are known to be denuded in rotavirus infection,

Fig. 1. OBSERVED CALORIE INTAKE IN STUDY PERIOD OF 8 DAYS - LATE CONVALESCENT (L.C) STAGE FOR EACH GROUP (MEAN ± SEM)

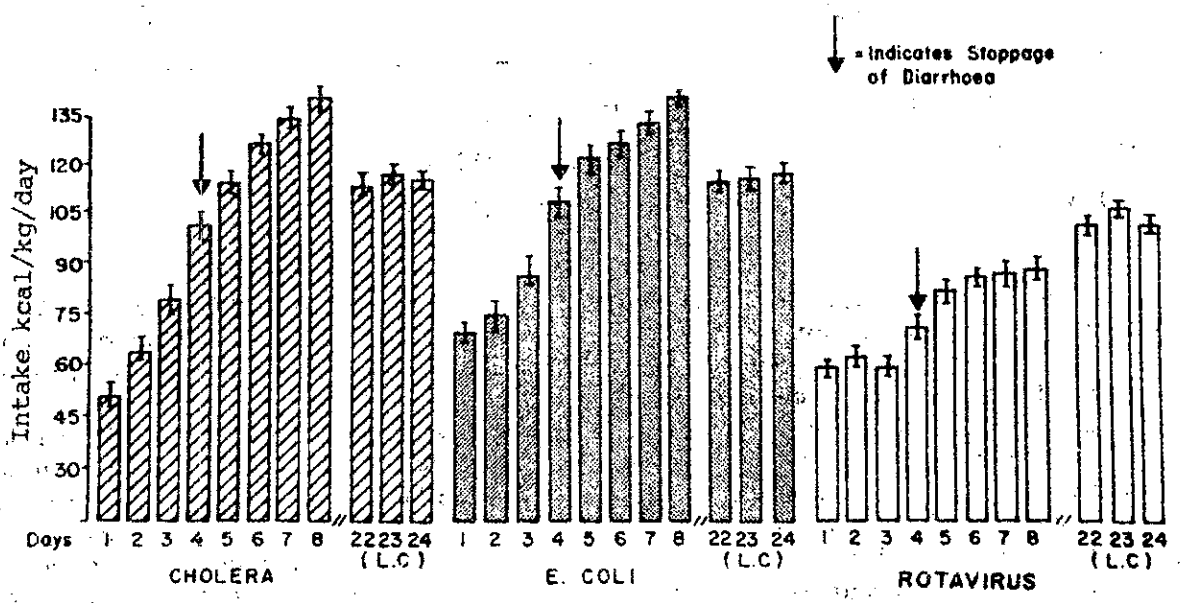


TABLE III--OBSERVED CALORIE INTAKE (KCAL/KG/DAY) IN EACH GROUP FOR THE THREE STAGES OF DIARRHOEAL ILLNESS (MEAN ± SEM)

	Acute	Convalescent	Late Convalescent
Cholera	71 ± 8 (A)	128 ± 6 (B)	115 ± 4 (C)
E.coli	80 ± 6 (D)	126 ± 6 (E)	114 ± 6 (F)
Rotavirus	63 ± 4 (G)	84 ± 6 (H)	100 ± 7 (I)

(A) vs (B) P<.001 (C) vs (B) P<.05

(D) vs (E) P<.001 (F) vs (E) P<.05

(G) vs (H) P<.01 (H) vs (I) P<.05

an association between inability of the gut to handle food and anorexia would not be surprising. It may be noted here that rotavirus children were younger than those of cholera and *E.coli* groups. It was thought that the solid food offered to rotavirus patients may have been unfamiliar to some of them, resulting in lowered intake. To minimise this, the rotavirus patients were at liberty to take milk or solid food according to the habit of the child. Moreover this study was conducted in the hospital, and not home environment, which is likely to have influence on the food intake of the children. Attempts were also made to minimise this effect to some extent by offering food by the mother. In all three study groups we observed that early feeding did not seem to have any adverse effect on diarrhoeal course as in all cases the daily stool volume gradually decreased and children who reached the maximum intake level progressively gained weight. The inverse relationship between the volume of stool passed and intake of food may also reflect the degree of physiological changes affecting the appetite during the acute stage of diarrhoea. Since only small amount of stool was passed in rotavirus diarrhoea, perhaps there was relatively little disturbance in the physiology of the affected children. There may be other mechanisms besides diarrhoea responsible for lower intake of food. It may be mentioned that one of the important clinical symptom of rotavirus diarrhoea is the presence of nausea, vomiting and fever (16).

