Journal of Umm Al-Qura University for Medical Sciences

Journal homepage: https://uqu.edu.sa/en/mj

Research Article

Nutritional Status of Short Stature Children under Growth Hormone Therapy

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ARTICLE INFO

Received: 11/04/2023
Revised: 28/05/2023
Accepted: 08/06/2023

Keywords:
Undernutrition, paediatric, hormonal treatment, growth impairment, nutrient intake, stunting.

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ABSTRACT

Background: Childhood stunting is one of our community's most prevalent public health nutrition problems. Many factors may lead to the development of stunning. Growth hormones and diet might play a role in the treatment. This study aims to investigate the effect of nutritional status on the growth rate among children with short stature who underwent growth hormone therapy the previous year.

Methods: A one-year retrospective, cross-sectional study was carried out among 4-10-year-old children with stunting. Laboratory tests, anthropometric measurements, and dietary intake were measured at the start of the research and one year after the application of growth hormone therapy.

Results: A significantly higher growth rate was observed among males than females (P = 0.040). Also, males had significantly higher calorie intake (P). This study found that the patients had a less than 8.5% difference in energy intake vs. total energy requirement. There is a significant association between food consumption from two food groups (milk and meat) (P = 0.04 and 0.021, respectively.

Conclusion: Diet plays a significant role in the improvement of growth velocity.

1. INTRODUCTION

Short stature, defined as ″ height below the 2.3rd percentile on the WHO growth standard", is the most common manifestation of childhood malnutrition worldwide (Richmond & Rogol, 2021). Globally, in 2016, 22.9% (or 154.8 million) of children under five years of age suffered from stunting, defined as a low height-for-age (UNICEF/WHO/The World Bank Group Joint Child Malnutrition Estimates, 2020). A study by De Onis et al. (2013), which included data from 110 countries, found that the average relative annual decrease in the rate of childhood stunting is 1.8% per annum. This is far below the 3.9% rate needed to achieve the World Health Assembly's goal to reduce the global incidence of stunting to 100 million by 2025 (De Onis et al., 2013). In modern society, short-statured individuals in otherwise good general health are often under physical and psychological stress; furthermore, children with short stature are more susceptible to being intimidated by others or to report feeling less satisfied, easily frustrated, and introverted (Fernald & Grantham-McGregor, 2002). Children with short stature were more susceptible to being intimidated by others or to report feeling less satisfied, easily frustrated, and introverted (Fernald & Grantham-McGregor, 2002). In 2008, short stature led to 2.1 million deaths (Black et al., 2008). Short stature is not an illness. Genetic factors determine about 70-90% of growth, while environmental factors such as dietary intake, living environment, and physical

Doi: https://doi.org/10.54940/ms64260830

activity are also influences (Hammond et al., 1994). The impact of environmental factors on growth compared to genetic factors is relatively low. However, interventions can alter environmental factors and are considered important for maximising growth potential. Nutritional management is the most important factor, as it is key in preserving and synthesizing body tissues throughout the growth period. Nutritional deficits among subjects in the short stature category have been observed compared to the normal group. They also determined that the increased number of children with tall stature despite their parents' short stature resulted from proper nutrition (Lee et al., 2020). Children’s eating habits and preferences were closely linked to those of their mothers; proper maternal nutrition guidance and a high interest in children’s eating habits at home were considered to be very important, based on findings that children with short stature had low interest in meals and poor eating behaviours (Lee et al., 2020).

Despite possibly contributing to a decrease in morbidity and mortality, no single nutritional intervention has shown effectiveness for normalising linear growth rates and reversing the effects of stunting. Based on an assessment of multiple approaches to combating stunting, it has been suggested that scaling up nutrition-specific interventions might correct about 20% of cases (Fanzo et al., 2018). Since stunting is the product of exposure to a complex mix of detrimental impacts over time, effective treatment may entail tackling the problems of recurrent pathogenic and adverse environmental exposures and consuming low-quality, low-diversity diets (Grantham-McGregor et al., 2007).

Research among Korean children with short stature found that they had significantly lower protein, fat, calcium, and iron intakes than their taller peers. The observed lower protein intake is consistent with findings of protein deficiencies in many children with short stature (Lee et al., 2020). Other studies have also shown lower animal protein intake and higher carbohydrate intake in children with short stature (El Okda et al., 2015).

Almost 82% of severely stunted and 75% of severely malnourished patients had anaemia, while 43% of anaemic patients also had rickets. There was also a strong connection between rickets and stunting; 44% of severely stunted patients, 34% of moderately stunted patients, and 29% of slightly stunted patients had rickets (Shabana Ejaz &Latif, 2020).

Other studies done during the first year of growth hormone treatment found a strong first-year growth response in 11 out of 13 children with increased total energy intake (Straetemans et al., 2019).

