

Locally Made Ready-to-Use Therapeutic Food for Treatment of Malnutrition: A Randomized Controlled Trial

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Objective: To evaluate the effectiveness of a locally made ready-to-use therapeutic food (RUTF) in decreasing mild to moderate malnutrition.

Design: A randomized open label, controlled trial.

Setting: Pre-schools run by the Department of Community Health in Kaniyambadi administrative block, Vellore, India; duration of follow-up – 3 months from the date of recruitment.

Participants: Pupils aged 18-60 months with Weight-for-Age ≤ 2 SD.

Interventions: A locally produced energy-dense supplement (RUTF), and the current standard of care [teaching caregivers how to make a fortified cereal-milk supplement called High Calorie Cereal Milk (HCCM)].

Main outcome measures: Increase in weight-for-age status; increase in levels of plasma zinc, vitamin B₁₂, serum albumin and haemoglobin.

Results: The Mean (SD) weight gain at 3 months was higher in the RUTF group: RUTF ($n=51$): 0.54 kg; (SE = 0.05; 95% CI = 0.44 – 0.65) vs HCCM ($n=45$): 0.38 kg; (SE = 0.06; 95% CI = 0.25 – 0.51), $P = 0.047$. The weight gain per kilogram of body weight was directly proportional to the severity of malnutrition.

Conclusions: Community-based treatment showed weight gain in both groups, the gain being higher with RUTF.

Key words: India, Indigenous, Management, Malnutrition, Nutrition therapy.

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The third National Family Health Survey estimated that 45.9% of Indian children and 33.2% of children in Tamil Nadu below 3 years of age are underweight(1). Mild-to-moderate malnutrition has been associated with an increased risk of childhood mortality(2,3). Treatment of malnutrition has largely been restricted to health education directed at increasing the caloric and protein content of a young child's diet. Severe malnutrition has been treated in a hospital setting.

Ready to use high energy foods to be provided to the caregiver of a malnourished child has been a paradigm shift in the management of malnutrition. Evidence is largely restricted to severe malnutrition, where home-based and community-based therapy

with nutrient-dense foods has been found to be more cost-effective than in-patient care of severe acute malnutrition (SAM). Home-based treatment has been recommended during the rehabilitation phase of treatment for malnutrition in areas where follow up is possible(4). The use of ready-to-use therapeutic foods (RUTF) for the treatment of moderate malnutrition has been reported to result in an average weight gain of 12.7% over a period of 28 days in moderately malnourished children(5).

This trial was designed to evaluate the effectiveness of community-based therapy with a locally produced RUTF in comparison with the standard of care, for treatment of all grades of malnutrition, by anthropometry, measurement of

micronutrient levels, and intestinal function in children < 60 months attending local pre-schools.

METHODS

This study was an open-labeled randomized controlled trial. Children were randomly assigned to either receive a locally produced energy-dense RUTF, administered in pre-schools by teachers, compared to the current standard of care: to teach caregivers to prepare a fortified cereal-milk supplement (High-Calorie Cereal Milk; HCCM), and advised 2 x 100 ml feeds per day. Both arms included continuation of family diets.

Sample size estimation

A total of 120 children (60 in each intervention group), assuming a 5% drop-out had 80% power to detect a difference of 50% of reduction in the proportion of malnutrition between groups, with an overall type I error of 5%.

334 children between the ages of 18 to 59 months were screened in 16 pre-schools, information leaflets sent home with the parents, the parents met at a later date, and 128 children recruited after obtaining written informed consent. Ten were later excluded. The study was approved by the Institutional Review Board of the Christian Medical College, Vellore, India.

Block randomization was done in blocks of ten using a computer-generated sequence, generated by the statistician. The children were allocated to either group by one of the investigators. Measurement of anthropometry, measurement of micronutrient levels and intestinal function were done.

