Relation between changes in weight parameters and height parameters in prepubertal children: daily weight gain and BMI changes in relation to linear growth during nutritional rehabilitation of underweight children

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Summary. *Background:* Early detection of abnormal weight loss or gain in childhood may be important for preventive purposes. Variable growth response to nutrition rehabilitation have been reported in children with failure to thrive (FTT) who do not have any chronic disease or systematic illness due to different clinical and nutritional approach in their management. *Aim of the study*: To analyze the association of different body mass index (BMI) and BMI- SDS, to linear growth (Ht-SDS) in different BMI categories of prepubertal children. In addition, we studied the effect of weight changes on linear growth in a randomly selected group of prepubertal underweight children who received nutritional rehabilitation (NR) for 9±2 months. *Subjects and methods:* 102 children, between 1 and 9 years, followed at the General Pediatric Clinic, between January 2017 to December 2017, because of abnormal weight gain (decreased or increased) which was not associated with any acute or chronic illness were included in the study. Anthropometric measurements included weigh, height, Ht-SDS, BMI, and BMI-SDS. Children BMI-SDS were categorized into 4 groups: Group 1: BMI-SDS <-2, group 2: BMI-SDS <-1 but >-2, group 3 BMI-SDS >-1 but <2, group 4 BMI-SDS >2. We also evaluated the effects of weight changes on linear growth in a randomly selected group of underweight children who received nutritional counselling and oral nutritional supplementation (n = 51) for 9±months. *Results:* HT-SDS in children of groups 1 and 2 (underweight and at risk of underweight children) was significantly lower than Ht-SDS of groups 3 and 4 (normal and overweight children). Ht-SDS in children of group 4 was significantly higher than the Ht-SDS of children in group 3. A significant linear correlation was found between BMI-SDS and Ht-SDS in these prepubertal children. *Discussion:* After nutritional rehabilitation for a year, 55% of underweight children increased their BMI-SDS and 43% increased their Ht-SDS. Children who had weight gain >7g/d, over the whole period of follow-up, (n =14) increased their BMI-SDS and Ht-SDS significantly after versus before NR. The BMI-SDS and Ht-SDS did not increase significantly in the group of children who had weight gain <7 g/day. 28 children out of 51 improved their BMI-SDS after nutritional rehabilitation (group A) and 23 did not have improvement in their BMI-SDS (Group B). Group A had higher weight gain per day versus group B. Height growth velocity was significantly higher in Group B (7.4±3.6 cm/yr) versus group A (5.7±2.8 cm/yr). Ht-SDS increased significantly in the group of patients who had lower Ht-SDS before NR. Children who had faster linear growth velocity, after nutritional rehabilitation, did not increase their BMI-SDS. Linear regression showed a significant correlation between BMI-SDS and Ht-SDS supporting the notion that proper nutrition and maintaining normal BMI-SDS is essential for adequate gain in height. *Conclusion:* It appears that calculating the weight gain per day, BMI-SDS and Ht-SDS are clinically useful parameters to detect the effect of weight gain on linear growth and to monitor the nutritional management. Daily weight gain was correlated significantly to height growth rate during nutritional rehabilitation. Based on our findings and literature reports, we suggest an algorithm for follow-up of underweight/ malnourished children based mainly on anthropometric assessment. (www.actabiomedica.it)

Key words: linear growth, weight gain, nutritional rehabilitation, underweight children

Introduction

Underweight, as well as overweight and obesity, are currently highlighted as being among the most important threats to human health. According to the UNICEF, WHO and The World Bank joint report, linear growth restriction or stunting (height below minus two standard deviations from the median height for age of the reference population) due to chronic malnutrition affects an average of 25% of all children younger than five years worldwide (1). Therefore, monitoring both linear growth and weight dimensions of population is critical, because of the persistent growth failure globally as well as the emergence of obesity as a global epidemic (2-4).

It is possible not to find any specific cause for a child's apparent poor weight gain. A well looking child with normal neurodevelopmental progress, who shows apparent isolated poor weight gain, with no specific cause evident from history, examination and possibly some simple investigations, will have an excellent prognosis for future health, wellbeing and development. These children should be monitored over time to ensure that no specific causes of poor growth become evident.

A large study in the US found that most infants (77%) aged from birth to 6 months cross weight-for-age percentile lines, with 39% of infants either moving up or moving down two percentile lines. As children got older, they are much less likely to cross two weight-for-age percentile lines, but this did still happen. Six to 15% of children cross 2 percentile lines weight for height and 1-5% of children cross 2 percentile lines (weight for-age) between 2 and 5 years (5, 6).

Body mass index (BMI) as well as BMI z-scores are reasonably good references for predicting the body composition and adiposity status in children. In addition, calculation of normal weight gain/day for children according to their age and gender, although is a less used measurement, allows more precise estimation of weight growth rate and adiposity during periods of nutritional rehabilitation (7-15).