On the other hand, not all studies found a relationship between diet and the impact of growth hormone treatment. A study examined boys with a constitutional delay of growth and maturation (CDGM), who use energy accelerated—an imbalance not resolved by added nutrition. Growth hormone (GH) therapy increased growth in these patients, with or without added nutrition (Han et al., 2011). However, there are not enough studies and no direct literature on the relationship between short stature and the nutritional status of children, especially in Saudi Arabia. This study hypothesises that nutritional status may improve linear growth in short-statured children undergoing GH therapy.

Children with systemic disorders such as GI diseases (particularly Crohn’s and celiac diseases), rheumatologic disease, renal disease, pulmonary disease, endocrine disease, genetic diseases; Turner syndrome, Noonan syndrome, and Silver-Russell syndrome were excluded due to either delayed bone age, sluggish height velocity, or both (Richmond & Rogol, 2021).

The proposed study was undertaken to evaluate the interrelationship between nutritional status and GH therapy’s effect on short-statured children in Saudi Arabia. We also sought to determine whether nutritional status provided relevant information that might contribute to developing nutritional strategies to prevent short stature in Saudi Arabian children.

2. MATERIALS AND METHODS

2.1 Study Setting

A retrospective, cross-sectional study was conducted at Taif Children's Hospital. Recruitment took place between July 2020 and November 2020. During regular hospital follow-up, an informed consent form was obtained from the participants.

Patients were selected via hospital record review of their diagnoses, dietary plans, ages, heights, lab results, length of treatment, and prescription of growth hormones. Inclusion criteria were children aged 4-10 years with short stature who had been treated with GH for the past year. Exclusion criteria were: children under 4 years of age or older than 10; those who had been treated with GH for less than one year; or patients with chronic diseases, including renal and gastrointestinal disorders or genetic diseases with primary effects on growth, such as Turner syndrome and Down syndrome.

2.2 Data Collection

2.2.1 Clinical measurements

Laboratory investigations were collected at baseline, including fasting complete blood count (CBC), electrolyte measurements, and GH records.

And after a year of treatment.

Weight was measured to the nearest 0.1 kg with a digital weighing scale (Seca, Hamburg, Germany). Height was measured to the nearest millimetre with a wall-mounted stadiometer (Gima, Milano, Italy). Height velocity was calculated as a change in height over a 12-month interval. The height percentile was determined using the standards for the child’s age on a graphic chart. For the assessment of linear growth, a height-for-age index was used. The height was plotted on the WHO chart against the patient's age, with the 50^{th} percentile for their age and sex considered as the normally expected height. For stunting, patients were categorized into normal stature (95-100%, +2SD to -1SD), mild (90-94%, -1SD to -2SD), moderate (85-89%, -2SD to -3SD), and severe stunting (less than 85%, less than -3SD) (*WHO | World Health Organization*, 2021). The study was approved by the

Institutional Review Board (IRB number HAP-02-T-067, approval no. 398).

2..2.2 Sociodemographic Profile

The children's parents or guardians were asked to complete a questionnaire that included sociodemographic data such as age, gender, parental education and occupations, monthly income and area of residence, as well as personal habits such as diet, physical activity, consumption of medications, developmental and family history.

2..2.3 Dietary intake

Dietary intake was estimated using a food frequency questionnaire (FFQ) for young children (Mumena & Kutbi, 2022; Zheng et al., 2020). Mothers were interviewed in the nutrition clinic. Standardized measuring utensils and pictures of foods with various portions were used to help mothers objectively quantify their children's food consumption for one week. Intake was then analysed using "LOSE IT" nutrition software (Nutritional Analysis Program, Version 12.2). Energy and macronutrient intake were estimated using the results of the FFQ and then compared with dietary requirements for the relevant age group.

2.3 Statistical Analysis

The sample size selection was based on a review of other literary studies (Lee et al., 2020; Shabana Ejaz & Latif, 2020). A sample of 105 children with short stature was selected from the hospital records. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) (IBM SPSS Statistics for Windows, Version 26.0; Armonk, NY: IBM Corp). Frequency and percentages were used to display categorical variables. Means and standard deviations were used to display numerical variables. A chi-square test was used to test for the presence of an association between categorical variables. An independent t-test and an ANOVA were also used to test for association. The level of significance was set at $P \leq 0.05$.

3. RESULTS

Sociodemographic data are shown in **Table 1**. There were 50 male and 55 female patients with short stature. 35.2% of first-born children were diagnosed with short stature, while only 2.8% of seventh-born children had short stature. Regarding the parents' educational level, a large proportion of parents held a bachelor's degree (54.3% and 60.0%, respectively).

Table 1: Sociodémographique data of participants.

