

Principal Investigator Dr. P. H. H. Trainer Investigator (if any) _____
 Application No 78-026 Supporting Agency (if Non-CRL) _____
 Title of study Assessment of ... Project status:
 () New Study
 () Continuation with change
 () No change (do not fill out rest of form)

Provide the appropriate answer to each of the following (If Not Applicable write NA):

1. Source of Population:
 a) Ill subjects Yes No
 b) Non-ill subjects Yes No
 c) Minors or persons under guardianship Yes No
 Does the study involve:
 a) Physical risks to subjects Yes No
 b) Social risks Yes No
 c) Psychological risks Yes No
 d) Discomfort to subjects Yes No
 e) Invasion of Privacy Yes No
 f) Disclosure of information possibly damaging to subject or others Yes No
 2. Does the study involve:
 a) Use of records (hospital, medical, death, birth or other) Yes No
 b) Use of fetal tissue or abortus Yes No
 c) Use of organs or body fluids Yes No
 3. Are subjects clearly informed about:
 a) Nature and purposes of study Yes No
 b) Procedures to be followed including alternatives used Yes No
 c) Physical risks Yes No
 d) Sensitive questions Yes No
 e) Benefits to be derived Yes No
 f) Right to refuse to participate or to withdraw from study Yes No
 g) Confidential handling of data Yes No

4. Will signed consent form be required:
 a) From subjects Yes No
 b) From parent or guardian (if subjects are minors) Yes No
 5. Will precautions be taken to protect anonymity of subjects: Yes No
 6. Check documents being submitted herewith to Committee:
☒ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
☒ Protocol (Required)
☐ Abstract summary (Required)
☐ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (REQUIRED)
☐ Informed consent form for subjects
☐ Informed consent form for parent or guardian
☐ Procedure for maintaining confidentiality
☐ Questionnaire or interview schedule
 * If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
 1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
 2. Examples of the type of specific questions to be asked in the sensitive areas.
 3. An indication as to when the questionnaire will be presented to the Board for review.

We agree to obtain approval of the Review Board on Use of Human Volunteers for any changes involving the rights and welfare of subjects before making such change.

in Children.

Starting Date;

1st January

Completion Date:

Expected date of completion within 6 months of starting the study.

METHODS AND PROCEDURES:

1. Subjects:

a) Patients

Children between 1-5 years of age of all sex suffering from acute watery diarrhoea due to vibrio cholerae, E.coli and rotavirus with moderate to severe dehydration will be selected for this study. A total of 80 children, as far as possible equally distributed to each group will be selected. Patients with complications, like pneumonia, tuberculosis, high fever and severe malnutrition will be excluded from this study. Those patients who received antibiotics prior to admission will also be excluded from this study.

ADDENDUM 2

b) Controls

Age and sex matched healthy children without any apparent illness will be studied as per study procedure. The children who will be studied as patients will also serve as control when they will again be studied at convalescent phase during follow up.

Locations :

The study will be carried out in CRL.

Time Period:

From 1st January 1979 and expected date of completion within 6 months from the starting of the study:

Follow Up

1st follow up:

The patients will be followed up initially after 2 weeks from the day of discharge. At this stage if the patient is found to have worms will be treated after the study procedure is completed.

During follow up studies, patients will be given test diet after a marker. Stool and urine collection will be started after the appearance of the marker in the stool on 24 hourly basis for 72 hours.

2nd Follow Up:

After 2 weeks of first follow up patients will be followed up again. From the first day of study some of the patients will receive multi-vitamins and others placed at random basis. Improvement in their food absorption will be compared and this may help us in assessing the importance of vitamins in the function of nutrient absorption of the gut.

Laboratory Tests:

Test for toxigenic E.coli (ST and LT) will be done.

D-Xylose Test will be done on the 2nd day of all admission - 5gm. of D-xylose will be given to each child and 5 hours of urine or 1 hour blood sample whichever possible will be done for D-xylose estimation.

