

SMALL INTESTINAL ENTEROPATHY IN UNDERNOURISHED CHILDREN IN THREE URBAN SLUMS IN SOUTH INDIA

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ABSTRACT

Introduction: Growth faltering is a common health issue in the developing countries. At times we are unable to attribute this growth faltering to lack of adequate nutrients in food or ongoing disease conditions alone. With this study we aim to assess the possibility of the existence of subclinical malabsorption in children with undernutrition. **Methods:** A cross sectional study was conducted on a sample of 161 children from a birth cohort of 377 children who were under follow up from birth for health and disease in three of the urban slums of Vellore. The prevalence of small intestinal enteropathy, as assessed by a 5 hour urinary d-xylose excretion test, was compared between undernourished and well-nourished children. Correlation between undernutrition, d-xylose malabsorption and previous documented illnesses including viral, bacterial or parasitic infections/ infestations was also studied. **Results:** Xylose test result was abnormal in 41% (25 of 61) of undernourished children as against 26% (26 of 100) of well-nourished children, with p value of 0.047 and Odds ratio of 1.976 with 95% confidence interval between 1.003 and 3.895. **Conclusion:** There is a statistically significant association between undernutrition and small intestinal enteropathy.

INTRODUCTION

There is a high prevalence of undernutrition in the developing and the least developed countries. In India the proportion of children who are moderately and severely underweight (below minus 2 standard deviations (SD) from median weight for age of reference population) is 43% and those who are severely underweight (below minus 3 SDs from median weight for age of reference population) is 16%. This is higher than the prevalence in the world which is 15% and 9% respectively. Similarly, the proportion of children who are moderately and severely stunted (below minus 2 SDs from median height for age of reference population) is 48% in India as against 25% in the world^[1]. Children from developing countries grow more slowly and achieve a shorter adult height than those from wealthier regions^[2]. Of the various possible factors, dietary inadequacy and disease prevalence are generally believed to have the greatest impact on growth. But there is frequently an inability to attribute long-term growth faltering to either nutritional factors or overt clinical disease. This has led to speculation about the role of gastrointestinal tract, and particularly the mucosa of the small intestine, as this represents a major interface between the body and the environment^[3]. Environmentally induced damage to the mucosa could compromise both nutrient uptake and barrier function, both of which could lead to impaired growth^[4, 5]. Several studies have suggested an association between abnormal intestinal function and growth failure. There is a lack of Indian studies looking into this issue. We had the opportunity to undertake this study in a group of children who were being closely monitored for health and disease.

We also attempt to study the relationship between infection/infestations, malnutrition and malabsorption.

AIM AND OBJECTIVES

1. To compare the prevalence of small intestinal enteropathy as assessed by d-xylose absorption test among undernourished and well-nourished children in a birth cohort of 377 children in three of the urban slums of Vellore.
2. To study the association of small intestinal enteropathy in undernourished children with prior gastrointestinal infections / infestations.

MATERIALS AND METHODS

Study Design: A cross sectional study.

Study Population: Three urban slums of Vellore namely Ramnaickan palayam, Chinna allapuram and Kaspas which are geographically adjacent to each other and well demarcated covering an area of about 2.2 sq kms. The study population included a birth cohort comprising of 377 children who were being followed up for health and disease through a clinic run in the area. The study area was mapped and pregnant women were identified through repeated household surveys and from local antenatal clinics. The babies of those intending to remain in the area for 3 years were eligible for enrolment. Those who lived in brick-built houses with 5 or more rooms (to exclude the higher socio economic group which may not

be compliant) and those who had babies born with gross congenital anomalies or a birth weight of less than 1500 g were excluded from the cohort. Recruitment was done consecutively. Ethical clearance was obtained. Informed consent was taken from those enrolled in the study. The original cohort consisted of 452 children. 75 children had dropped out by the time this study was started. Reasons for drop out included death of 4 children, migration of 44 children and refusal of 27 children to continue to be part of the cohort. Therefore 377 children were under follow-up.