Participants in the study were children recruited from 16 village pre-schools run by the Community Health and Development (CHAD) Hospital of the Christian Medical College, Vellore. Children aged 18-60 months, -2 SD weight-for-age and below but not requiring hospitalization for malnutrition, were considered eligible. Children younger than 18 months were excluded as several of them were receiving a predominantly milk diet, as chosen by their parents.

The children received supplementation for three months from recruitment, the study running from January to the end of May 2008. Baseline assessment of nutritional status, micronutrient levels and intestinal function were carried out immediately following recruitment. Weight and height were measured, and blood samples taken for estimation of serum albumin, plasma zinc, plasma vitamin B12, hemo-globin and red cell indices. The micronutrients chosen for assay were those that were considered clinically useful. All children underwent D-Xylose testing for evaluation of intestinal function.

Weight was measured to the nearest 100g on a regularly calibrated electronic scale with the child standing barefoot and undressed. Height was measured to the nearest 1 mm using standard measuring techniques, the mean of two readings was calculated for each child. Weight and height at day 30, day 60, and day 90 after recruitment, with a window of +5 days to allow for holidays and weekends (*Fig. 1*). All measurements were done by one investigator. Blood were drawn by a research nurse. Definition of anemia was as defined by the World Health Organization for children aged 6 months to 5 years (Hb<11 g/dL)(8). Five mL of venous blood was drawn, at recruitment and final follow-up. The tests for hemoglobin and red cell indices were conducted using the Sysmex KX21 auto analyzer. Plasma zinc was tested using an atomic absorption spectrometer (Perkin Elmer AAnalyst200). Serum albumin was tested by a colorimetric method using bromocresol green as an indicator on an Olympus/Hitachi 912 auto analyzer. Vitamin B₁₂ was tested using the Roche Immunoassay system. Five-hour urine samples were collected after the oral administration of D-Xylose according to the child's weight, to measure intestinal barrier function. This was done at recruitment and final follow-up. Urine D-Xylose testing was estimated by colorimetry using Phloroglucinol(6). Body impedance anthropometry was done on day 60 and day 90 following recruitment. Baseline measurements are not available.

The primary outcome of the study was recovery, defined as the attainment of a Weight-for-Age Z score >-2. Secondary outcomes were changes in the vitamin B₁₂, plasma Zinc, serum albumin levels and iron status of the children.