Variables		**Growth velocity**			**Total**		***P. value***
		High	**Normal**	**Low**		**%**	
Gender	Male	27	20	3	50	47.6	0.04*
	Female	20	23	12	55	52.4	
Child's Birth Order	First	17	14	6	37	35.2	0.94
	Second	15	9	3	27	25.7	
	Third	6	8	3	17	16.1	
	Forth	5	4	1	10	9.5	
	Fifth	1	4	1	6	5.7	
	Sixth	1	2	0	3	2.8	
	Seventh	2	2	1	5	4.7	
Mother's Education Level	Middle School	3	2	0	5	4.8	0.28
	High School	12	16	3	31	29.5	
	Bachelor's	27	24	12	63	60.0	
	Post-Graduate	5	1	0	6	5.7	
Father's Education Level	Middle School	0	0	0	0	0	0.98
	High School	17	15	5	37	35.2	
	Bachelor's	25	23	9	57	54.3	
	Post-Graduate	5	5	1	11	10.5	

Mother's Income SAR/month	No income	13	7	4	24	22.9	0.56
	<2000	24	22	6	52	49.5	
	2000-5000	10	14	5	29	27.6	
	6000-10000	0	0	0	0	0	
	>10000	0	0	0	0	0	
Father's Income SAR/month	No income	11	2	1	14	13.3	0.07
	<2000	10	15	6	31	29.5	
	2000-5000	5	4	1	10	9.5	
	6000-10000	2	7	0	9	8.6	
	>10000	19	15	7	41	39.0	
	Total	**47**	**43**	**15**	**105**	**100**	

*$P \leq 0.05$, Saudi Arabian Riyal (SAR

Table 2 presents differences between the sexes in response to a year of GH therapy. The growth response varies significantly based on sex; 47 males had a high growth rate versus only 20 females (P = 0.040). Both male and female subjects (101) committed to adhere to one year of GH therapy; three were mostly committed, while only one patient did not commit at all. A significant difference between sexes was observed in terms of physical activity, with male subjects more active than females (P = 0.053).

Table 3 shows the influence of gender on growth velocity, haemoglobin, vitamin D, calcium, albumin, and calorie intake. Males had a higher growth velocity than females (P = 0.003). Additionally, males had significantly higher calorie intake (P = 0.001).

Table 2: Sex differences in growth velocity, commitment to growth hormone treatment and physical activity.

Variables		**M**	**F**	***Total***	**Chi²**	***P. value***
Growth Velocity	High	27	20	47	6.42	0.04*
	Normal	20	23	43		
	Low	3	12	15		
Commitment to GH Therapy	Yes	50	51	101	3.78	0.15
	No	0	1	1		
	Sometimes	0	3	3		
PA	Yes	3	5	8	5.87	0.05*
	No	17	30	47		
	Sometimes	30	20	50		

Male (M), Female (F), Physical Activity (PA), *P =0.05

Table 3: Sex influences patients' growth velocity and calorie intake.

Variables	**Gender**	**N**	**Mean ± SD**	***P. value***
GV cm/year	Male	50	7.00 ± 1.65	0.003*
	Female	55	6.01 ± 1.68	
Calorie intake	Male	50	1674.76 ± 256.62	<0.001*
	Female	55	1457.56 ± 208.55	

GV (Growth velocity),*$P \leq$ 0.001

After one year of GH therapy, blood values significantly differed depending on GV. Patients had significantly different albumin levels across all three GV categories. There was no significant difference in haemoglobin between the three GV categories; however, haemoglobin was significantly higher in the high-velocity group versus the low-velocity group. Additionally, there was no discernible difference in calorie intake across the three GV categories (**Table 4)**.

Table 5 illustrates the difference between the participants' energy requirements and energy intakes. Patients consumed 8.5% less energy than they required (<0.001).

GV increased significantly with GH treatment. Participants grew taller after 12 months of GH treatment [110.154 vs +114.648 17.42 (p = 0.001)]. Similarly, their weights increased significantly after 12 months of GH treatment [17.897 4.18 vs. 20.061 4.629 (p<0.001)] (**Table 6**).

There was no significant effect of grains, vegetables, fruits, and fat consumption on growth velocity P = (0.795, 0.144, 0.063, 0.821), respectively (**Table 7**).

Table 8 demonstrates a significant association between milk and meat consumption and GV (P = 0.042 and 0.021, respectively). The more frequent the consumption, the more regular and higher GV was achieved. Patients consumed different dairy products such as milk, laban, yoghurt and labna. The most popular food items among participants were milk, laban, yoghurt, and labna respectively. The average consumption was 1-3 portions a day. The chicken was the most ingested food item in the meat group. The most common frequency of chicken consumption was 1-3 times per day (72.3%), then 4-6 times per week (15.2%). Those who did not consume chicken or consumed it 1-3 times per month were in the minority, with only 1% of subjects in each group. Fish and sausage were the least consumed food items in the meat group.

