Physical growth and bone age of survivors of protein energy malnutrition

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SUMMARY   Early postnatal malnutrition produces delay in growth and developmental processes, and children from a low socioeconomical level where undernutrition is prevalent are shorter than those from higher socioeconomic levels. We examined the effects of severe and early protein energy malnutrition on growth and bone maturation. We studied 40 preschool children who had been admitted to hospital in infancy with protein energy malnutrition and 38 children from the same socioeconomic level, paired for age and sex, who had never been malnourished. Growth measurements were made over a period of 4–6 years, and bone age was determined in a subgroup through wrist roentgenograms. Results showed a correlation between protein energy malnutrition, birth weight of infants, and mother's height and head circumference. The group with protein energy malnutrition showed a significant delay in stature after four years, especially the girls ($p<0.001$). Weight:height ratio was reduced in boys compared with controls but not in girls. Both groups showed a delay in bone maturation, but there were no significant differences between them. We found a positive correlation between bone age and arm fat area in control boys and between bone age and height for age in boys with protein energy malnutrition. The finding that rehabilitated children were shorter than the control group but had similar bone age at follow up suggests that genetic or prenatal factors were important in their later poor growth, and this suggestion is supported by their smaller birth size and the smaller size of their mothers.

The physical effects of undernutrition on growth have been well defined in animals. The effects vary from species to species, but on the whole the earlier in life it occurs and the more severe and protracted the state, the more likely it is to reduce the stature of the adult. This is so even if the animal is perfectly nourished for the rest of its life.[1] A lifetime of poor nutrition reduces adult size,[2] but if the starvation is only the result of a mild energy deficiency the growth of the skeleton may proceed at a faster rate than the growth of other tissues.[3] Under these circumstances the animal seems almost as long and tall as a littermate of the same age, but much leaner.

The skeleton provides a sensitive index of the long term effect of metabolic and nutritional diseases, and there are many studies that have shown that chronic undernutrition slows down the rate of skeletal maturation, delays the onset of menarche, and retards epiphyseal fusion period. This presumably represents an adaptation to a lower functional level in the presence of adverse nutritional circumstances. Such children apparently have a longer time in which to overcome their growth deficit and in which to attain their adult height.

There is no general agreement about whether growth retardation caused by malnutrition during early infancy is a reversible or an irreversible phenomenon. Prolonged observations in children who have survived protein energy malnutrition have shown that severe malnutrition in early life affects their postmalnutritional growth, reducing their adult height and head size.[4][5] Other clinical and epidemiological studies have shown, however, that the catch up growth, subsequent to malnutrition, compensates for the previous growth retardation and results in normal stature of previously malnourished children.[6][7]

To investigate this problem further we studied a group of children who suffered from protein energy malnutrition in infancy, were treated in a nutritional recovery centre, discharged nutritionally recuperated, and followed up for six years; this group was compared with a group of children of the same age and socioeconomic level who had never suffered

from undernutrition. Comparative anthropometric studies of the mothers of the two groups of children were also carried out.

We have tried to answer the following questions. (1) Are there any significant differences in anthropometric measurements of survivors of protein energy malnutrition compared with those of the children who had never been clinically malnourished? (2) Are there any differences between bone age measurements of the two groups? (3) Are there any anthropometric differences between the mothers in the two groups of children?

Patients and methods

Patients. Subjects for study were selected on the basis of the following criteria:

(a) Chronological age: 4 to 6 years.

(b) Nutritional state: depending on whether or not there was a history of protein energy malnutrition during the first or second year of age.

(c) Ethnic background: Chilean population, white Amerindian origin.

(d) Geographical origin: Santiago, Chile.

(e) Health: absence of overt hormonal imbalance or debilitation disease other than due to nutritional causes.

(f) Socioeconomic level: 5 or 6 according to a modified Graffar scale.[8]

Informed parental consent for inclusion of children and parents themselves in the investigation was obtained for all subjects.

The undernourished group consisted of 18 boys and 22 girls who had been admitted to a nutritional recovery centre unit severely malnourished at a mean age of 16 months (8–20 months), having less than 60% of appropriate weight for age and less than 85% of appropriate weight for length. They stayed 90–180 days in the unit before being discharged nutritionally recuperated. All of them have been followed, during the period of their hospital admission and after discharge, by the same group of professionals for six years.

They were compared with a group of 18 boys and 20 girls who had never been undernourished, belonging to the same socioeconomic level and matched for age and sex. This group was obtained from five nursery schools that the previously malnourished children were also attending. We examined all the children in these schools, selecting those with normal weight and height for their age according to World Health Organisation (WHO) standards. We then examined their anthropometrical charts in the outpatient clinic where they were being followed to make sure they had never been undernourished.

As all the children included in this investigation belonged to a poor urban community, both groups were regularly receiving free medical care, immunisations, and food supplementation.