Logistical Support:

Several variables like protein, fat, calories and electrolytes will be studied against patients with different disease conditions, acute stage and at different times during the convalescent phase also.

Analysis of variance (F-test) technique will be applied for statistical test..

SECTION 1 - RESEARCH PROTOCOL

- (1) Title: Good Absorption in Diarrhoea in Children.
- (2) Principal Investigator: DR. A. M. Molla.
- Co-Investigator: DR. Aysha Molla.
- (3) Starting Date: Feb. 1979.
- (4) Completion Date: Dec. 1980.
- (5) Total Direct Cost: US \$ 12,000. (Twelve thousand)
- (6) Scientific Program Head:

This protocol has been approved by the Pathogenesis and Therapy
Working Group.

Signature of Scientific Program Head: [Signature]

Date: 6/15/1980

Ref
2/11
78-026

SECTION - 1 RESEARCH PROTOCOL

Title: Absorption of Foods During Attack of Diarrhoea in Children

Investigators: A.M. Molla, M.A. Wahed, Ayesha Molla and M.Mujibur Rahaman

Starting Date: November 1, 1978

Completion Date: April 30, 1979

Total Direct Cost: \$ 6,211.00

Abstract Summary:

Diarrhoea is known to interfere with the intake, digestion and absorption of food. A total of 80 children below 5 years of age with diarrhoea and shigella dysentery both during acute and convalescent phases will be studied. The main objective will be to study the quantitative absorption of foods in these diarrhoeal disease. In many communities of Bangladesh, food is withdrawn during and after the attack of diarrhoea. This obviously leads to malnutrition and as such the effect of recurrent attacks of diarrhoea on the nutritional status of this affected children will also be studied.

Reviews:

- a) Research Involving Human Subjects: _____
- b) Research Committee: _____
- c) BMRC: _____
- d) Director: _____
- e) Controller/Administrator: _____

SECTION 11 - RESEARCH PLAN

A. INTRODUCTION:

1. Objective: The objective of this study are:

- (i) To find out the quantitative aspect of net absorption of foods in different diarrhoeal diseases in children.
- (ii) To study the effect of diarrhoea on the nutritional status of children.
- (iii) To assess the rationale in withholding diet during the diarrhoeal disease as practiced in the communities of Bangladesh.

2. Background: Diarrhoea in children is one of the major causes of mortality and morbidity in the developing world. One study in Latin America (Puffer and Serrano, 1973) attributed one third of all the mortality to diarrhoea. In another major study WHO showed that the mean incidences of diarrhoea is about 100-200 attacks per one hundred children (Van Jijl, 1966) and 1-4% of these episodes were fatal bringing the death rate from diarrhoea to 20-55 per 1000 children per year. In Jakarta, the mortality from diarrhoea ranged from 14-22% in children (J. Rhode, 1976). Mackay has shown that the malnutrition and diarrhoea accounted for 41% of the total deaths in 1-5 years of age groups (Rahaman MM, 1974). In Bangladesh, malnutrition and diarrhoea, both are extremely common and in many cases one may be the effect of the other. Diarrhoea is known to interfere with the intake, digestion and absorption of food, thus resulting in malnutrition. Because of many cultural practices and taboos in many communities in rural Bangladesh, withdrawal of food or a modification of food is very common. As frequency of diarrhoea is very high, and in many instances diarrhoea becomes a chronic affair, this kind of caloric restriction or caloric deprivation per se may explain part of the severe malnutrition in our paediatric population.