4. DISCUSSION

Stunting among children in the Middle East is highly prevalent. According to a community-based study, the % of children in Saudi Arabia with stunted growth was 10.9% (M. El Mouzan et al., 2010). This is worrying, as stunted children may experience delayed mental development, poor school performance, and reduced intellectual capacity. In turn, this affects economic productivity at the national level. The primary treatment approach for stunting in children is GH therapy. However, stunting is often a result of long-term nutritional deprivation, and diet might play a role in treatment. Therefore, this study aimed to investigate the effect and efficiency of GH therapy and nutrition on childhood stunting. Stunting distribution varied by sex. We found that 52.4% of study subjects with stunting were female, compared to 47.6% male. This finding is different from that of previous studies; in the West Bank,

Table 4: Haemoglobin, vitamin D, calcium, and calorie intake values and growth velocity.

Parameters		**Growth velocity categories**			***P. value***
		High	**Normal**	**Low**	
Haemoglobin (g/dl)	**Mean ± SD**	13.35 ± 0.79[a]	13.11 ± 0.81[ab]	12.4 ± 3.27[b]	0.08
	No.	47	43	15	
Vitamin D (nmol/L)	**Mean ± SD**	35.59 ± 16.73[a]	36.73 ± 16.24[a]	34.62 ± 21.54[a]	0.90
	No.	47	43	15	
Calcium (mg/dl)	**Mean ± SD**	9.13 ± 0.39[a]	8.87 ± 1.12[a]	9.015 ± 0.49[a]	0.31
	No.	47	43	15	
Calorie Intake (Kcal/day)	**Mean ± SD**	1606 ± 247[a]	1514 ± 241[a]	1553 ± 309[a]	0.23
	No.	47	43	15	

[a]Significantly different within the group, [b] significantly different from high GV, [ab] significantly different from both GV

Table 5: Relationship between calorie requirements and calorie intakes.

Parameters		**Mean ± SD**	***P. value***
Calories	Calorie requirements	1699 ± 263	0.001*
	Calorie intakes	1560 ± 255	

*P <0.001

Table 6: Effects of growth hormone therapy on height and weight after 1 year of treatment.

Parameters		**Mean ± SD**	***P. value***
Height	Before GH treatment	110.154 ± 10.18	0.001*
	After 1 year of GH treatment	114.648 ± 17.42	
Weight	Before by GH treatment	17.897 ± 4.18	<0.001*
	After 1 year of GH treatment	20.061 ± 4.629	

*$P \leq 0.001$

Table 7: Effect of frequent grain, vegetable, fruit and fat group consumption on growth velocity during 1 year of growth hormone therapy.

Food Groups	**Frequency of Consumption**	**Growth Velocity**			**Total**	***P. value***
		High	**Normal**	**Low**		
Vegetable Group	No consumption	2	2	0	4	0.14
	1-3 monthly	3	8	5	16	
	1-3 weekly	3	3	3	9	
	4-6 weekly	12	11	3	26	
	1-3 daily	24	19	4	47	
	4-6 daily	3	0	0	3	
	7 or more daily	0	0	0	0	
Grain Group	No consumption	16	18	5	39	0.79
	1-3 monthly	7	7	3	17	
	1-3 weekly	2	4	1	7	
	4-6 weekly	4	1	0	5	
	1-3 daily	18	13	6	37	
	4-6 daily	0	0	0	0	
	7 or more daily	0	0	0	0	
Fruit Group	No consumption	5	6	2	13	0.06
	1-3 monthly	4	6	4	14	
	1-3 weekly	7	15	1	23	
	4-6 weekly	6	6	3	15	
	1-3 daily	25	10	5	40	
	4-6 daily	0	0	0	0	
	7 or more daily	0	0	0	0	
Fat Group	No consumption	0	0	0	0	0.82
	1-3 monthly	41	37	14	92	
	1-3 weekly	2	1	1	4	
	4-6 weekly	2	3	0	5	
	1-3 daily	2	2	0	4	
	4-6 daily	0	0	0	0	
	7 or more daily	0	0	0	0	

Table 8 : Effect of frequent meat and milk group consumption on growth velocity during 1 year of growth hormone therapy.