Sample Population: Weight and height measurements taken at the start of this study were used to classify the population into well-nourished and undernourished groups. Weight for age (WAZ) and weight for height Z scores (WHZ) with standard deviations (SD), with reference to Centers for Disease Control and Prevention (CDC) growth data were calculated using Nutstat program (Epi Info software).

Inclusion Criteria: Undernourished and well-nourished children were selected from the cohort based on the following criteria: Undernourished children were those who had WAZ and WHZ lesser than -2 SD, well-nourished children were those children with WAZ and WHZ greater than -2 SD.

Exclusion Criteria: Those who had only one of these values below -2 SD were not included into the study.

Sample Size: Sample size for this study was determined using Epi Info software^[6]. The expected prevalence of malabsorption among well-nourished and undernourished children was considered to be 10% and 30% respectively. A sample size was calculated for 80% power and 95% confidence interval. The sample size thus determined was 51 undernourished children and 102 well-nourished children. The well-nourished group was randomized and 119 children were called to participate in the study. Sixty three most undernourished children were called to participate. Sixteen of these well-nourished children and one undernourished child refused to take part in the study. Parents of these children were contacted at home by the field workers explaining the study and asking them to come to the clinic to take part in the study. Thus 62 most undernourished and 103 well-nourished children were included in the study after informed consent was taken from the parents. Four children (1 from undernourished group and 3 from well-nourished group) had to be excluded due to inability to collect the urine sample satisfactorily in spite of repeated attempts. Final analysis was done on 61 undernourished and 100 well-nourished children.

Data Collection: Baseline data including date of birth, sex, current nutritional status as per Z scores and history of diarrheal episodes in the past were collected from previously available records. Stool samples from children in the cohort were being collected periodically for rotavirus testing. An enzyme linked immunosorbent assay (ELISA) (DakoCytomation Ltd, United Kingdom) was being used for this purpose. Stool samples were also collected for culture and microscopy if and when the children developed a diarrheal disease. Correlation between positive tests from these samples, xylose malabsorption and malnutrition was also studied. A 5 hour urinary d-xylose excretion test was

performed on all the children enrolled into the study after an informed consent of a parent.

Procedure:

1. Child was kept nil per oral from 4: 30 am on the study day.
2. Urine voided by the child at around 7: 30 am was discarded.
3. 0.1g/kg of d-xylose was given orally.
4. Urine voided during the next 5 hours was collected.
5. Child was allowed to drink liberal amounts of water during this period.
6. Child was allowed to eat an hour after starting sample collection.
7. The test was repeated on a later date if the sample collected was less than 200 ml or obvious spillage of large volumes of urine had occurred.
8. Urinary samples collected in the urban clinic were transported to the hospital immediately for analysis.
9. Samples were analyzed for d-xylose using a calorimetric method.
10. Values below 18% of the dose given were considered indicative of malabsorption as per the standards used by the laboratory.

The test had to be repeated on 8 children due to inability to collect the entire sample the first time. Samples could not be satisfactorily collected from 4 children and hence they were excluded from the study.

Statistical analysis: The comparison of d-xylose absorption in undernourished and well-nourished children was done by the t- test for equality of means. Pearson chi-square test was used to assess the statistical significance. P value of less than 0.01 indicates highly significant and value of less than 0.05 indicates significant. The odds ratio was used to estimate the relative risk.

RESULTS:

Out of the total cohort of 377 children, there were 242 children (119 males and 123 females) who had WAZ below 2 SD. Of them 182 fulfilled the inclusion criteria and 195 were excluded.

Table 1: Nutritional Status of study population who fulfilled the inclusion criteria

Sex	Nutritional Status		Total
	Undernourished	Well-nourished	
Male	36(57.1%)	62(52.1%)	98
Female	27(42.9%)	57(47.9%)	84
Total	63	119	182

Data from the sample population, which included 61 undernourished and 100 well-nourished (161 totally) children was analyzed.

Table 2: Sample Population

Sex	Nutritional Status		Total
	Undernourished	Well-nourished	
Male	26(42.6%)	47(47%)	73
Female	35(57.4%)	53(53%)	88
Total	61	100	161

There was no statistically significant difference in the nutritional status between the two sexes in the sample population. P = 0.588.