Although anorexia with 30-40% reduction in intake, was observed in the acute stage, consumption of 60-80 Kcal/kg/day during that period could effectively interrupt the diarrhoea malnutrition cycle. This amount of calories is necessary for normal physiological activities of the child, when food is withheld, this amount would be provided from metabolic breakdown of body's own

FIG. 2. STOOL OUTPUT (ML/KG/DAY) AND CALORIE INTAKE IN CHOLERA, *E.COLI* AND ROTAVIRUS STUDY GROUPS. THE FINE CURVE IS A LOGARITHMIC ONE AND FORM Y=A+B IN X

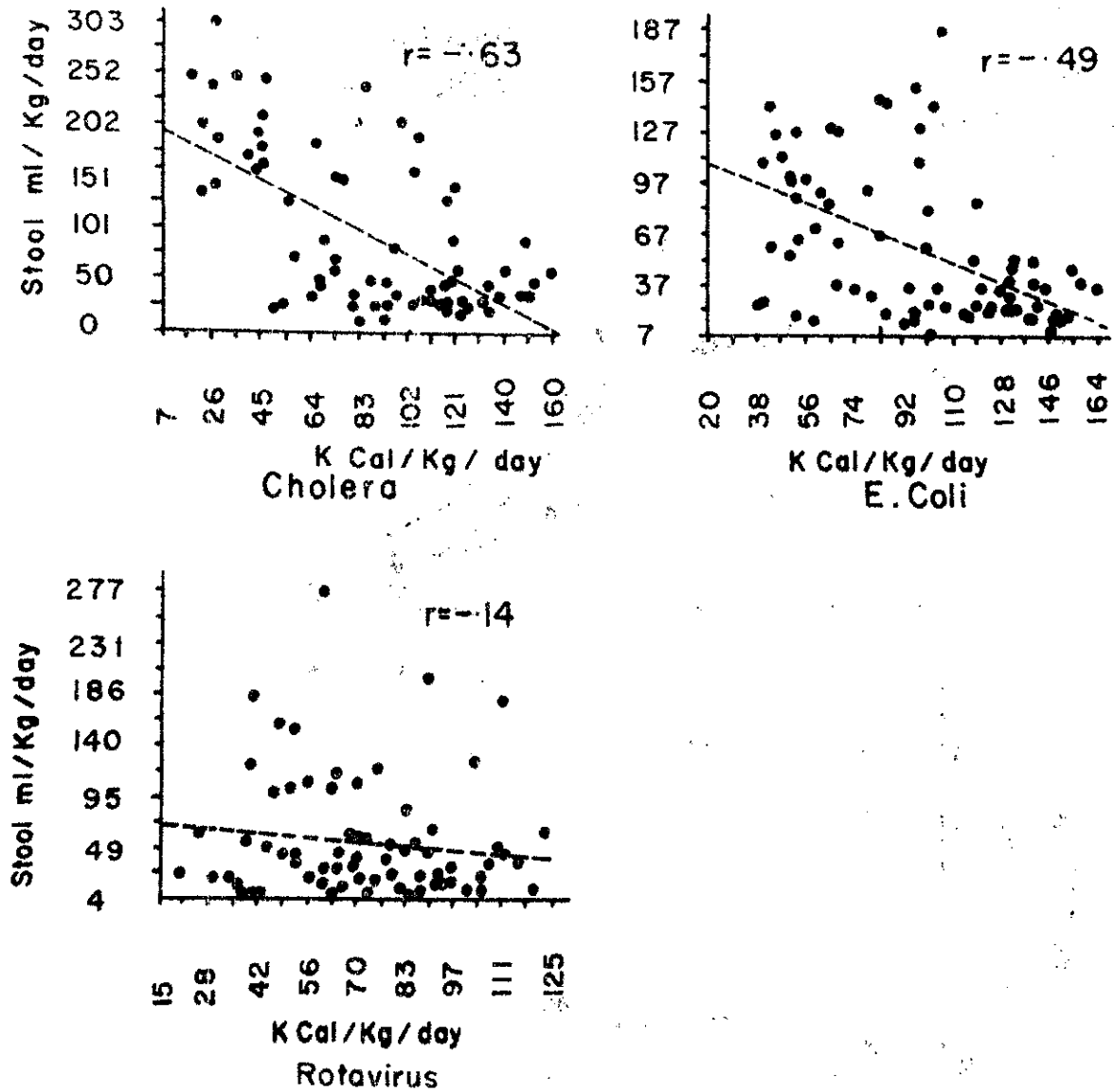
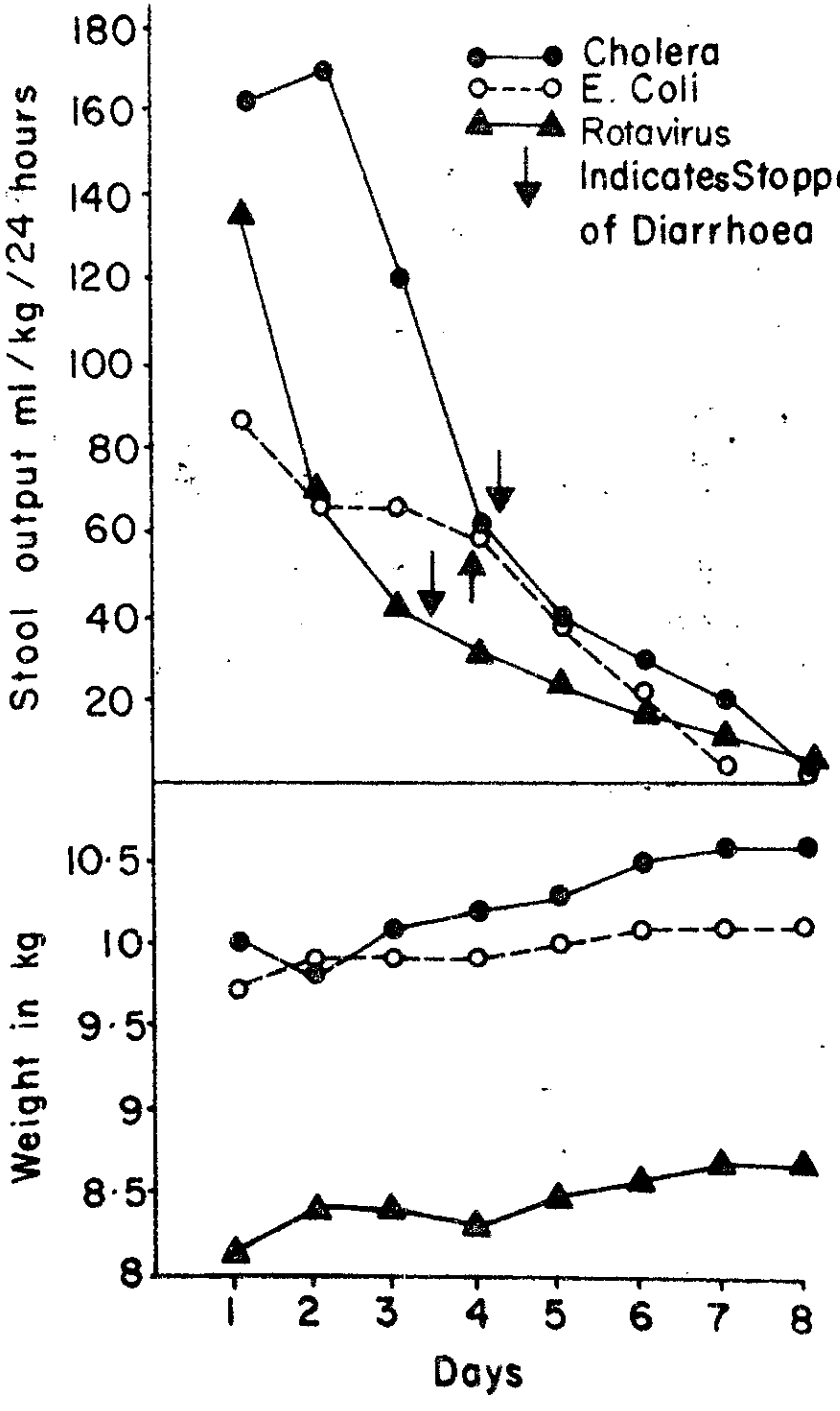