It is suggested that the content of adipose tissue influences the regulation of the biological maturation, including bone and linear growth as well as pubertal growth spurt. It has also been demonstrated that chil-

dren with changes in BMI and adiposity can affect the timing and tempo of puberty and consequently the pubertal growth spurt (16, 17).

Malnutrition is considered a leading cause of growth attenuation in children. When food is replenished, spontaneous catch-up (CU) growth usually occurs, bringing the child back to its original growth trajectory. However, in some cases, the CU growth is not complete, leading to a permanent growth deficit (7).

There is no clear consensus on the correct definition of ideal body weight (IBW) (ideal weight for growth and health) in children or on the best method used to calculate IBW.

The BMI method has many advantages that include: 1) the BMI is age specific, 2) BMI-for-age accounts for "adiposity" rebound, which is the normal pattern during puberty and adolescence, 3) BMI fit well with both weight-for-height measurements and measures of body fat and, 4) BMI carries into the adult lifecycle. However, BMI cutoff values have high specificity but low sensitivity to identify adiposity. Moreover, BMI does not provide information on the proportions of multi components of weight, such as fat mass (FM), lean mass (FFM) and bone mass. BMI is correlated with each of these parameters but, it cannot differentiate between them. BMI differences among thinner children can be largely due to FFM, and it is more important in underweight children (7, 18-25).

Stunting is a primary manifestation of malnutrition (undernutrition). In malnourished and underweight children slowing of linear growth and the association between short stature and underweight has been reported in many population studies. The relation/association between weights changes (BMI-SDS and weight gain/day) and linear growth [height, Ht-SDS and growth velocity (GV)] has not been adequately studied in older children with underweight before and after nutritional rehabilitation.

The aim of this study was to analyze the effect of different BMI and BMI-SDS, if any, on linear growth (Ht-SDS) in different BMI categories of prepubertal children (n = 102). In addition, we assessed the effects of weight changes (weight gain/day, and BMI-SDS) in relation to linear growth (growth velocity and Ht-SDS) in a randomly selected group of underweight children, after nutritional rehabilitation.

Subjects and methods

All children, between 1 and 9 years, followed at the General Pediatric Clinic of Hamad Medical Centre, Doha (Qatar), between January 2017 to December 2017, because of abnormal weight gain (decreased or increased) which was not associated with any acute or chronic illness were included in the study. Physical exam and routine lab tests did not show any abnormality. Children with any organic or systematic disease were excluded from the study. The study was approved by the Institutional Review Board of Hamad Medical Centre, Doha, Qatar.

Anthropometric measurements included weigh, height, Ht-SDS, weight for height, BMI (Kg/m²), and BMI-SDS. The height-for-age Z-score (Ht-SDS) and the BMI-for-age Z-score (BMI-SDS) for each child were calculated using the WHO standard population as the reference (14, 18).

We categorized Ht-SDS <–2.0 (approximately the 3rd percentile) as stunted, BMI-Z score <–1.00 (approximately the 15th percentile) as mild underweight, BMI-SDS <–2.00 as moderate-severe underweight, BMI-SDS >1.00 (approximately the 85th percentile) as overweight, and BMI-SDS >2.00 (approximately the 97th percentile) as obese.

According to BMI-SDS our children were categorized into 4 groups: Group 1 (N=19) BMI-SDS <-2 , Group 2 (N=33) BMI-SDS >-2 - <-1, Group 3 (N=20) BMI-SDS >-1 <2, and Group 4 (N=30) BMI-SDS >2.

In addition, we evaluated the effect of nutritional rehabilitation on weight changes (weight gain g/day and BMI-SDS changes) and linear growth (height growth velocity and Ht-SDS changes) in a randomly selected group of underweight children (n = 51) who received nutritional counselling and oral nutritional supplementation.

Nutritional rehabilitation (NR) included nutrition counseling to increase energy and protein intake. Energy requirements were calculated using catch up growth method and protein requirements were calculated using catch up growth method up to 3 g/kg/d (18). Pamphlets were handed out for patients for education and My Plate food model was used for demonstration of food types and serving sizes. In addition,

high energy (1:1 or 1:1.5) and high protein nutrition supplementation were monthly supplied for free to all patients who had BMI-SDS ≤ -1 (18).

The effects of weight changes (g/day) and BMI on linear growth measured by height GV and Ht-SDS were studied.

Student- t test was used to compare the variables among different groups when the data was normally distributed and Wilcoxon test was used when the data was not normally distributed. ANOVA test was used to compare variables among the 4 groups categorized according to their BMI-SDS. Linear correlation equation was used to investigate possible relations between different variables. Significance was accepted when was ≤0.05.