Methods. The following data were collected and recorded for every child in both malnourished and control groups: social level; sex; date of birth; weight and length at birth and measurements of height (cm), weight (kg), head circumference (cm), arm fat area (mm^2), and arm muscle area (mm^2). Bone age was measured in two subgroups matched for age and sex. Weight, height, and head circumference were measured in the mothers of all the children.

Socioeconomic level of the family was determined according to a modified Graffar scale. This scale includes schooling, activity of the head of the family, and housing facilities. There are six grades, grade 1 being the highest and grade 6 the lowest in social state.[8]

Weight and length at birth were obtained from the clinical files kept at the outpatient clinic. These measurements were done in hospital at birth.

Standing heights were determined to the next succeeding 0·5 cm. Readings were taken with the shoes removed, feet together, and heels, buttocks, shoulders, and head touching the scale. Body weight was measured on a beam scale to the nearest 50 g. Children and mothers were weighed nude at the same hour of the day. Head circumference was measured with a metallic tape measure to the next succeeding 0·1 cm. We analysed the nutritional state of the children by expressing their measurements as a percentage of the expected weight for height, height for age, and head circumference for age according to WHO standards.[9]

Arm fat and muscle areas were determined using the relation between mid-arm circumference, measured with a metallic tape measure to the next succeeding 0·1 cm, and triceps skinfold thickness measured with a Harpenden caliper to the next succeeding 0·1 mm and analysed according to Frisancho's standards.[10]

Skeletal age assessment was made at four years of follow up in a group of 12 boys and 13 girls of the undernourished group and nine boys and 11 girls of the control group. They were matched by sex and age. Evaluation of skeletal age was performed double blind by two observers from a series of roentgenograms of the left hand and wrist, using the Greulich-Pyle atlas for standards of reference.[11]

The degree of maturation asymmetry demonstrable in each roentgenogram was quantified by the Red Graph method,[12] in which ages assigned to the most advanced and least advanced bones are plotted

to delineate a zone, which includes the maturational times of all the other ossification centres in the hand.

The results were analysed statistically using the Student *t* test, the Pearson coefficient of correlation, and the Fisher test.[13]

Results

Socioeconomic state. There were no significant differences in the socioeconomic characteristics of the two groups except in the schooling and social security of the head of the family, which favoured the control group.

Birth measurements. There were significant differences in birth weight and length at birth between the groups when analysed according to sex. The difference was greatest in girls (p<0·001) (Table 1).

Maternal data. The mean age of the mothers of both groups was the same. There were significant differences in height and head circumference favouring the control group (Table 2), but not in weight.

Weight gain and linear growth. The nutritional state of children in the study group showed significant differences in weight:height, height:age, and head

circumference:age ratios at admission and at discharge during the initial period of hospital treatment in both boys and girls. During four years of follow up, however, the study group grew at a consistently slower rate than that observed during the period of hospital treatment. In comparison with the control group they were significantly shorter (p<0·001), and the girls had smaller head circumference (p<0·05). The weight:height ratio was smaller in boys only (p<0·02) (Figures 1 and 2).

Arm muscle and fat areas. There was no significant increase in arm muscle area after four years of follow up in either boys or girls of the malnourished group (Table 3). There was a significant decline in arm fat area after four years of follow up, however, in both boys and girls. There was a significant difference in arm fat area between the sexes at discharge from hospital, which disappeared during the follow up (Table 3).

When the malnourished group was compared with the control group there were no significant differences in arm muscle area, but arm fat area was significantly greater in the controls, particularly in the girls (Table 4).

Bone age. There was a significant sex difference in bone age in the malnourished group but not in the

Table 1 *Nutritional state at birth in previously malnourished (study) and control groups*

	Birth weight (g)		Length at birth (cm)	
	Boys (n=18)	Girls (n=22 in study, 20 in control)	Boys (n=18)	Girls (n=22 in study, 20 in control)
Study group:				
Mean (SD)	3018·2 (490·3)	2654·6 (579·0)	48·4 (2·2)	46·8 (2·6)
Control group:				
Mean (SD)	3453·5 (522·3)	3328·4 (563·4)	51·1 (2·3)	49·5 (2·2)
t	3·62	3·7	3·48	3·63
p	<0·01	<0·001	<0·01	<0·001

Table 2 *Nutritional state of mothers of previously malnourished (study) and control groups (separated by sex of their children)*

	Weight (kg)		Height (cm)		Head circumference (cm)	
	Boys	Girls	Boys	Girls	Boys	Girls
Study group						
No	11	13	11	13	11	13
Mean (SD)	60·5 (13·5)	54·1 (13·4)	151 (3·2)	149 (3·8)	53·2 (2·2)	53·3 (1·1)
Control group						
No	18	17	18	17	18	17
Mean (SD)	63·7 (11·2)	62·9 (10·2)	155·3 (4·9)	154·2 (7·7)	55 (1·5)	54·9 (1·9)
t			2·75	2·19	2·38	2·77
p			<0·02	<0·05	<0·05	<0·01

controls (Table 5). There were no significant differences in bone age between the malnourished children and the controls either as a group or when analysed by sex.