Food Groups	**Frequency of Consumption**	**Growth Velocity**			**Total**	***P. value***
		High	**Normal**	**Low**		
Meat Group	No consumption	5	14	3	22	0.02*
	1-3 Monthly	13	17	8	38	
	1-3 weekly	12	4	2	18	
	4-6 weekly	6	5	2	13	
	1-3 Daily	11	3	0	14	
	4-6 Daily	0	0	0	0	
	7 or more daily	0	0	0	0	
Total		**47**	**43**	**15**	**105**	
Milk Group	No consumption	1	0	0	1	0.04*
	1-3 Monthly	2	3	5	10	
	1-3 weekly	4	9	1	14	
	4-6 weekly	11	5	3	19	
	1-3 Daily	28	26	6	60	
	4-6 Daily	1	0	0	1	
	7 or more daily	0	0	0	0	
Total		**47**	**43**	**15**	**105**	

*$P \leq 0.05$

Palestine, the incidence of stunting among school-aged children aged 13-15 years was 9.2% for boys, 7.3% for girls in Ramallah 9.4% for boys and 4.2% for girls in Hebron (Mikki et al., 2009). A stunning study of South Indian teenagers aged 11-16 found that stunting was 38.8% in boys and 36.9% in girls (Haboubi & Shaikh, 2009). The average prevalence of stunting in the 11-16 age group is 14.4% for Saudi boys and 14.8% for Saudi girls (M. I. El Mouzan et al., 2011).

This difference may be due to the age range included in the study, as the age range in the current study was 4-10, whereas the age range in the other studies was 11-16. This could also explain the differences in body composition, as measured by a higher fat mass and a lower muscle mass in females. This may also contribute to the observed prepubertal differences in GH action (Juul et al., 2000). Additionally, prepubertal females exhibit significantly higher serum GH-binding protein levels than prepubertal boys and have a greater fat-to-muscle ratio (Cohen et al., 2002).

Socioeconomic factors have previously been linked with malnutrition; the prevalence of short stature is higher in children from poor families (Heshmat et al., 2020). A study conducted in Iran discovered a correlation between the prevalence of underweight and malnutrition and the mother's occupation, the parent’s education level, and the number of children in the family (Bahreynian et al., 2015). However, in the current study, there was no significant relationship between socioeconomic factors and the prevalence of short stature or growth velocity. This may be due to the free access to health care and nutritional support in Saudi Arabia and the ability to obtain financial support.

The results show that GH therapy significantly increased weight, height, and GV by 4%. There was a significantly higher GV rate, as measured by a mean value of 4.49 cm,

$P = 0.001$. Weight also increased by a mean of 2.16 kg, $P < 0.001$. GH stimulates growth by inducing a satisfying growth response in individuals. GH dosing levels may explain this increase. It has been demonstrated that an enhanced growth rate in short children with various etiologies following GH therapy is typically associated with increased appetite (Yackobovitch-Gavan et al., 2018). Appetite and food intake are controlled by the interaction of the central nervous system and endogenous appetite-regulating hormones. This agrees with our findings, as the results show a substantial weight gain after GH therapy.

However, GV was influenced by patients' sex. It has been discovered that sex has a significant effect on weight and height growth trends, with boys significantly heavier and taller than girls from birth to four years of age (Ghaemmaghami et al., 2018). This agrees with another study that observed that sex significantly affected weight growth trends, with boys having a higher mean weight from birth to two years of age (Hosseini et al., 2021).

Although total calorie intake was not significantly correlated with GV, certain food groups, such as meat and milk, were associated with increased height and weight. These two groups have nutrients that support growth, such as protein and calcium. Research indicates that higher protein consumption during childhood correlates with increased height and weight (Thorisdottir et al., 2013). A high animal protein intake among one-year-old children was attributed to increased height, weight, and BMI for children up to age two (Koletzko et al., 2009). The introduction of protein in early childhood might increase growth. Diet is a critical factor in children's development. Proteins provide essential amino acids that stimulate growth. Achieving optimal protein intake, particularly from animal sources such as red meat, eggs, and dairy products, protects against stunting (E et al., 2015). Besides protein, dairy products positively influence stunted growth and children at risk for stunting. It has been reported that consuming 150 mL of milk and one egg daily for 90 days and 1 RDA of multiple micronutrient powder for 60 days improved length-for-age z ratings (Iannotti et al., 2017). 100 grams of whole cow's milk contains 64 calories and 3.5 grams of protein. Additionally, it includes essential micronutrients and bioactive components that may be responsible for its impact on linear growth (Hoppe et al., 2006). A 55 g egg provides approximately 75 calories, 7 g protein, 5 g fat, 1.6 g saturated fat, vitamins, minerals, and carotenoids. Along with promoting linear growth in young children, egg supplementation has been shown to increase choline and docosahexaenoic acid status, which is essential for growth and neurocognitive progress (Lutter et al., 2018). The current study's findings report that milk was the most consumed dairy product, with an average of 1-3 portions/day (58.1%), while egg consumption was high, with 1-3 weekly portions (44.8%).