Results

We evaluated growth parameters in 102 pre-pubertal children (age 1-9 years), with abnormal weight gain without systematic or organic illness, followed at Pediatric General Dietitian Clinic of Hamad General Hospital of Doha (Qatar).

Children were divided according to their BMI-SDS (Table 1). Ht-SDS of children in groups 1 and 2 (moderate/severe underweight and mild underweight) was significantly lower than Ht-SDS of groups 3 and 4 (normal and overweight children). Ht-SDS in children of group 4 (obese) was significantly higher than the Ht-SDS of children in group 3 (controls).

Both underweight and obese groups (1 and 4) had significantly higher percent of vitamin D insufficiency, compared to the other groups (p: <0.00001). The BMISDS was correlated significantly with Ht-SDS (r=0.72, p: <0.0001) (Table 2, Figure 1).

Serum albumin and hemoglobin concentrations were normal and did not differ among the four groups (Table 1). Vitamin D insufficiency was present in 71% of the children in group 1, 40% of the children in group 2, 23% of the children in group 3 and 75% of the children in group 4.

In the 51 children who received nutritional rehabilitation (NR) followed up for 9±2 months, the weight gain/day increased significantly between the last and first visit.

Table 1. Anthropometric and biochemical data (mean ±SD) of children with abnormal weight gain

	N.	Age (yr)	Height SD	BMI-SD	Hb (g/dl)	Vit D (ng/ml)	Alb (g/l)
Group 1 (BMI-SDS <-2) Moderate/ severe under-wt	19	4.9±4.4	-1.5±1.3 *#	-2.8±1.0 *#	11.6±1.1	20.1±7.4	40.9±3.6
Group 2 (BMI-SDS >-2 <-1) mild under-wt	33	5.6±4.0	-1.76±0.9 *#	-1.5±0.2 *#	12.2±1.3	24.3±12.7	41.8±3.3
Group 3 (BMI-SDS >-1 <2) Controls	20	3.1±2.7	-1.26±0.9 #	-0.2±0.5 #	11.7±1.2	29.5±11.7	40.4±5.1
Group 4 (BMI-SD >2) Obese	30	8.9±3.9	1.0±0.9*	3.5±0.9 *	12.7±1.1	19.0±13.5	41.1±3.3

Legend: * P: <0.05 groups vs controls; # P: <0.05, groups vs. obese group (Group 4)

Table 2. Correlation between Body Mass Index (BMI- Kg/m^2) and Height-SDS

|	Height- SDS	BMI (Kg/m^2)	BMI-SDS
Height-SDS	1.00	-	-
BMI (Kg/m^2)	0.68*	1.00	-
BMI SDS	0.72**	0.85**	1.00*

P: <0.01; ** P :<0.001

We divided the 51 children into 2 groups according to their weight gain/day response. Group A: included 14 children who had weight gain >7 g/d over the whole period of follow-up (average normal weight gain for the average age and gender is 6.5 g/d); Group B: included 37 children who gained weight <7 g/d during the follow up period.

The BMI-SDS of group A increased significantly after versus before nutrition rehabilitation, whereas, BMI-SDS did not increase significantly in group B (p: 0.06).

The Ht-SDS of group A increased significantly after 9±2 months of NR while the Ht-SDS of group B did not improve significantly (Table 3).
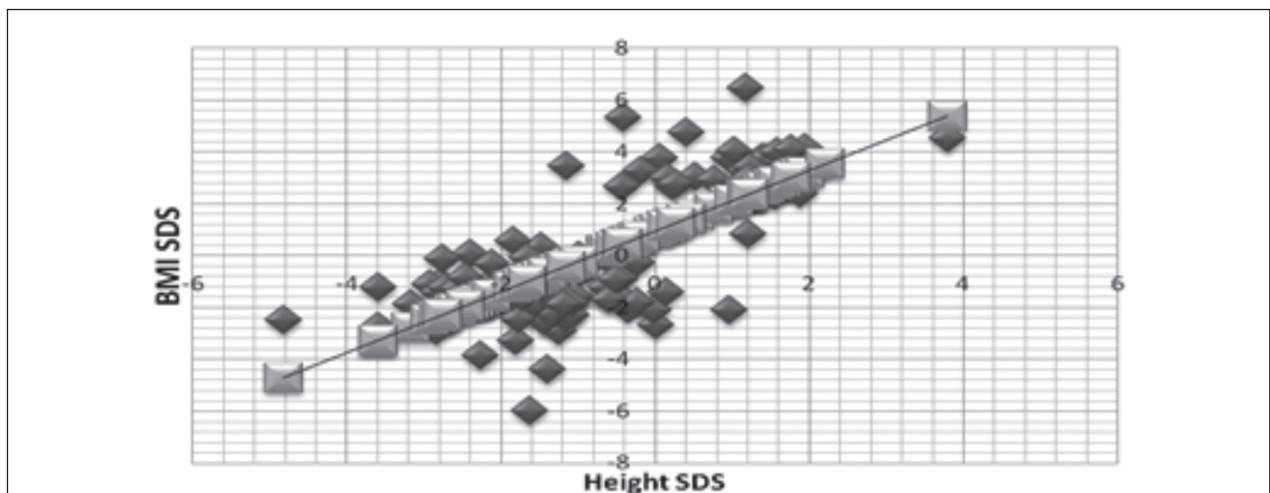