The age of the children in the sample population ranged from 21 to 38 months.

Table 3: Age Distribution

Age Group in months	Nutritional Status		Total
	Undernourished	Well-nourished	
18-24	3(4.9%)	4(4%)	7
24-30	27(44.3%)	40(40%)	67
30-36	23(37.7%)	52(52%)	75
36-42	8(13.1%)	4(4%)	12
Total	61	100	161

There was no statistically significant difference in the distribution of age groups among the well-nourished and undernourished groups. P = 0.106.

Xylose test result was abnormal in 41% (25) of undernourished children as against only 26% (26) of well-nourished children.

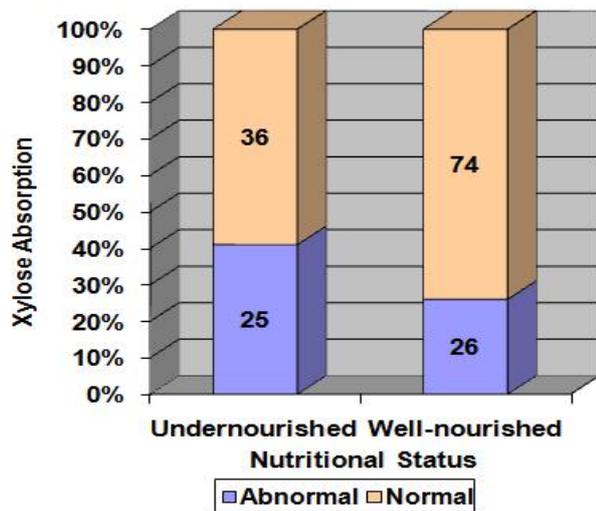


Figure 1: Xylose Absorption in Well-nourished and Undernourished Children

There was a statistically significant difference in the xylose absorption results between the well-nourished and the undernourished children. This implies that there is significantly more malabsorption as assessed by a 5 hour urinary d-xylose test in undernourished children as compared to well-nourished children. P value = 0.047.

Odds ratio = 1.976; 95% confidence interval is 1.003 to 3.895.

Most of children in the cohort had also suffered from a diarrheal illness at some point of time. Only 9 of the 161 children (5.6%) had not had even a single diarrheal illness in the past reflecting the high prevalence of diarrheal illnesses in this community. Of the 9 children who did not have diarrhea 4 had xylose malabsorption and 5 had normal xylose absorption, 4 were undernourished and 5 were well nourished. Of the 152 children who had history of diarrhea at some point 47 had xylose malabsorption and 105 had normal xylose absorption, 57 were undernourished and 95 were well nourished. The differences were not statistically significant. Forty-three of the 152 children who had had diarrheal illnesses had positive results on stool examination or culture at least during one of these episodes. Organisms detected were Shigella, Salmonella, Aeromonas, Vibrio cholerae, Giardia lamblia, Cryptosporidium and occasionally Trichuris trichura, Hymenolepis nana and Ascaris lumbricoides. Rotavirus surveillance test was positive in 130 of 161 children. Of these 130, 43 had xylose malabsorption, as against 8 of the 31 who did not have rotavirus positivity. But this difference was not statistically significant, p value 0.434. Six children had history of persistent diarrhea in the past. Of these 6 children, none had xylose malabsorption and only one was undernourished. The difference however, was not statistically significant, p values 0.089 and 0.275 for xylose absorption and nutritional status respectively.

DISCUSSION

In our study, it was found that nearly two thirds (64.2%) of our children had WAZ below -2 SD and nearly half (48.3%) had both WAZ and WHZ below -2 SD. This is much higher than the reported prevalence in India (1). Though the children in this cohort are constantly being monitored and essential nutritional advice and medical services are rendered to them, the prevalence of undernutrition is very high. This favours the concept that there could be an underlying malabsorption in these children. There was no statistically significant difference in undernutrition or malabsorption among the two sexes. This is against what would be expected in our community with preference to male children. A cross-sectional study done in an urban slum of Kolkata on 130 under-five children showed the prevalence of malnutrition, as per IAP classification, to be 55.38% with a marked female preponderance (females 77.6%; males 31.7%; P <0.001) [7]. The observed difference can possibly be explained by the fact that our cohort of children is constantly being monitored. This study was undertaken to demonstrate the existence of an enteropathy in children with undernutrition. Xylose absorption was assessed using a 5 hour urinary xylose excretion test. Though this test is not the preferred method in children and infants as compared to a serum xylose measurement, this was chosen in view of its ease of administration, non invasiveness and possibly better compliance. This required constant supervision of the children while collecting the samples by medical personnel. First attempt to collect the sample in twelve children (7.27%) failed. Only four children