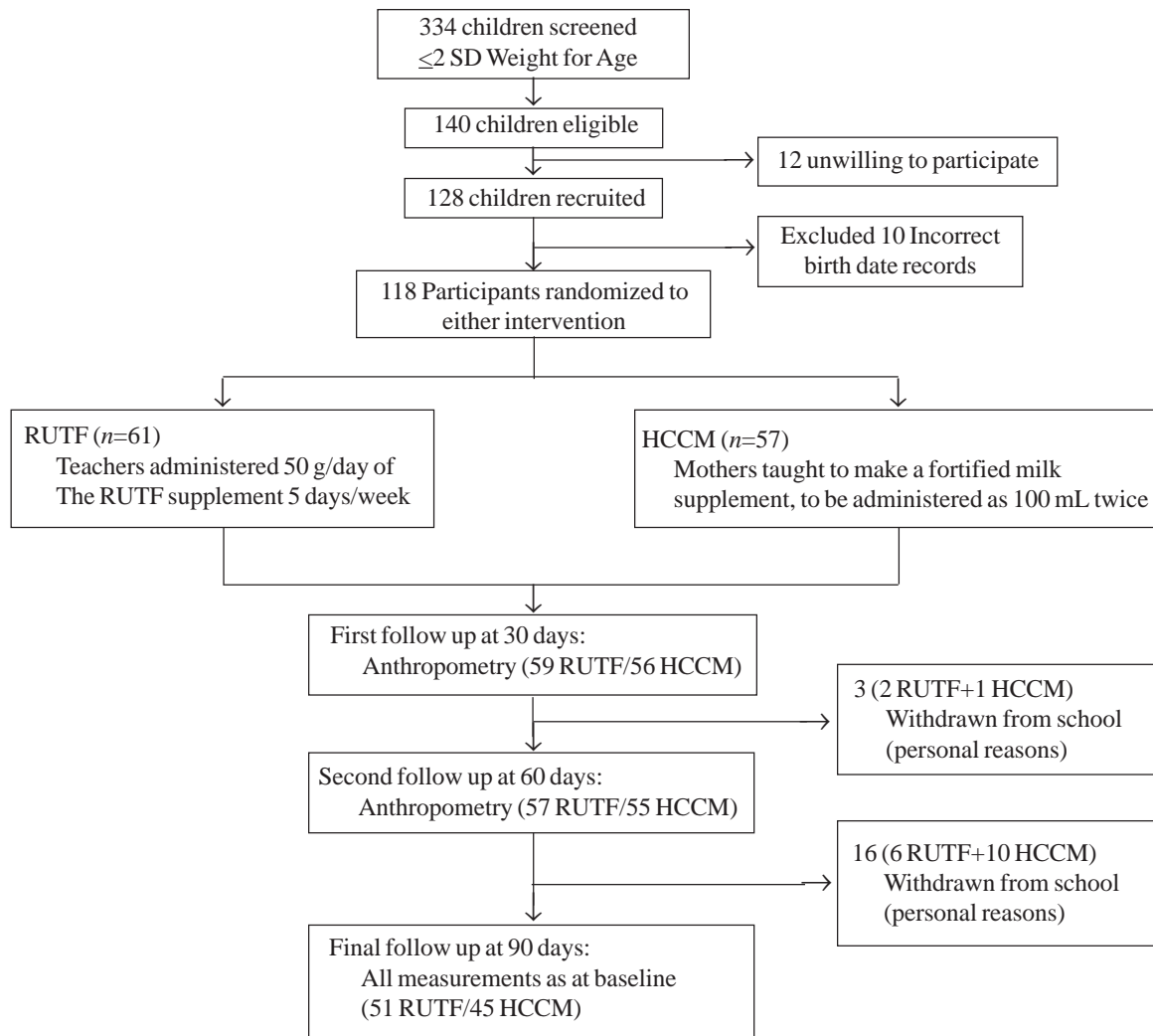


FIG. 1 Study Flow Chart.

Dietary Interventions

The RUTF was prepared weekly, under supervision, at a local bakery and packed into new polythene bags (250 g per bag), heat-sealed and distributed to the pre-schools. The RUTF was produced by mixing together ground roasted peanut powder, milk powder, and sugar in a ratio of 30:28:25 (grams), along with 15 grams of gingili oil. Multivitamin supplements of 2 grams to the above ratio of mix resulted in a medicinal after-taste after a week, which was unacceptable to the children and this quantity was reduced to 1 tablet per 100 g of mix. Oral multivitamins were supplemented. The teachers were

weekly provided with one 250 g bag of RUTF for each child, to be administered at a rate of 50 g per child per working day, at 5.5 Calories per Gram. The RUTF was given during the mid morning and mid afternoon breaks, approximately 50 g per working day, equal to about 1.5 tablespoons per helping.

Mothers of the children receiving, High Caloric Cereal Milk (HCCM) were taught how to make the supplement. HCCM consisted of 100 mL milk fortified with 15 g flour of mother's choice, 5 mL oil and 2 teaspoons of sugar, cooked to a porridge-like consistency. Two servings of HCCM made with 100 mL of milk each, were advised, and were to be given at home.

All children additionally continued to receive their normal diets, including one hot meal provided by the preschool every working day as part of the PTMGR Nutritious Meal Program, where each child below six years of age receives a nutritious noon meal prepared with rice, dhal, oil and vegetables containing a caloric value of 358.2 to 780.3 and 8.62 g to 12.55 g of protein served every school day(7). The nutritive values of the 2 products are dissimilar, RUTF containing 550 Cal per 100 g of product and HCCM containing 187 Calories per 100 mL.