There were positive correlations between arm fat area and bone age in control boys (Fig. 3), and between bone age and height for age in boys with protein energy malnutrition (Fig. 4).
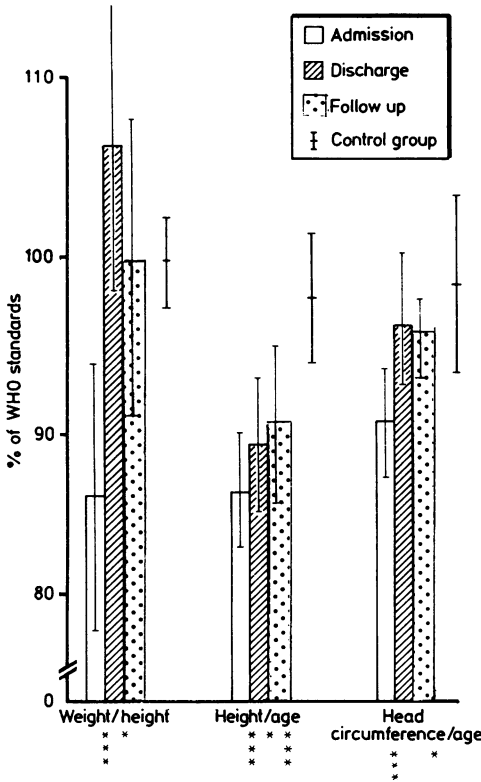

Fig. 1 *Nutritional state in girls in study group (% of World Health Organisation (WHO) standards) at various times compared with control group.*

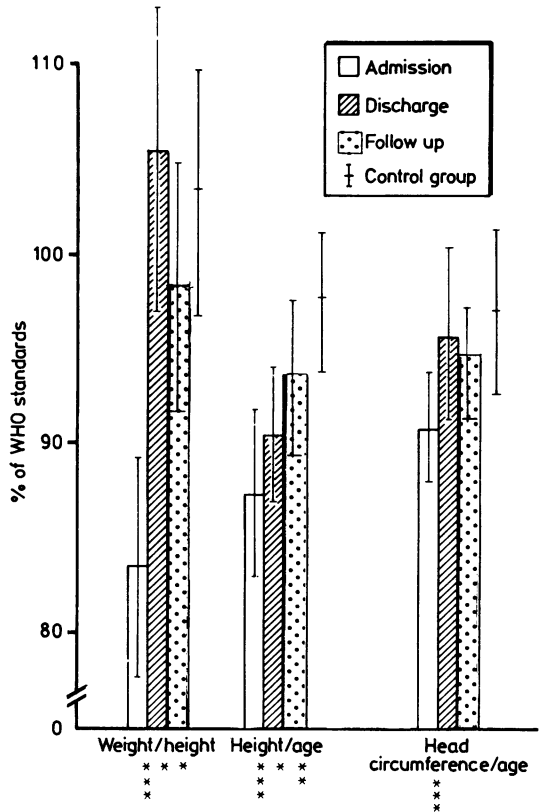*p<0·02, >0·05; **p<0·01; ***p<0·001.

Fig. 2 *Nutritional state in boys in study group (% of WHO standards) at various times compared with control group.*

*p<0·02, >0·05; **p<0·01; ***p<0·001.

Table 3 *Arm muscle area and arm fat area (% of adequacy Frisancho standards) previously malnourished (study) of group at discharge and four years of follow up*

	Arm muscle area (%)		Arm fat area (%)		
	Boys (n=18)	*Girls (n=22)*	*Boys (n=18)*	*Girls (n=22)*	
At discharge					
Mean (SD)	89·9 (11·2)	89·7 (12·7)	92·0 (12·0)	77·5 (18·9)	(t=2·5, p<0·05)
Follow up					
Mean (SD)	92·0 (12·0)	93·5 (11·5)	73·5 (15·3)	64·5 (16·4)	
t			3·92	2·38	
p			<0·001	<0·05	

Table 4 *Arm muscle area and arm fat area (% of adequacy Frisancho standards) of previously malnourished (study) and control group*

	Arm muscle area		Arm fat area	
	Boys (n=18)	Girls (n=22 in study, 20 in control)	Boys (n=18)	Girls (n=22 in study, 20 in control)
Study group:				
Mean (SD)	92·0 (12·5)	93·5 (11·5)	73·5 (15·3)	64·5 (16·5)
Control group:				
Mean (SD)	96·1 (11·8)	92·0 (9·7)	91·0 (24·7)	95·7 (28·5)
t			2·48	4·18
p			<0·05	<0·001