Figure 1. Regression analysis of BMI-SD score on Height SDS (r = 0.723, P: <0.0001)

When children were divided according to their BMI-SDS changes in response to rehabilitation, 28 children out of 51 improved their BMI-SDS after nutritional rehabilitation (Group A) and 23 did not have improvement in their BMI-SDS (Group B).

Group A had higher weight gain per day (8.6±5.8 g/day) versus Group B (3.3±2.2 g/day). Height growth velocity (cm/y) was significantly higher in Group B (7.4±3.6 cm/yr) versus Group A (5.7±2.8 cm/yr).

Children who had higher linear growth velocity after nutritional rehabilitation did not increase their BMI-SDS (Table 4). Weight gain/day and BMI-SDS were correlated significantly with height growth velocity (r = 0.38, p: 0.02) and (r = 0.4, p: 0.018) (Figure 2). Ht-SDS was not correlated with weight gain/day (r = 0.09) or BMI-SDS (r = -0.04).

Children who presented with Ht-SDS <- 2 (n= 17) had slightly higher height gain SDS (0.15±0.37) compared to those who presented with Ht-SDS >-2 (n = 34) (0.02±0.4) (p: 0.09). Children who presented with BMI-SDS >- 1.5 (n= 26) had an higher BMI-SDS gain (0.12 ±0.29) compared to those who presented with BMI-SDS <-1.5 (n = 25) (0.02 ±0.46) (p: 0.05), with no difference in the Ht-SDS gain between the two groups.
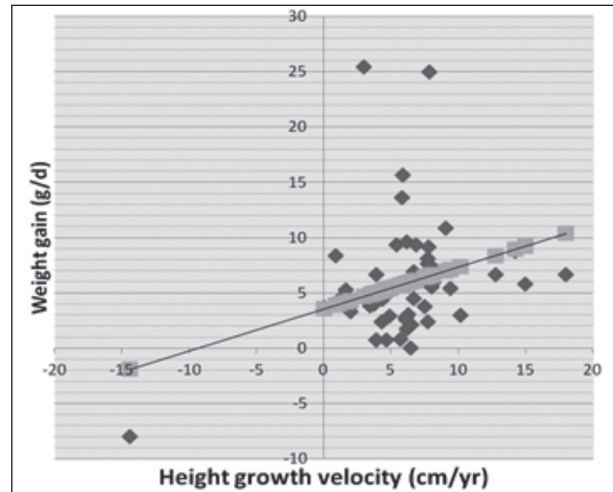
Figure 2. Correlation between growth velocity (cm/y) and weight gain g/day (r = 0.4, P: 0.02)

Table 5 shows the results of Ht-SDS changes after average of 4 and 9 months of treatment. After 4 months, 20 children increased their Ht-SDS and this was associated by decreased BMI-SDS by 0.1. They continued to have a catch- up growth also in the following 9 months of NR (0.2 at 4 months and 0.31 at 9 months associated to a decrease in BMI-SDS, after 4 and 9 months, of 0.12 and 0.13 respectively).

Table 3. Linear growth of children who gained >7g/day during nutritional rehabilitation (NR) (mean±SD)

	Age (yr)	Ht-SDS (1)	BMI-SDS (1)	Ht-SDS (2)	BMI SD (2)	GV cm/y
Wt gain >7 g/day Group A (n = 14)	7.6±3.5	-1.1±1.3 *	-1.5±0.8	1.0±1.2 *	-0.9±0.9 #*	6.9±3.0 #
Wt gain <7 g/day Group B (n = 37)	5.4±3.3	-1.7±1.04	-1.5±1.1	-1.6±0.9	-1.6±1.0	6.0±3.4

Legend: 1 = after 4 months; 2 after 9 months of nutritional rehabilitation (NR). * P: <0.05. group A vs group B; # P: <0.05. after vs before NR

Table 4. Linear growth of children who increased their mass index (BMI) SDS during nutritional rehabilitation (NR) (mean±SD)

Groups	Age	Duration months	Ht-SDS (1)	BMI- SD (1)	Ht-SDS (2)	BMI-SD (2)	GV cm/y
BMI-SDS Gain group (n:28)	6.3±3.5	9.5±2.9	-1.2±1.1	-1.3±1.2	-1.3±1.0	-1.1±1.0 #*	5.7±2.8
BMI-SDS No gain group (n: 23)	5.1± 3.3	8.5±2.4	-2.0±1.1*	-1.2±1.0	-1.8±0.9#*	-1.7±1.0	7.4±3.6*

Legend: 1 = after 4 months; 2 after 9 months. # P: <0.05, after versus before rehabilitation; *P: <0.05 between groups

Table 5. Growth data of children who increased their Height-SDS (Ht-SDS) versus those who did not during nutritional rehabilitation (NR) (mean±SD).