The deleterious effect of diarrhoea has clearly been recognised by various (Avery et al 1968, Gall and Hamilton 1974). Starvation has been shown to produce jejunal villous changes and disaccharide intolerance (Knudsen et al 1966). Chronic malnutrition and starvation

can also result in chronic secondary diarrhoea in children (Anderson, 1966; Stanfield et al 1965, Donoso et al 1965). The minimum calorie requirement for a child to maintain body weight is 75 cal/kg and more is to be added to maintain growth (Heird et al 1972). The devastating effect of diarrhoeal diseases in children is partly due to calorie restriction or deprivation either due to anorexia due to diarrhoea or because of food withdrawal as a measure to control diarrhoea. Calorie restriction as described above can alter gut function and structure, thus setting up a vicious circle. In some cases wrong or modified food like barley water or only sugar solution may be fed to the children which may aggravate diarrhoea in children with monosaccharide intolerance as noted in chronic diarrhoea (Lifshitz F et al 1970).

3. Rationale: It is known that diarrhoea may affect the nutritional status of the affected children. It may be due to decreased digestion or absorption, or both and partly increased catabolism during the diarrhoeal state. But which of the factors affected during diarrhoea can not be clearly stated. To our knowledge quantitative aspects of absorption of food has not been studied. Hence informations are needed in this field by doing balance studies or by other absorption studies to elucidate the effect of diarrhoea on the gut functions. It is also important to study the rationale of withholding diet in diarrhoeal diseases and advise the parents and the other related people in this regard.

B. SPECIFIC AIMS:

This study aims specifically at finding out the quantitative aspect of absorption of foods (carbohydrates, fat and protein) during the acute phase of diarrhoeal disease in children in comparison to convalescence.

C. METHODS OF PROCEDURE:

1. Subjects:

Children between 1-5 year suffering from acute diarrhoea due to vibrio cholerae, E.coli, NAG and Reovirus will be selected for this study. A total of 80 children as far as possible equally distributed to each group will be studied. Patients with complications like pneumonia, tuberculosis or high fever will be excluded. Those who receive antibiotics prior to admission will

2. Locations:

Subjects will be selected from patients coming to CRL or children nutrition unit and the study will be carried out in either place as necessary.

3. Time Period:

From 1st November 1978 to 30th April 1979.

4. Study Procedure:

Children with active diarrhoea will be selected for the study after initial dehydration and acidosis has been corrected. Unless definitely indicated no antibiotic will be given. Those patients who will receive antibiotic will be studied as a separate group. Test diet "khichuri" (consisting of rice, dal and vegetable oil) as designed by Dr. K. Brown and Dr. B. Clemens to each child. The amount offered will be determined by calculating the calorie required per kilogram per day, children who are on the bottle feedings will receive measured amount of standard milk formula at 4 hourly intervals. Breast fed babies will receive mother's milk at 3/4 hourly intervals and each time the baby will be weighed before and after breast feedings to find out the amount fed.* Any unconsumed food will be measured and deducted from the amount offered. Calculation will be made to show the effect of anorexia due to diarrhea. Test diet at usual intervals will be continued for 72 hours or for shorter period if diarrhoea stops earlier.

* Weaning children who on breast feeds as well as solid feeds will receive both at regular intervals in measured quantity.

Collection of Stool & Urine:

Before giving diet, a harmless marker (Tab. ultracarbon) will be given to facilitate the timing of collection. As soon as the marker will appear in the stool, collection of stool and urine will be started on 24 hourly basis upto 72 hours. Each 24 hours stool and urine will be measured and mixed separately. Duplicate samples from each 24 hours stool and urine will be done. Another marker will again be fed at convalescent stage (a) when the stool will be formed and frequency will be normal (b) sometimes, if the patient does not want to stay for long, patient will be allowed to go home and brought back after 3 weeks. Sample collection will be done as before. To prevent bacterial infection...

