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ARAŞTIRMA / RESEARCH

Evaluation of prevalence, demographic characteristics, associated risk factors and effects of enteral nutrition products in children with primary malnutrition

Primer malnutrisyonlu çocukların prevalansının, demografik özelliklerinin, ilişkili risk faktörlerinin ve kullanılan enteral beslenme ürünlerinin etkilerinin değerlendirilmesi

Adnan Barutçu[1], Saliha Barutçu[2]

[1]Şanlıurfa Halfeti Devlet Hastanesi, Çocuk Sağlığı ve Hastalıkları Bölümü, [2]Aile Hekimliği Bölümü, Şanlıurfa, Turkey

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Abstract

Purpose: The present study aims to evaluate the prevalence, demographic characteristics, associated risk factors and effects of enteral nutrition products in malnourished children.

Materials and Methods: A total of 229 pediatric outpatients aged 1-18 years with primary malnutrition related growth failure and prescribed with hypercaloric enteral feeding regimen were included. A total of 73 healthy children with normal growth served as the control group. Anthropometric measurements included height (cm), weight (kg), body mass index (kg/m^2), height for age Z score and weight for age Z score.

Results: When the malnourished patients were compared with the control group; patients were aged younger and associated with higher likelihood of having a birth weight >3001 , shorter duration of breastfeeding, lower number of siblings, family with lower monthly income and illiterate mothers. In the malnourished group, height, weight, body mass index and height for age and weight for age Z scores improved significantly during 3rd month and 6th month as compared with baseline scores, regardless of gender, sibling number, maternal education and monthly income level.

Conclusion: Our findings show the efficacy and tolerability of 6-month high-calorie enteral nutritional support given to children with primary malnutrition, regardless of initial symptoms and socio-economic risk factors.

Keywords:. Primary malnutrition, high-calorie enteral feeding, anthropometrics, gastrointestinal tolerance, risk factors

Öz

Amaç: Çalışmamız; malnütrisyonlu çocukların prevalansının, demografik özelliklerinin, ilişkili risk faktörlerinin ve kullanılan enteral beslenme ürünlerinin etkilerinin değerlendirilmesini amaçlamıştır.

Gereç ve Yöntem: Primer malnütrisyona bağlı büyüme yetersizliği olan ve hiperkalorik enteral beslenme rejimi başlanmış 1-18 yaşları arasında toplam 229 pediatrik hasta çalışmaya dahil edildi. Büyümesi normal 73 sağlıklı çocuk kontrol grubunu oluşturdu. Antropometrik ölçümlere; boy (cm), ağırlık (kg), vücut kitle indeksi (kg/m^2), yaşa göre boy Z skoru ve yaşa göre ağırlık Z skoru dahil edildi.

Bulgular: Malnutrisyonlu hastalar kontrol grubu ile kıyaslandığında; daha küçük yaşta ve doğum ağırlığı >3001 g olanlarda malnütrisyonun görülme olasılığının daha fazla olduğu, bu hastaların emzirme sürelerinin daha kısa, kardeş sayısının daha az, ailelerinin düşük aylık gelirli ve annelerinin okuma yazma bilmiyor oldukları gözlendi. Malnütrisyonlu grupta boy, ağırlık (, vücut kitle indeksi, yaşa göre boy ve yaşa göre ağırlık Z skorları; cinsiyet, kardeş sayısı, anne eğitimi ve aylık gelir düzeyinden bağımsız olarak, başlangıç değerlerine kıyasla, 3. ve 6. ay kontrollerinde önemli ölçüde iyileşmiştir.

Sonuç: Bulgularımız başlangıç semptomları ve sosyo-ekonomik risk faktörlerinden bağımsız olarak, primer malnutrisyonlu çocuklarda verilen 6 aylık yüksek kalorili enteral beslenme desteğinin etkililiğini ve tolere edilebilirliğini göstermektedir.

Anahtar kelimeler: Primer malnütrisyon, yüksek kalorili enteral beslenme, antropometri, gastrointestinal tolerans, risk faktörleri

Yazışma Adresi/Address for Correspondence: Dr. Adnan Barutçu, Şanlıurfa Halfeti Devlet Hastanesi, Çocuk Sağlığı ve Hastalıkları Bölümü, Şanlıurfa, Turkey E-mail: adnan_barutcu@hotmail.com
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INTRODUCTION

Pediatric malnutrition is considered a major global public health problem, estimated to be associated with 45% of child deaths worldwide[1,2]. Malnutrition and inadequate intake of nutrients together with environmental, behavioral, biological factors lead to growth failure, impaired cognitive and physical development and increased risk of morbidity and mortality in children[1-3].

However, while prevalence and consequences of malnutrition are well studied for children aged ≤5 years, scarce amount of data are available for children and adolescents ages 5–19 years, despite profound consequences of malnutrition on education and health outcomes in the middle childhood and adolescence such as increased risk of cardio-metabolic diseases, poor school performance and poor health outcomes and reduced quality of life[3-6].