had to be rejected because of inability to complete the study process on a subsequent attempt.

There was a significantly high prevalence of malabsorption among the undernourished children than the well-nourished children (41% vs. 26%, P value 0.047, Odds ratio 1.976, 95% confidence interval 1.003 to 3.895) proving that there is significant enteropathy in children with undernutrition. Further prospective studies employing serial small intestinal function tests are required to identify the causative factor between the two states. It was noticed that 130 of 161 children (80.7%) had stool rotavirus positivity at one time or the other reflecting continued exposure to this virus though they were mostly asymptomatic. This is comparable to data from Brazil and the United States. In Brazil, the serum rotavirus antibody prevalence in children aged 2 to 4 years measured by blocking enzyme immunoassay (bELISA) was 50% to 60% and by hemagglutination inhibition antibody (HIA) test was 70% to 81%^[8]. In the United States, nearly every child is infected with rotavirus by age 5 years^[9]. In our study, the rotavirus positive state did not affect either the nutritional status or the ability to absorb xylose.

Our study proves the existence of malabsorption in undernourished children which has been suspected by others as early as in the 1960s, when lesions of the small intestinal mucosa of severely malnourished children were described. In their case, the 'enteropathy of malnutrition' was assumed to occur as a result of a reduced rate of enterocyte renewal due to poor or inadequate diet, i.e. it was believed that the enteropathy occurred as a consequence of the child's malnutrition. It is now generally accepted that the etiology is similar to tropical enteropathy of adults, i.e. it is caused by chronic exposure to enteric pathogens, and moreover, that the enteropathy may be an important cause of malnutrition, particularly stunting, rather than a consequence^[10,11]. Our study however failed to show any significant correlation between prior gastrointestinal infections or infestations with malabsorption. Earlier in 1991, Lunn had also demonstrated negative correlation between intestinal disease and growth performance. A lactulose:mannitol permeability test was done regularly on children aged 2-15 months. Their growth was monitored over a mean of 7.5 months. The study revealed persistent abnormalities of small bowel mucosa of 2-15 month old Gambian infants and a negative correlation between these abnormalities and growth. Up to 43% of observed growth faltering in Gambian infants could be explained on the basis of these long-term intestinal lesions^[12]. Goto et al. based on the observations made in a dual-sugar intestinal permeability test reported positive association between stunting and poor lactulose:mannitol ratios in children with *Giardia* infection^[13]. Similarly, our study demonstrates the existence of a small intestinal enteropathy in undernourished children, but further studies are needed to evaluate its role as a causative agent for undernutrition.

Limitations: In this study, the statistical analysis identified a significant difference in the ability to absorb xylose between under-nourished and normal children. However, there was no statistically significant association between any two parameters when undernutrition or malabsorption were associated with

history of previous diarrheal illnesses, chronic diarrhea, stool rotavirus positivity or proven bacterial/ parasitic gastrointestinal infections. It is possible that testing techniques may have been insufficiently discriminatory, in that xylose absorption may not have identified all children with malabsorption or that all enteric infections in these children were not identified. It is also possible that application of more sophisticated statistical analytic techniques such as multivariate analyses would permit identification of associations not noted by the techniques applied in this study.

CONCLUSION

There is a definite statistically significant association between undernutrition and small intestinal enteropathy. There is an urgent need to conduct further prospective studies employing serial small intestinal function tests to determine if malabsorption is an etiological factor or an outcome of childhood undernutrition.

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CONFLICT OF INTEREST: Nil.

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