Laboratory Tests:

- i. At the time of marker be given, a catheter specimen of stool will be taken under oil for electrolytes.
- ii. In between the marker given and its appearance in the stool, a sample of both stool and urine (0hr specimen) for protein, fat, carbohydrate and protein respectively.
- iii. On all 24 hours specimen of stool, the assays, protein fat, and calorie will be done. Only protein will be done on urine.
- iv. ELISA assays will be done to diagnose the rota-virus.
- v. All diets will be analysed in terms of protein, fat and calorie.
Protein estimation will be done as per microkjeldal method.
Fat estimation will be done as per Ether extraction procedure (Van de kamer)
Calorie estimation will be done in bomb calorimeter.
Glucose will be estimated on both pre and post hydrolysed stool sample.
- vi. Xylose will be fed (30 ml of 16.5 gm%) and xylose will be determined on urine specimen, usually on the second hospital day.

Besides these test routine tests may be done as and when indicated for patients' routine care.

FACILITIES REQUIRED:

1. Office space: Existing office space of the investigators will be sufficient.
2. Laboratory space: Already exists in CRL - Dacca.
3. Hospital Resources: CRL ward facilities will be used.
4. Logistical support: Data processing support from statistical branch.
5. Major items of equipment: Existing equipments in Biochemistry Branch will be used.
6. Extra Personnel: Nursing assistance will be needed in addition to the investigators. One technician on daily basis may be required, if technician is not available from Biochemistry.

REFERENCES

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4. Avery G.B., Villa Vin Cercio O., Libby T.R. and Randolph J.C.: Intractable diarrhoea in early infancy. Pediatrics 41, 712, 1968.
5. Gall D.C., and Hamilton J.R.: Chronic diarrhoea in childhood. Pediatric Clinics of North America. 1974.
6. Knudsen K.B, Bellamy H.M., Lecocq F.R., Bradley E.M. and Welsh J.P. The influence of fasting and refeeding in Jejunal disaccharidases. Southern Soc. Clin. Invest. Jan 28, 1966.
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8. Donoso G, and Moncheberg F: Desnutricion infantil 1. Consideraciones generales Epidemiologica. Rev. Chile. Pediat. 36: 301, 1965.
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ABSTRACT SUMMARY

Diarrhoea is known to interfere with the intake, digestion and absorption of foods. 80 children below 5 years of age with diarrhoea and dysentery will be studied at both acute and convalescent phases. The object of this study is to see the quantitative absorption of food during diarrhoeal diseases. Food is withdrawn during and after attack of diarrhoea in many communities of Bangladesh. This obviously leads to malnutrition and as such the effect of recurrent attacks of diarrhoea on the nutritional status of the affected children will also be studied.

1. 80 children of 1-5 yr. age group suffering from diarrhoea due to *V. cholerae*, *E. coli*, NAG and R. virus will be studied. Subjects will be equally distributed according to different group of diarrhoea.
2. No potential risks.
3. Not applicable.
4. Not applicable.
5. As there is no potential risks and we will not collect any blood, we think that it is not necessary to obtain any signed consent. But it is understood that we shall not force any subject to stay in the hospital beyond their will and also beyond the day after they become fit to leave the hospital.
 - a) Not applicable
 - b) Not applicable
6. No involvement of interview except to obtain the clinical history.
7. This study aims at quantitative aspect of absorption and loss of foods (interms of Fat, Carbohydrate and Protein) in various diarrhoeal diseases. These informations which till now are not known will enable us to assess the impact of diarrhoea on the nutritional status of the children. This will also evaluate the rationale of withholding food during diarrhoea which is practiced in Bangladesh. Therefore, these informations will be very useful to the society for deciding the nutritional guidelines in paediatric diarrhoea.
8. We shall use patient records. We shall collect stool and urine for necessary assays indicated in the protocol.