Table 5 *Percentage of expected bone age (Greulich and Pyle standards) for previously malnourished (study) and control group at 4 years of age*

	Bone age		
	Boys	Girls	
Study group			
No	12	13	t=3·38
Mean (SD)	60·3 (8·6)	76·7 (14·2)	p<0·01
Control group			
No	9	11	
Mean (SD)	69·2 (9·7)	86·7 (27·2)	

Fig. 4 *Correlation between height/age and bone age (%) in undernourished boys at different times.*
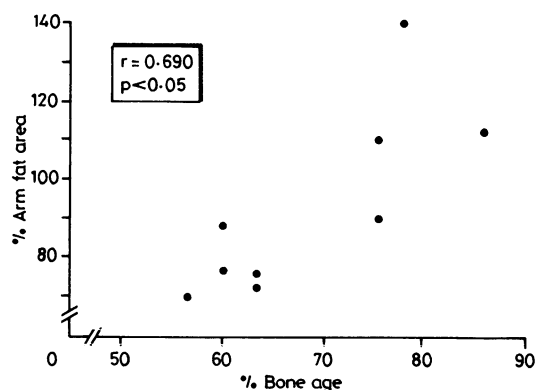

Fig. 3 *Correlation between arm fat area and bone age (%) in control boys.*

Discussion

The controversy regarding growth and ultimate physical stature of survivors from malnutrition cannot be easily solved, as follow up studies in human subjects cannot be conducted under fully controlled experimental conditions. For this reason attempts to isolate malnutrition as an independent variable have been only partially successful.
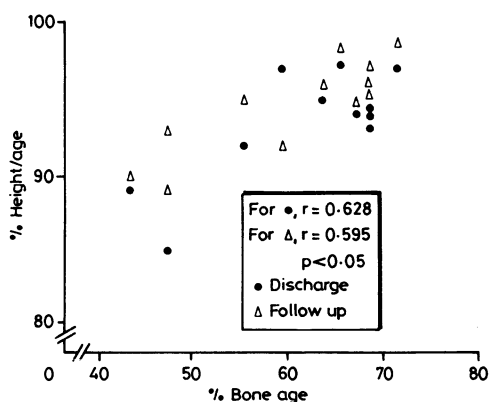
The malnourished infants admitted to our nutritional recovery centre at the Institute of Nutrition and Food Technology come from extremely poor families in the peripheral slums of Santiago. They live in one or two room shacks, without flooring, windows, running water, sewage, or electricity and are usually the fourth or fifth born to a mother whose 'husband' is often the second in line, works sporadically, and drinks to excess. Both the malnourished and the control infants came from this environment in our study.

It is important to emphasise that the children of our control group were able to grow up to WHO standards in spite of their inadequate living conditions. This might depend on the head of the family having social security (permanent work) and better schooling and is a fact that shows the inadvisability of using local standards for height and weight in an undernourished community, as these norms will reflect suboptional growth in the population.

We found that admission to hospital was capable of reverting the undernutrition and of giving better living expectation to the children with protein

energy malnutrition. They were able to grow at a faster rate, probably because of the extra amount of fat saved during admission to hospital, but they were not capable of attaining the growth of the children who were not malnourished.

When we analysed bone age maturity of the study group we found it to be delayed as previously reported.[14-17] Interestingly, there were significant differences in bone age of boys and girls in the study group. This had been reported by Pryor,[18] but we found a more pronounced effect. This could have a genetic reason as proposed by Valenzuela.[19 20]

It is important to note the positive correlation between bone age and height for age in boys with protein energy malnutrition. This could be explained by the extra amount of fat gained during hospital treatment. The correlation between arm fat area and bone age observed in controls could indicate that adequate nutrition is related to bone age. The extra amount of fat saved by the boys of the study group could determine an acceleration of growth and therefore of bone age. This finding has also been observed in obese children whose bone ages were significantly accelerated when compared with normal patients.[21]

The results obtained confirm the experience in animals and other follow up studies of malnourished children. The amount of information compiled suggests that the effects of severe and protracted malnutrition in early life produce limitation of growth. It is important to emphasise that, although there was a small acceleration in linear growth velocity in the malnourished group, the bone age observed in them suggests that they are not going to attain normal adult height.

The evidence presented in this study suggests that mother's height influences birth weight of their children and that protein energy malnutrition is related to birth weight, so it seems important to give special nutritional support to low birthweight infants, especially if they have precarious living conditions.

The design of this study does not allow us to estimate the influence of maternal nutrition upon growth of their children, but this is probably an important factor because the children of short mothers (who themselves were probably malnourished in childhood) are at disadvantage when placed in bad living·conditions.

We wonder whether these children would have had better growth if placed in a better environment, as the living conditions of the study group have been far from ideal.

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