Ht-SDS	Age	Ht-SDS (1)	BMI-SDS (1)	Ht-SDS (2)	BMI-SDS (2)	Δ Ht-SDS (2)	Δ BMI-SDS (2)	Ht-SDS (3)	BMI-SDS (3)	Δ Ht-SDS (3)	Δ BMI-SDS (3)
Increased/ 4 mo. (n : 20)	5.3±3.8	-1.9±1.3	-1.1±1.0	-1.6±1.2	-1.2±1.3	0.3±0.3	-0.1±0.8	-1.6±1.2	-1.2±1.0	0.3±0.3	-0.1±0.5
Not increased 4 mo. (n : 31)	6.3±3.3	-1.3±0.9	-1.8±0.8	-1.5±0.9	-1.7±1.0	-0.1±0.2	0.1±0.6	-1.4±0.8	-1.6±1.0	-0.1±0.2	0.1±0.7
Increased 9 mo. (n : 28)	5.6±3.6	-1.9±1.2	-1.2±0.9	-1.7±1.1	-1.3±1.1	0.1±0.3	-0.1±0.6	-1.6±1.1	-1.3±1.0	0.3±0.3	-0.1±0.5
Not increased 9 mo. (n : 23)	6.3±3.4	-1.0±0.8	-1.9±0.9	-1.3± 0.8	-1.6±1.2	-0.2±0.2	0.2±0.7	-1.3±0.8	-1.5±1.0	-0.2±0.1	0.3±0.7

Legend: 1 = at presentation; 2= after 4 months of NR; 3 = after 9 months of NR

Children who did not increase their Ht-SDS after 4 months on NR (n = 31) had significant increase in BMI-SDS by 0.15. After 9 months of NR, 8 of them increased their Ht-SDS. Those children who didn't show catch up in height (n = 23) had increased BMI-SDS at 9 months of NR.

Discussion

We examined the Ht-SDS in 4 different BMI-SDS categories of prepubertal children. Our study showed that the Ht-SDS of children in groups 1 and 2 (children with mild and moderate/severe underweight) was significantly lower than normal and overweight children. Ht-SDS in obese children was significantly higher compared to the Ht-SDS of normal children.

Our cross-sectional data are reinforced by other studies in underweight and overweight children (26-31).

Pomeroy et al. (32) found that height was positively associated with BMI among urban lowland peruvian children. Freedman et al. (33) reported that relatively tall children had a higher BMI in early adulthood. Other authors show positive correlations between height and adiposity (34-35). Mukuddem-Petersen et al. (36) showed that stunted children living in rural areas and informal settlements, had significantly lower mean BMI than non-stunted children. However this relationship was not supported by others (37).

In support of our findings, Bonthuis et al. (38) studied BMI in children with different height distributions: short stature (mean height SDS: -1.6), normal stature (height SDS: 0), and tall stature (height SDS: +1.6). It was shown that at a given age, BMI was distributed towards lower values in short, and towards higher values in tall subjects as compared to a population with average height distribution.

In our study, the BMI-SDS was highly correlated with Ht-SDS in prepubertal children between 2 and 9 years of age (r = 0.7) (Figure 1). In addition, Kain et al. (39,40) found an association between BMI-SDS and Ht-SDS in a large cohort of children after 3 years of age.

The relation between tall stature (high Ht-SDS) and adiposity (increased BMI) can be explained by accelerated epiphyseal growth plate maturation possibly due to early estrogenization and the action of insulin

on the IGF-1 receptor. IGF-I serum values are higher in obese children compared to normal subjects for both genders. A positive relationship was found between IGF-1 SDS for serum IGF-1 and anthropometric parameters (P <0.0001) with greater effects observed for height than for BMI.In addition, the degree of body fatness may trigger the neuroendocrine events that lead to the onset of puberty; these may explain the findings that obese girls tend to mature earlier than lean girls (41-45).

Nutritional intake is an important systemic factor that strongly modulates growth. Malnutrition transiently inhibits growth, but this resolves with nutritional rehabilitation. The growth rate generally does not just return to normal but rather exceeds the normal rate for chronological age to achieve catch up growth (46). To allow for this catch-up growth, dietitian usually increase both caloric and protein intake, based on the ideal body weigh (IBW) -BMI method or other methods.