Recruitment was done in January and the intervention started from the date of recruitment. Measurements were taken on day 1, day 30, 60 and 90, with a window of 5 days after the scheduled date, allowing for holidays and weekends. The last measurement of the children recruited last was completed at the end of May 2008.

Anthropometric indices were calculated using WHO Anthro (v 2.0.2; Department of Nutrition, World Health Organization). To compare the differences between the two groups, the chi square test was performed for dichotomous outcomes and one-way ANOVA or *t*-test for continuous outcomes. Weight gain in the two groups was compared using the linear regression analysis. All analysis were performed using SPSS version 15.0 and Epiinfo version 2002.

RESULTS

Of the 140 malnourished children identified, 128

were recruited (**Fig 1**). Confirmation of dates of birth and rechecking weight resulted in 10 children being excluded. 118 children were enrolled (**Table I**). At the end of the study, 96 children remained for follow-up, of whom 51 received RUTF and 45 received HCCM. Mean (SD) weight gain in 3 months was as follows: RUTF ($n=51$): 0.54 kg; (SE = 0.05; 95% CI = 0.44 – 0.65) and in the group that received HCCM ($n=45$): 0.38 kg; (SE = 0.06; 95% CI = 0.25 – 0.51). The linear regression analysis showed that the group receiving RUTF gained 0.168 kg (95% CI 0.002 – 0.333; $P=0.046$) more than the other group. The data for the individual children in the group were aggregated. **Table II** shows the weight gain (g)/kg body weight/day during the subsequent month for the different weight-for-age Z score classifications in the children in the two groups daily categorized according to the degree of malnutrition. The table shows that the greater the degree of malnutrition, the higher the weight gain; with a seemingly higher weight gain in the RUTF group, though the results are not statistically significant. The gain in weight persisted in the third month only in the children who were <-3 SD weight for age. **Figure 2** shows scatter plots of the weight gain per kilogram of body weight per day of the groups receiving the two supplements. In both groups it is evident that the weight gain per kilogram is higher, the greater the degree of malnutrition.

Significant increases in serum albumin was seen in both the RUTF [$P=0.045$] and the HCCM

TABLE I BASELINE DATA FOR ALL CHILDREN (N=118) WHO COMPLETED THE STUDY AND THOSE WHO DROPPED OUT, SHOWN SEPARATELY

Characteristics	Intervention			
	Ready-to-use Food (RUTF)		High Calorie Cereal Milk(HCCM)	
	Participants ($n=61$)	Dropouts ($n=10$)	Participants ($n=51$)	Dropouts ($n=12$)
Gender: Male	29 (47.5%)	5 (50%)	26 (45.6%)	5 (41.7%)
Mean (SD) age (in years) at recruitment	3.53 (0.87)	3.61 (0.77)	3.59 (0.85)	3.50 (1.06)
Median (IQR) number of siblings ($n=108$)	1 (1 – 2)	1 (1 – 1)	1 (1 – 2)	2 (1 – 2.5)
Maternal education > Grade V ($n=110$)	35 (57.4%)	8 (80%)	29 (50.9%)	5 (41.7%)
Mean (SD) weight (in kg) at recruitment	10.79 (1.28)	11.07 (1.37)	10.98 (1.34)	10.93 (1.58)

TABLE II MEAN (SD) WEIGHT GAIN (g)/kg BODY WEIGHT/DAY FOR THE DIFFERENT WEIGHT-FOR-AGE Z SCORE CLASSIFICATIONS IN THE TWO GROUPS

Weight-for-age Z Score	Intervention					
	Month 1	RUTF*			High Calorie Cereal Milk*	
	Month 1	Month 2	Month 3	Month 1	Month 2	Month 3
< 0 to -1	–	–	–	–	–	–
< -1 to -2	–	0.53 (1.40)	-0.90 (0.93)	–	0.40 (1.37)	-1.02 (1.02)
< -2 to -3	1.00 (0.91)	0.61 (1.05)	-0.07 (0.90)	0.65 (1.12)	0.51 (0.93)	-0.09 (0.95)
< -3 to -4	1.54 (1.42)	0.50 (0.90)	0.86 (0.64)	0.74 (1.06)	1.61 (1.54)	0.24 (0.62)
< -4	0.92	–	–	–	–	–

* Differences not statistically significant.