SECTION III - FINANCIAL

A. DETAILED BUDGET

1. PERSONNEL SERVICES

<u>Name</u>	<u>Position</u>	<u>% of Effort</u>	<u>Annual Salary</u>	<u>Project Requirement</u>
Dr. Majid Molla	Investigator	30	90,920	Tk. 13,638
Mr. M.A. Wahed	Co-investigator	30	31,580	Tk. 3,158
Dr. Ayesha Molla	Co-investigator	10	72,630	Tk. 3,631
Dr.M.M.Rahaman	Co-investigator	5	116,740	Tk. 2,918
Mr. M.A.Rahim	Res. Assistant	30	20,910	Tk. 3,136
Study Nurse		25	16,600	Tk. 2,075
Field Assistant		20	9,600	Tk. 960
Microbiology Technician		10	15,000	Tk. 1,500
				<u>31,016</u>

2. SUPPLIES AND MATERIALS

<u>Items</u>	<u>Unit Cost</u>	<u>Amount Required</u>	<u>Project Requirement</u>
			<u>Tk.</u> <u>U.S.\$</u>
Ethyl Alcohol	\$17.00/4pt	68 pt	289.00
Toluene	4.20	22 pt	92.40
Hydrochloric acid	7.55	5 pt X 2	15.10
Potassium Hydroxide	6.45	2 lbs.	12.90
Boric Acid	5.65	2 lbs.	11.30
Sulfuric acid	6.27	1 pt	6.27
Acetone	4.05	4 pt	16.20
Nitrogen gas cylinder (refill)	TK.90.00	3	270.00
Oxygen gas cylinder (refill)	20.00	3	60.00
Zinc Sulfate	\$ 2.90	1 850	2.90
Sodium Sulfate	2.20	1 850	2.20
Sodium Carbonate	4.75	1 850	4.75
Sodium-K-Tartrate	4.75	1 850	4.75
Sodium bicarbonate	1.80	1 850	1.80

<u>Items</u>	<u>Unit Cost</u>	<u>Amt. req.</u>	<u>Project. req.</u>
			Tk. \$
Copper sulfate	\$ 3.40	1 Btl	\$ 3.40
Ammonium molybdate	5.75	1 Btl	5.75
Sodium orthoarsenate	4.50	1 Btl	4.50
Barium hydroxide	2.50	1 Btl	2.50
Acetic acid	4.50	1 Btl	4.50
Thiourea	1.00	1 Btl	1.00
P-bromoaniline	7.90	1 Btl	7.90
50ul disposable pipette	5.00 each	6 pkt	30.00
			<u>519.12</u>

For ELISA Assay

Tk. 2.50/test

Tk. 250.00

Tk. 250.00 \$519.12

3.	<u>EQUIPMENT</u>	Nil	
4.	<u>PATIENT HOSPITALIZATION</u>		
	340 pt. days	150 X340	Tk. 51000.00
5.	<u>OUTPATIENT CARE</u>	Nil	
6.	<u>CRL TRANSPORT</u>		
	500 miles	3.40 X500	1700.00
7.	<u>TRAVEL AND TRANSPORTATION OF PERSONS</u>	-	
8.	<u>TRANSPORTATION OF THINGS</u>	-	
9.	<u>PRINTING AND REPRODUCTION</u>		
	Mimeograph	300 copies	150.00
	Xeroxing	100 copies	150.00
			<u>300.00</u>
10.	<u>OTHER CONTRACTUAL SERVICES</u>	Nil	
11.	<u>CONSTRUCTION, RENOVATION, ALTERATIONS</u>	Nil	

BUDGET SUMMARY

<u>CATEGORY</u>		<u>YEAR - 1</u>	
		<u>Taka</u>	<u>Dollar</u>
1.	Personnel	31016.00	
2.	Supplies	580.00	519.12
3.	Equipment		
4.	Patient hospitalization	51000.00	
5.	Outpatient care	-	-
6.	CRL Transport	1700.00	
7.	Travel Persons	-	-
8.	Transportation of things		52.00
9.	Printing & reproduction	300.00	
10.	Contractual services	-	-
11.	Construction	-	-
12.	Rent/Communication	-	-
Total		84596.00	571.12

Total U.S.\$ 5,640.00

Grand total U.S.\$ 6,211.00

Tk. 15.00 = 1 U.S. \$

CONSENT FORM

Food Absorption During Attack of Diarrhoea

The Cholera Research Laboratory (ICDDR,B) is carrying out research to see the absorption of foods during attack of diarrhoea both at acute and convalescent phase. We would like your child to participate in this study. Information out of the study will enable us to assess the impact of diarrhoea on the nutritional status of your children and also help us to evaluate the rationale of withholding foods during diarrhoea as practiced in Bangladesh.