After a year of GH therapy, haemoglobin (HGB), Vitamin D, and calcium blood values were significantly associated with GV in both sexes. There was a significant relationship between calorie intake and GV during GH treatment. It has been reported that haemoglobin concentration and RBC count were substantially lower in small-stature cases than in a control group (E et al., 2015). The lower serum iron levels reported can clarify this result: Iron is a critical component of haemoglobin and RBCs. Patients with high GV had significantly higher haemoglobin levels.

By comparing caloric intakes and requirements of children with short stature, we discovered that patients did not meet their caloric requirements and that, despite this deficiency, iron and albumin levels returned to normal, and the growth rate was excellent.

The consumption level of multiple food groups was investigated in this research (Lee et al., 2020) to understand better the disparity between dietary intakes in standard and short-stature classes as they relate to more difficult eating habits. The five food groups' analysis revealed that the consumption level of fruit and vegetables, beef, seafood, eggs, legumes, fat, calcium, and iron was slightly lower in the small stature population. In contrast, our study's findings indicated that only meat consumption was significant and was consumed in large quantities by children of small stature. It has been confirmed GH's short- and long-term effectiveness in treating GH deficiency, as height and peak velocity improved in all patients after one year of treatment (Pozzobon et al., 2019). These observations corroborate our research, which demonstrated improved height velocity following GH; use by the conclusion of treatment, 44.7% of patients tended to have achieved a growth rate greater than 7 cm/year, and 40.9% of patients were near their goal growth rate of 5-6.5 cm/year, except for fifteen patients (14.2%) who had a growth rate of less than 5cm/year.

Incorporating many variables can increase the scope of care and accuracy of objective solutions. This study is the first of its kind in Saudi Arabia. Limitations include not having baseline anthropometric measurements for patients and the memory bias of using an FFQ.

5. CONCLUSION AND RECOMMENDATION

Our findings suggest that stunted children and those at risk for stunting who receive GH treatment can have better health outcomes, and these outcomes improve by combining the therapy with meat and dairy product consumption and physical activity. Further randomized control trials and cohort studies should be carried out to determine the optimal amount of nutrients and physical activity levels to increase the efficiency of GH therapy.

The study's recommendations emphasize the importance of increasing energy intake to meet children's energy requirements, mainly from meat and dairy products, due to their benefits in increasing height in children of short stature.

AUTHOR CONTRIBUTION

AQ, HA and KG made substantial contributions to the concept and design of the study. WFA, NA and NAA conducted the literature search. WEA, AQ, TB, WEA, and TB, acquisition, analysis, and interpretation of data. DN, MG, AQ and KG wrote the initial draft. DN, MG, KG and SOA reviewed and edited the manuscript. SOA and WA, critical review of the manuscript for important, intellectual content. KG agreed to be accountable for all aspects of the work. FA, KG, and AQ reviewed the final version to be published.

SOURCE OF FUNDING

No funding was received.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

Bahreynian, M., Kelishadi, R., Qorbani, M., Motlagh, M. E., Kasaeian, A., Ardalan, G., Rad, T. A., Najafi, F., Asayesh, H. & Heshmat, R. (2015). Weight disorders and anthropometric indices according to socioeconomic status of living place in Iranian children and adolescents: The CASPIAN-IV study. In *Journal of Research in Medical Sciences*.

Black, R. E., Allen, L. H., Bhutta, Z. A., Caulfield, L. E., de Onis, M., Ezzati, M., Mathers, C. & Rivera, J. (2008). Maternal and child undernutrition: global and regional exposures and health consequences. *The Lancet*, *371*(9608), 243–260. https://doi.org/10.1016/S0140-6736(07)61690-0

Cohen, P., Bright, G. M., Rogol, A. D., Kappelgaard, A. M. & Rosenfeld, R. G. (2002). Effects of Dose and Gender on the Growth and Growth Factor Response to GH in GH-Deficient Children: Implications for Efficacy and Safety. *The Journal of Clinical Endocrinology & Metabolism*, *87*(1), 90–98. https://doi.org/10.1210/JCEM.87.1.8150

De Onis, M., Dewey, K. G., Borghi, E., Onyango, A. W., Blössner, M., Daelmans, B., Piwoz, E. & Branca, F. (2013). The World Health Organization's global target for reducing childhood stunting by 2025: rationale and proposed actions. *Maternal & Child Nutrition*, *9*(2), 6–26. https://doi.org/10.1111/MCN.12075

E, E. O., MA, A.-H., F, G. & I, S. (2015). IRON AND ZINC STATUS IN CHILDREN WITH SHORT STATURE. *Egyptian Journal of Occupational Medicine*, *39*(1), 105–118. https://doi.org/10.21608/EJOM.2015.814

El Mouzan, M., Foster, P., Al Herbish, A., Al Salloum, A., Al Omar, A. & Qurachi, M. (2010). Prevalence of malnutrition in Saudi children: a community-based study. *Annals of Saudi Medicine*, *30*(5), 20–67. https://doi.org/10.4103/0256-4947.67076