Conditional coordination of growth is observed during malnutrition. Malnutrition/undernutrition generally cause widespread inhibition of growth in multiple organs however, body proportions tend to be maintained. When growth-inhibiting conditions resolve (with nutritional rehabilitation), catch-up growth is observed in multiple organs, again tending to maintain body proportions. However, this tendency to maintain body proportions is not absolute. It appears that although the growth rates of different organs are typically affected in the same direction but not to the same extent (47-52).

One of the biological variables with the greatest impact on the long-term health of undernourished children is the recovery of stature. Most studies on growth in malnourished children have focused on weight. However, few studies have also documented a catch-up growth in height after malnutrition, either in the immediate recovery period or in the long term. We analyzed the outcome of our group of underweight children (n = 51) in response to nutritional rehabilitation (NR) according to the changes of weight (weight gain/day and BMI-SDS) and height (Ht-SDS and GV) over the period of 9±2 months.

20/51 of children started their height catch-up after 4 months of NR, whereas 28/52 of children showed increased Ht-SDS, after 9 months of NR. Children who had significant height catch-up did not increase their BMI-SDS. (i.e. the change in height was more than weight gain in the BMI equation). However, children who had weight gain >7 g/d over the whole period of follow-up (average normal weight gain for their average age and gender was 6.5 g/d), (n =14) had significant increase in BMI-SDS and Ht-SDS after versus before NR compared to those who gained weight <7 g/d (n = 37) during the follow up period. These findings suggested that during NR, weight gain more than the average weight gain for age and sex provides enough energy for catch-up in stature .

In our study underweight children who had increased BMI-SDS after NR (n = 28) had higher weight gain per day (8.6±5.8 g/day) versus children who did not increase their BMI-SDS (n = 23) with lower weight gain per day (3.3± 2.2 g/d). The height growth velocity (cm/y) was significantly higher in the latter group (7.4±3.6 cm/yr) versus the former group (5.7±2.8 cm/yr). These data denoted that children, who had faster linear growth velocity, after nutritional rehabilitation, did not increase their BMI-SDS. This effect can be clearly explained by the fact that changes in the BMI-SDS represent the relative changes in weight compared to height. Therefore, an increase of BMI-SDS can occur if an underweight child increases his weight while he is not catching-up in height or if his weight gain is relatively in excess of his height growth. In support of this view, weight gain/day was correlated significantly with height growth velocity (r = 0.4, p: 0.018). Ht-SDS was not correlated with weight gain/day (r = 0.09) or BMI-SDS (r = -0.04). Furthermore, a prospective population-based birth cohort study in Brazil found that the weight gain was positively correlated to length/height gain (height growth velocity) in the same age range (53). Stein et al. (54) analyzed a series of cross-sectional surveys, conducted between 1968 and 2007, in 4 villages in eastern Guatemala. The authors observed an improvement in child growth, as measured by Ht-SDS, without concurrent increases in BMI.

At presentation, our underweight children, who started their catch-up growth as early as 4 months after NR (n = 20/51), were significantly shorter and had a higher BMI-SDS compared to those who did not

show early catch up (Table 5). In addition, our undernourished children with BMI-SDS >-1.5 at presentation, had a significantly better height gain after NR versus those with BMI-SDS <-1.5. In support of our findings, Walker et al. (55) and Doherty et al. (56) reported a catch-up growth in height and knee -heel length in a subgroup of severely malnourished children. On the other hand, Grantham-McGregor et al. (57) did not find any improvement in length /height in the immediate recovery period in their malnourished children. This may be due to the severe degree of malnutrition of their cohort that required longer time to start catch-up.

The number of children who had catch-up in Ht-SDS increased from 20/51 after 4 months of NR to 28 /51 after 9 months of NR. Similarly, Alves et al. (58) studied 51 undernourished children after nutritional rehabilitation. Height catch-up occurred in 39% of children, after 4 months, and in 55% of them after 9 months of NR. Das Neves et al. (59) reported that among their 106 malnourished children, 67.9% recovered in both weight and height after an average of 16.4 months. Almost half of their children presented a nutritional recovery of more than 0.50 in Ht-SDS (46.2%) and about 40% in weight-for-age (WAZ) (38.7%). They also found that a longer treatment was associated with a greater gain in both WAZ and Ht-SDS. Picot et al. (60) reported a significant height gain (0.2±0.33 mm/day) and weight gain (3.7±4.3 g/kg/day) in malnourished children (n = 532) during their first 8 weeks of home-based nutritional rehabilitation.

Long-term studies on height prognosis, after an episode of severe malnutrition, have produced conflicting results. Studies from Guatemala, India, and Brazil have reported that rapid infant weight and length gain are positively associated with subsequent height and lean mass rather than adiposity (61-64). A complete recovery to a normal adult height was reported in some studies (65, 66).