If you decide on behalf of your child to participate in the study, the following procedures will be carried out:

1. Your child will be fed a measured special diet made of rice, dal, sugar and vegetable oil.
2. Before this diet, a harmless marker will also be fed.
3. Stool and urine will be collected before and after the diet 24 hourly basis till diarrhoea stops.
4. Your child has to stay for another 72 hours after diarrhoea stops.
5. We shall bring your child to carryout the above again after 2 weeks and 4 weeks of discharge. During follow up, we shall give your child necessary medicine and vitamins.
6. Routine patient care for all associated diseases will be taken care of.
7. It is ^{your} right to withdraw your child from the study at any time and in that case you should not be afraid of your child's care in terms of treatment in the hospital.

If you agree, please sign below:

Signature

Relative _____

জামিনী। চল্লিশালীন বেলার মাঝে ২৬শে মে মাসে
জামিনীয়ার একটি জামিনী চান্নাড়ে। আমতা চাই, আম
হাচ্চা এই জামিনীয়া অংশ গ্রহন করুক।

জামিনীয়ার জন্য যে মুক্তি শাস্তি হয়, সেই জামিনীয়ার ফলে তার
নির্ভর করা মাঝে। তাইনাভেদে প্রায়ই দেখা যায় যে, জামিনীয়ার
সময় বাচ্চাদের যোজা বেড়ে যাওয়া বলে তাদের মাঝার সেও দেখা
হয়না। প্রায়শ চলিত সহজাতের জুলিয়ায়নাও ২৬ এই এই জামিনীয়া।
আমতার আমতা না মাঝে, আমতার বাচ্চা এই জামিনীয়া অংশ
নির্ভর এবং নিম্নলিখিত ব্যক্তি গ্রহন করা হবে।

(১) আমতার বাচ্চাকে পরিমিত মত চাল, ডাল, তেল এবং চিনি প্রদান
করা মাঝার দেখা হবে।

(২) এই মাঝার খাওয়ার আগে একটি উমর মাঝারনা হবে।

(৩) জামিনীয়া বন্ধ ২৩শার পূর্ব পর্যন্ত প্রতি ২৪ ঘণ্টার প্রায় এবং
জামিনীয়া পরীক্ষার জন্য নিম্না ২৬।

(৪) জামিনীয়া বন্ধ ২৩শার ১২ ঘণ্টা পর্যন্ত বাচ্চাকে খাওয়ানো
হবে।

(৫) আমতার বাচ্চা বামাস চলে মাঝার ২ সপ্তাহ এবং ৪ সপ্তাহ
পর আমতা আরো উপস্থাপিত জামিনীয়া করা-জানু আমতার
বাচ্চাকে খাওয়ানো আমতার উপদেশ দেবে। এই সময় প্রায়-
জন মত উমর ও ডিটোমিত আমতার-বাচ্চাকে দেখা হবে।

(৬) সকল প্রকার মেডের মাঝার জন্য আমতার-বাচ্চাকে নির্ধারিত
চিকিৎসা করা হবে।

(৭) যে কোন সময় আমতার বাচ্চাকে এই জামিনী থেকে প্রত্যাহার
করে নিও পারবেন, তাও আমতার বাচ্চার আত্মিক চিকিৎসার
কোন অতি হবেনা।

এই জামিনীয়া মাসের ২৬ রাজী থাকল মাঝার করুন।

স্বাক্ষর