El Mouzan, M. I., Al Herbish, A. S., Al Salloum, A. A., Foster, P. J., Al Omer, A. A. & Qurachi, M. M. (2011). Prevalence of short stature in Saudi children and adolescents. *Annals of Saudi Medicine*, *31*(5), 498–501. https://doi.org/10.4103/0256-4947.84628

ElOkda E, Abdel-Hamid MA, Gadalla F & Sabry I. (2015). Iron and Zinc Status in Children with Short Stature. *Egyptian Journal of Occupational Medicine*, *39*(1). https://doi.org/10.21608/ejom.2015.814

Fanzo, J., Hawkes, C., Udomkesmalee, E., Afshin, A., Allemandi, L., Assery, O., Baker, P., Battersby, J., Bhutta, Z., Chen, K., Corvalan, C., Di Cesare, M., Dolan, C., Fonseca, J., Grummer-Strawn, L., Hayashi, C., McArthur, J., Rao, A., Rosenzweig, C. & Schofield, D. (2018). *2018 Global Nutrition Report: Shining a light to spur action on nutrition*. Bristol, UK: Development Initiatives.

Fernald, L. C. & Grantham-McGregor, S. M. (2002). Growth Retardation Is Associated with Changes in the Stress Response System and Behavior in School-Aged Jamaican Children. *The Journal of Nutrition*, *132*(12), 3674–3679. https://doi.org/10.1093/JN/132.12.3674

Ghaemmaghami, P., Ayatollahi, S. M. T., Alinejad, V. & Sharafi, Z. (2018). Growth curves and their associated weight and height factors in children from birth to 4 years old in West Azerbaijan Province, northwest Iran. *Archives de Pédiatrie*, *25*(6), 389–393. https://doi.org/10.1016/J.ARCPED.2018.06.010

Grantham-McGregor, S., Cheung, Y. B., Cueto, S., Glewwe, P., Richter, L. & Strupp, B. (2007). Developmental potential in the first 5 years for children in developing countries. *The Lancet*, *369*(9555), 60–70. https://doi.org/10.1016/S0140-6736(07)60032-4

Haboubi, G. J. & Shaikh, R. B. (2009). A Comparison of the Nutritional Status of Adolescents from Selected Schools of South India and UAE: A Cross-sectional Study. *Indian Journal of Community Medicine : Official Publication of Indian Association of Preventive & Social Medicine*, *34*(2), 200. https://doi.org/10.4103/0970-0218.51230

Hammond, G. K., Barr, S. I. & McCargar, L. J. (1994). Teachers' perceptions and use of an innovative early childhood nutrition education program. *Journal of Nutrition Education*, *26*(5), 233–237. https://doi.org/10.1016/S0022-3182(12)80895-8

Han, J. C., Damaso, L., Welch, S., Balagopal, P., Hossain, J. & Mauras, N. (2011). Effects of Growth Hormone and Nutritional Therapy in Boys with Constitutional Growth Delay: A Randomized Controlled Trial. *The Journal of Pediatrics*, *158*(3), 427–432. https://doi.org/10.1016/J.JPEDS.2010.09.006

Heshmat, R., Qorbani, M., Mozafarian, N., Djalalinia, S., Sheidaei, A., Mansourian, M., Hajizadeh, N., Motlagh, M. E., Asayesh, H., Mahdavi-Gorabi, A. & Kelishadi, R. (2020). Economic inequality in prevalence of underweight and short stature in children and adolescents: the weight disorders survey of the CASPIAN-IV study. *Archives of Endocrinology and Metabolism*, *64*(5), 548–558. https://doi.org/10.20945/2359-3997000000280

Hoppe, C., Mølgaard, C. & Michaelsen, K. F. (2006). Cow's Milk and Linear Growth in Industrialized and Developing Countries. *Annual Review of Nutrtion*, *26*, 131–173. https://doi.org/10.1146/ANNUREV.NUTR.26.010506.103757

Hosseini, S. M., Maracy, M. R., Sarrafzade, S. & Kelishadi, R. (2021). Child Weight Growth Trajectory and its Determinants in a Sample of Iranian Children from Birth until 2 Years of Age. *International Journal of Preventive Medicine*, *5*(3), 400.