[$P=0.027$] groups, as were changes related to anemia, with improvement in both arms, the results of which are shown in **Table III**. D-Xylose absorption test showed improvement of intestinal function. (**Table III**) At baseline, 40 (75.5%) children in the RUTF and 42 (79.2%) in the HCCM group had abnormal function, while by the end of the study, 27 (57.4%) had abnormal absorption in the RUTF group and 23 (50%) in the HCCM group. There were no adverse events reported.

The cost of one month's supply of RUTF, at the rate of 250 g per week, or 50 g per week day, for each child was calculated to be approximately INR 135 (USD 2.95).

DISCUSSION

The RUTF in this study differed from the formulation recommended by the WHO in the micronutrient composition(9). There was significant improvement in the macro - and micro-nutritional status of participants. As the study was done in the time of year that included school holidays, with children moving on subsequently to other schools, 22 children did not complete 3 months of follow up. Nevertheless, the results expressed as weight gain per kilogram of body weight per day show that there is an increase in weight in both arms, with the degree of weight gain being directly proportional to the severity of the malnutrition. In the third month, there was no weight gain in the better nourished children, though the more severely malnourished continued to gain weight. It appears that RUTF results in a higher weight gain in the first month. The results are not statistically

significant, but this may be worth pursuing in subsequent studies with larger numbers. It is of note that both forms of therapy result in weight gain.

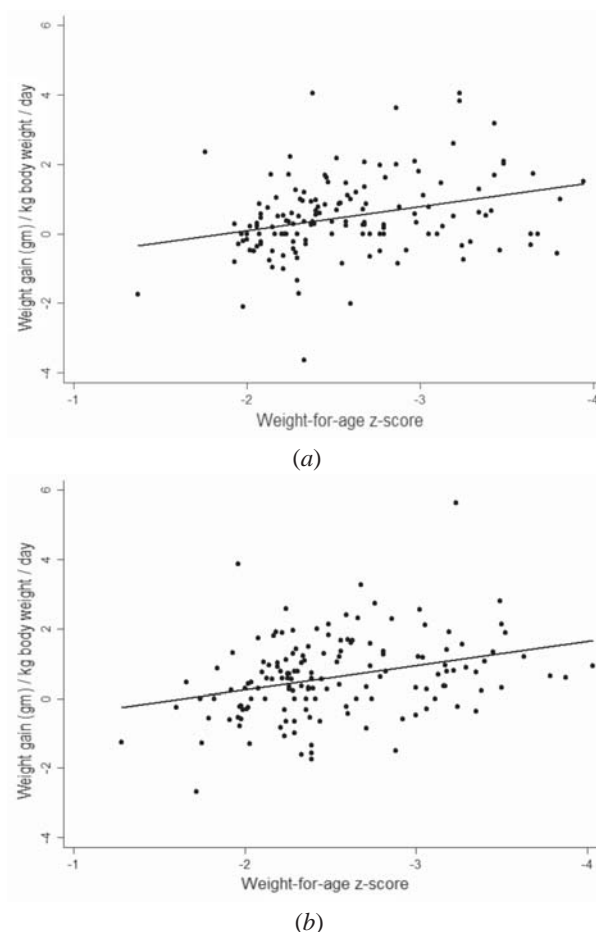


FIG. 2 Scatter plot showing the weight gain against the weight for age Z scores for the group receiving (a) high calorie cereal milk; and (b) the ready to use therapeutic food supplement.

WHAT IS ALREADY KNOWN?