The assumption that full catch-up growth is possible is supported by observations that the retardation of bone maturation is not significantly different from the height retardation (65-71). However, other investigators have suggested that severe malnutrition results in a permanent height deficit (67-70). The discrepancy between the outcome of these studies may be attribut-

ed to factors such as the control group with which previously malnourished children were compared, the degree of inadequacy of the home environment to which the children returned after discharge from hospital, and the more general problem that follow-up studies in human subjects cannot be conducted under fully controlled experimental conditions, thereby making isolation of malnutrition as an independent variable practically difficult to assess. However, relatively recent studies reported continuation of catch-up in height for years in malnourished children after NR (72, 73).

In addition, das Neved et al. (59) found that malnourished children (n = 94) who recovered from malnutrition had normal body composition. These results showed that height recovery fostered a normalization of the body composition and was followed by appropriate gain in lean body mass and bone mineral content. Therefore, it reduces the risk of chronic diseases in the adult life for previously malnourished children (59).

An important question is "why some children increase their height early during recovery of undernutrition while others recover later despite increased BMI and normal weight gain? " It has been suggested that three different types of catch-up growth can be distinguished (14, 15). In type A, when growth restriction ceases, height velocity increases to such an extent that the height deficit is swiftly eliminated. In type B, when growth restriction ceases, a delay in growth and somatic development persists. However, growth continues for longer than usual, so that ultimately the growth arrest is compensated. This type of catch-up growth has only a small or no increase of height velocity compared with the mean velocity for chronological age. Type C is a mixture of types A and B. When growth restriction ceases, there is an increase in height velocity as well as a delay and prolongation of growth. Although this subdivision of catch-up growth in different types appears reasonable, the borderlines between types A, B, and C are not sharply delineated and in practice a distinction cannot always be made (46-51, 74).

Studies in rats, rabbits, and humans, after various growth-inhibiting conditions, suggest that this local catch-up growth occurs because growth-inhibiting conditions (e.g. malnutrition) slow the normal loss of proliferative capacity in the growth plate. Thus, the

loss of growth capacity in the skeletal growth plate is driven, not simply by time, but rather by growth itself (75-78).

Recent findings suggest that body growth deceleration is driven by a growth-limiting genetic program that occurs in multiple organs. This growth-limiting program, which involves the down-regulation of a large set of growth-promoting genes, depends not simply on age but also on organ growth itself. Therefore, the adult body size limit appears to be imposed by a negative feedback loop. Organ growth leads to progression of a genetic program, which in turn causes growth of the organ to slow and eventually cease. Different organs seem to use different types of informa-

tion to precisely target the adult body size. This genetic growth-controlling program appears to be important during the growth-limiting periods as well as during catch-up periods (79).