Fig. 3. DAILY STOOL OUTPUT AND CHANGE OF WEIGHT OF THE PATIENT IN ALL AETIOLOGIES



tissue. It has been shown that for each day of starvation, enhanced feeding for one whole week was necessary to recover the lost weight (17). In acute diarrhoeal episodes the role of feeding is crucial. The vicious cycle of malnutrition and reinfection may set in if proper feeding is not continued during diarrhoea (18). Chung *et al.* had demonstrated that the duration and intensity of diarrhoea may be reduced by proper feeding (19).

The continued presence of food in the intestine may present carbohydrate intolerance and enzyme depletion (20,21). Fasting even for 3 to 5 days may substantially reduce the absorption of glucose, salt, water, aminoacid and dissacharidases, with or without changes in the histology of the intestine (22).

It is clear that, absorption is directly related to intake in children and considerable intestinal absorption takes place even during severe diarrhoea (15, 19,23).

This study demonstrated that feeding does not affect the diarrhoea in terms of volume and duration, and strong evidence exists that significant absorption occurs even during acute diarrhoea (15,19,23). Hence effort should be made to feed a child during diarrhoea of all etiologies to interrupt diarrhoea-malnutrition cycle. Considerable attention should be given in convalescent stage, to provide additional food supplementation to compensate for the reduced food intake during diarrhoea. Catch up growth to pre-illness period should be achieved during this period.

ACKNOWLEDGEMENTS

The authors wish to thank the staff of the department of biochemistry; the nurses and Ms. M. Khatoon, of the metabolic unit of ICDDR,B for their skillful assistance. We also wish to extend our sincere thanks to Mr. Abbasuddin Bhuiyan and Mr. Obaidur Rab, of the department of statistics for their help in data analysis. The authors gratefully acknowledge the valuable comments of Dr. Peter Barrett, Department of Medical Education, St. Mary Medical Center, Long Beach, USA, and editing by Ms. Shereen Rahman, Associate Editor, ICDDR,B.

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