Iannotti, L. L., Lutter, C. K., Stewart, C. P., Riofrío, C. A. G., Malo, C., Reinhart, G., Palacios, A., Karp, C., Chapnick, M., Cox, K. & Waters, W. F. (2017). Eggs in early complementary feeding and child growth: A randomized controlled trial. *Pediatrics*, *140*(1), 201–345. https://doi.org/10.1542/PEDS.2016-3459/37999

Juul, A., Fisker, S., Scheike, T., Hertel, T., Müller, J., Ørskov, H. & Skakkebæk, N. E. (2000). Serum levels of growth hormone binding protein in children with normal and precocious puberty: relation to age, gender, body composition and gonadal steroids. *Clinical Endocrinology*, *52*(2), 165–172. https://doi.org/10.1046/J.1365-2265.2000.00923.X

Koletzko, B., Von Kries, R., Closa, R., Escribano, J., Scaglioni, S., Giovannini, M., Beyer, J., Demmelmair, H., Gruszfeld, D., Dobrzanska, A., Sengier, A., Langhendries, J. P., Cachera, M. F. R. & Grote, V. (2009). Lower protein in infant formula is associated with lower weight up to age 2 y: a randomized clinical trial. *The American Journal of Clinical Nutrition*, *89*(6), 1836–1845. https://doi.org/10.3945/AJCN.2008.27091

Lee, E. M., Park, M. J., Ahn, H. S. & Lee, S. M. (2020). Differences in Dietary Intakes between Normal and Short Stature Korean Children Visiting a Growth Clinic. *Clinical Nutrition Research*, *1*(1), 23–29. https://doi.org/10.7762/CNR.2012.1.1.23

Levels and trends in child malnutrition: UNICEF/WHO/The World Bank Group joint child malnutrition estimates: key findings of the 2020 edition. (2020, 1. January). WHO. https://www.who.int/publications/i/item/jme-2020-edition

Lutter, C. K., Iannotti, L. L. & Stewart, C. P. (2018). The potential of a simple egg to improve maternal and child nutrition. *Maternal & Child Nutrition*, *14*(1), 126–510. https://doi.org/10.1111/MCN.12678

Mikki, N., Abdul-Rahim, H. F., Awartani, F. & Holmboe-Ottesen, G. (2009). Prevalence and sociodemographic correlates of stunting, underweight, and overweight among Palestinian school adolescents (13-15 years) in two major governorates in the West Bank. *BMC Public Health*, *9*(1), 1–12. https://doi.org/10.1186/1471-2458-9-485/TABLES/5

Mumena, W. A. & Kutbi, H. A. (2022). Development of a Food Frequency Questionnaire for Assessing Habitual Intake of Free Sugar Among Children in Saudi Arabia. *Frontiers in Nutrition*, *8*. https://doi.org/10.3389/fnut.2021.742737

Pozzobon, G., Partenope, C., Mora, S., Garbetta, G., Weber, G. & Barera, G. (2019). Growth hormone therapy in children: predictive factors and short-term and long-term response criteria. *Endocrine* , *66*(3), 614–621. https://doi.org/10.1007/S12020-019-02057-X

Richmond, E. J. & Rogol, A. D. (2021). Diagnostic Aproach to Children and Adolescents with Short Stature. *UpToDate*. Retrieved February 26, 2021, from https://www.uptodate.com/contents/diagnostic-approach-to-children-and-adolescents-with-short-stature

Shabana Ejaz, M. & Latif, N. (2020). Stunting and micronutrient deficiencies in malnourished children. *Journal Of Pakistan Medical Association*, *60*(7), 10–82.

Straetemans, S., Schott, D. A., Plasqui, G., Dotremont, H., Gerver-Jansen, A. J. G. M., Verrijken, A., Westerterp, K., Zimmermann, L. J. I. & Gerver, W. J. M. (2019). Effect of growth hormone treatment on energy expenditure and its relation to first-year growth response in children. *European Journal of Applied Physiology*, *119*(2), 409–418. https://doi.org/10.1007/S00421-018-4033-6/FIGURES/4

Thorisdottir, B., Gunnarsdottir, I., Thorisdottir, A. V., Palsson, G. I., Halldorsson, T. I. & Thorsdottir, I. (2013). Nutrient Intake in Infancy and Body Mass Index at Six Years in Two Population-Based Cohorts Recruited before and after Revision of Infant Dietary Recommendations. *Annals of Nutrition and Metabolism*, *63*(1–2), 145–151. https://doi.org/10.1159/000354431

WHO | World Health Organization. (2021, 1. January). WHO. https://www.who.int/

Yackobovitch-Gavan, M., Gat-Yablonski, G., Shtaif, B., Hadani, S., Abargil, S., Phillip, M. & Lazar, L. (2018). Growth hormone therapy in children with idiopathic short stature – the effect on appetite and appetite-regulating hormones: a pilot study. *Endocrine Research*, *44*(1–2), 16–26. https://doi.org/10.1080/07435800.2018.1493598

Zheng, M., Campbell, K. J., Scanlan, E. & McNaughton, S. A. (2020). Development and evaluation of a food frequency questionnaire for use among young children. *PLoS ONE*, *15*(3). https://doi.org/10.1371/journal.pone.0230669