Another fundamental biological variable with the greatest impact on the recovery of stature in undernourished children is the quality of the diet, especially the quality of protein and the essential amino acids consumed, to enable a gain in stature without an unwanted increase in energy provision that might favor the later development of obesity. As an example, a study in children of school age provided a protein-rich diet to one group while a second group received a diet with added oil. The group given a protein-rich diet
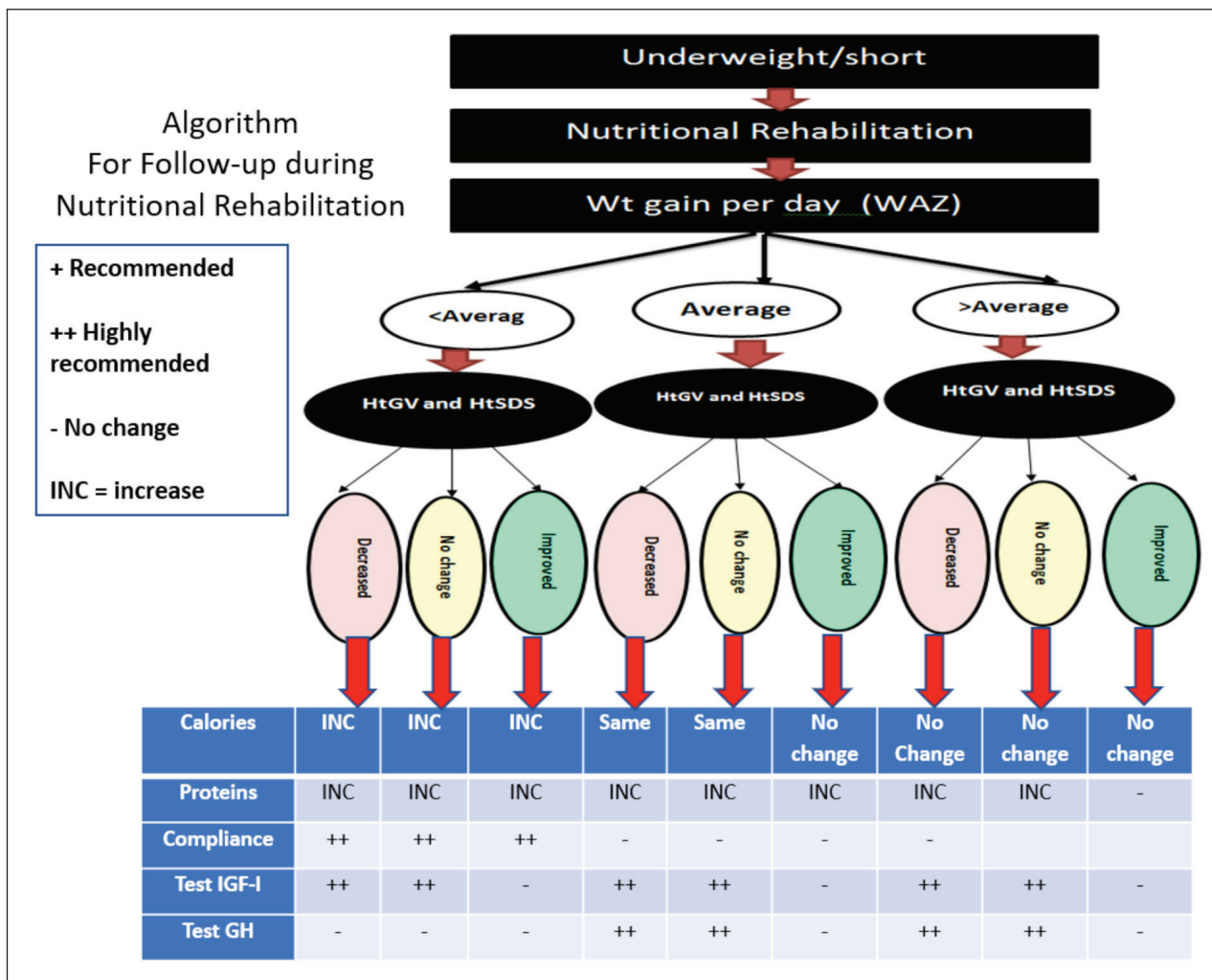
Figure 3. Algorithm for follow-up of underweight/ malnourished children based on anthropometric assessment.
Legend: INC = increase, ++ highly recommended, + = recommended; - no change recommended, weight-for-age (WAZ)

exhibited an increase in height directly related to the quantity of supplementary protein, while no detectable effect was present in the group consuming a diet with added oil (80).

It was also shown that the quantities of both protein and energy are important in the regulation of IGF-1, because these factors were essential in the restoration of the serum levels of IGF-1 (81-83). In one study, refeeding with a normo-caloric and normo-proteic diet after 5 days of fasting raised the levels of IGF-1 by up to 70% above basal levels before food restriction, meanwhile, refeeding with an iso-caloric but hypoproteic diet delayed the recovery in the levels of IGF-1 by 2 days, and the levels of this hormone failed to reach 50% of the values before restriction. In addition, refeeding with a low calorie and low protein diet, for more than 5 days, reduced the levels of IGF-1 even further (84). In India, Aykroyd and Krishnan (85) found that school children supplemented with skim milk grew faster in height. Malcolm (86) and Lampl et al. (87) showed that a skim milk supplement increased the height of stunted, low-protein-fed children in New Guinea. In the United States, Fomon et al. (88) found that infants fed skim milk (low energy, high protein) showed the same length growth but less weight gain than those fed the high energy formula. In Bangladesh, Kabir et al. (89) found that animal-source protein at 15% energy increased IGF-1 and linear growth more than did animal-source protein at 7.5% protein in children recovering from shigellosis.

A meta-analysis on the effect of protein intake on length gain in low-birthweight infants reported small but measurable effects of higher protein intake on improved linear growth. In very-low-birthweight babies, energy and the protein: energy ratio interacts synergistically to increase IGF-1 at high levels of both. The effect of protein on IGF-1 could be used as a marker of linear growth (90,91).

It has to be mentioned that inadequate compliance with nutrition regulations and/or supplement intake can explain some of the failures to achieve the proper weight gain in a number of our children. More intensive interference including hospital admission and/or tube feeding may be required in these cases.

In summary, different mechanisms and factors appear to control the process of catch-up during recovery from different degrees of undernutrition. Genetic control of catch up in the individual, the degree of his undernutrition at the beginning (BMI-SDS), the quantity and quality (energy: protein) offered during rehabilitation as well as compliance to the nutritional advice all share in the outcome. Frequent monitoring of weight changes (weight gain/day and WAZ), height changes (GV and Ht-SDS) and the BMI-SDS greatly help in tailoring the process of NR.

Based on our findings and literature reports, we suggest an algorithm for follow-up of underweight/malnourished children based mainly on anthropometric assessment (Figure 3).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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