- For the treatment of malnutrition, home-based and community-based therapy with nutrient-dense foods such as RUTF is more cost-effective

WHAT THIS STUDY ADDS?

- Using locally made RUTF in the community-based treatment of childhood malnutrition is feasible and effective in a rural South Indian setting.

The effects of the supplements on zinc are noteworthy, and though the explanation of the reduction of levels of zinc in both arms is unclear, it is possible that nutrient interactions with other micronutrients in the supplement, the presence of phytates or dietary fiber may have affected its absorption and bioavailability(11,12). It could perhaps be that the dose given was insufficient to cope with the increased demand for zinc with the increase in weight.

The WHO recommends treatment of uncomplicated severe acute malnutrition at home(9). The Indian Academy of Pediatrics (IAP) has made recommendations for recognition of those children who must be referred to a facility for treatment(13). The success of home-based treatment of severe malnutrition would require the provision of a nutrient-dense supplement which can be safely stored and administered without much preparation by the caregiver. Commercially available nutrient dense foods are expensive, and locally produced

nutritious mixes have not been compared to the present standard of care for home based treatment.

The RUTF used in this study was prepared from locally available ingredients and in a local bakery. The RUTF, or local modifications, can be prepared safely and in small or large quantities. A lower incidence of peanut allergies has been noted among children in developing countries, as compared to those in developed countries, especially as they may additionally suffer from severe malnutrition and comorbid conditions that further suppress immune function(14). However, this possibility must be considered whenever a peanut based product is used. In an Indian setting, the community-based treatment of malnutrition can find extensive application, and the involvement of pre-school teachers and mothers' groups in its delivery is a viable option. Any sustainable treatment for malnutrition has to rely on modifications of local foods. RUTF itself is used in the acute phase of rehabilitation and is prescribed as a therapeutic item, not a food.

TABLE III CHANGE IN MICRONUTRIENT STATUS AND URINE D-XYLOSE EXCRETION % OF CHILDREN AFTER THREE MONTHS OF SUPPLEMENTATION

	Vitamin B ₁₂		Plasma zinc		Albumin		Hemoglobin		D-Xylose excretion %	
	RUTF	HCC M	RUTF	HCCM	RUTF	HCCM	RUT F	HCC M	RUTF	HCCM
Mean	-70.23	-9.64	21.76	18.67	-0.98	-0.109	-0.447	-1.295	4.725 [†]	8.633 [†]
95% CI of the difference*	-135.74	-49.22	21.76	10.16	-0.98	0.204	-0.447	-4.247	0.517	4.227
	to	to	to	to	to	to	to	to	to	to
	-4.72	29.94	11.47	27.17	-0.193	-0.13	-0.899	1.657	8.933	13.039
Significance	0.036 [#]	0.626	0 [#]	0 [#]	0.045 [#]	0.027 [#]	0.053	0.381	0.029 [#]	0 [#]

*Difference calculated as baseline – final, therefore, positive values of the mean imply a decrease and negative values an increase in serum levels of the substance measuredF; [†]decreasing D-Xylose excretion % indicates improvement in intestinal barrier function: [#]statistically significant.

The study had several limitations. The numbers available for analysis at the end of the study were small. The study could have been done in the early part of the academic year, i.e. June to December, and the movement of children into other schools at the end of the school year should have been anticipated. The study is not ideal in that it was not blinded, but blinding would have been difficult for two very different but acceptable interventions.

To summarize, this study showed that community based treatment of malnutrition is a feasible, effective and well-accepted intervention. The ingredients for the RUTF are widely available and the supplement can be locally produced. The cost-effectiveness of this method of therapy needs to be evaluated.

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Contributors: AB: conceived and designed the study with GK and both revised the manuscript for important intellectual content. AB will act as guarantor of the study. AS: conducted the study, collected data and drafted the paper; AR: conducted the laboratory tests, and interpreted them; P analyzed the data with A and helped in manuscript writing. All authors approved the final manuscript.

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