In Turkey, prevalence of acute and chronic malnutrition in general pediatric population was reported to be 1.5% and 7.5% in children aged ≤5 years (n=396) and to be 5.7% and 1% in children aged 6–16 years (n=1576), respectively, while much higher rates (10.1-11.2% and 4.6-16.6%, respectively) have also been reported in hospitalized pediatric patients[7-10].

Primary malnutrition, more commonly seen in low- and middle-income countries, is due to combined effect of several factors including low birth weight, lack of adequate food, recurrent infections and environmental enteropathy[11]. Accordingly, the prevalence of underweight, stunting and wasting in children below 5 years of age was reported to be higher in more underdeveloped "Eastern regions" (19.7, 17.7 and 16.2%, respectively) of Turkey as compared with more developed "Western regions" (2.8-4.8%, 10.3-10.9% and 0.9-8.2%, respectively)[7,12,13]. Sanliurfa province located in Southeastern Turkey with the longest border with Syria, is considered an undeveloped region of the country with 63.6% of the population living in shantytowns in the city outskirts and in poor socio-economic and environmental conditions[14].

Use of enteral feeding regimens has been recommended as a first line treatment in clinical care of malnourished children with growth faltering, as associated with improved anthropometrics along with maintenance of gut function and immune functions[15-17].

This study was therefore designed to evaluate the utility of high-calorie enteral feeding regimen in 1 to 18 years old malnourished children living in Sanliurfa province, in terms of anthropometrics, laboratory markers of nutritional status and gastrointestinal tolerance and to determine demographic and socioeconomic risk factors for malnutrition in relation to healthy control subjects without growth failure.

MATERIALS AND METHODS

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the Non-Interventional Clinical Research Ethics Committee of Harran University Faculty of Medicine (Date of Approval: 04/11/2019; Reference number/Protocol No: 19/04/02). Written informed consent was obtained from children and/or children's parents or legal guardian following a detailed explanation of the objectives and protocol.

Study population

A total of 229 pediatric outpatients aged 1-18 years (mean(SD) age 67.0(46.5) months, ranged 12.0 to 195.0 months, 53.7% were boys) diagnosed with primary malnutrition related growth failure (weight and height below <2SD percentiles for age) and prescribed with hypercaloric enteral feeding regimen were included in this retrospective 6-month follow-up study. Patients aged <12 months, with tube-feeding or abnormal findings on acute infection screening (based on physical examination, complete blood count, complete urinalysis and fecal occult blood screening test) and fecal examination for parasites as well as those with co-morbidities such as celiac disease (based on Anti-tTG-IgA and Anti-EMA-IgA and IgA serology), hypothyroidism (based on thyroid function tests) or chronic diseases related to malnutrition were excluded from the study.

A total of 73 healthy children (mean(SD) age 95.3(53.92) months, ranged 13.0 to 202 months, 53.4% were boys) with normal growth parameters (weight and height below >2SD percentiles for age) who attended routine outpatient visits at the same hospital within the study period served as the control group.

Procedure

Data on demographic characteristics (age, gender),

birth weight (g), duration of breastfeeding (month), sibling number, monthly income level, maternal educational level, nationality were retrieved from medical records in both malnourished and control groups. Anthropometrics including height (cm), weight (kg), body mass index (BMI; kg/m^2), height for age (HFA) Z score and weight for age (WFA) Z score were recorded at baseline and 3rd month and 6th month visits in malnourished patients under nutritional support and in control subjects. Major symptoms on admission, energy need (kcal), daily nutritional support dosing frequency and laboratory findings including complete blood count and blood biochemistry [Vitamin B12 (pg/mL), folate (ng/ml), iron (µg/dL), ferritin (ng/mL), 25-OH Vit D (ng/mL) and CRP (mg/dL)] as well as gastrointestinal tolerance were recorded in malnourished patients. During 6-month follow up, change in anthropometrics were evaluated in both malnourished and control groups, while change in laboratory parameters and gastrointestinal tolerance were evaluated in the malnourished group.

Considering monthly income, the categories were based on Turkey's minimum wage level set by the government, while monetary results were converted by using average 4.67 USD/TL exchange rate within the study period. High-calorie enteral nutritional support was also evaluated. High-calorie (1.5 kcal/mL) enteric feeding was used as a supplement and per oral in all malnourished patients

Statistical analysis

Statistical analysis was made using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY). Chi-square (χ^2) test was used for the comparison of categorical data, while numerical data were analyzed using Student's t-test and One-way ANOVA for variables with normal distribution and with Mann-Whitney U and Kruskal Wallis tests for non-normally distributed variables.

ANOVA and post hoc Tukey test were used for the parametric variables applying Bonferroni correction for p values. Change over time is evaluated by repeated measures with variance analysis or by Friedman and Wilcoxon test depending on distribution pattern of continuous variables. Correlation analysis was performed via Spearman test. Data were expressed as mean (standard deviation, SD), median (minimum-maximum) and percent (%) where appropriate. $p<0.05$ was considered statistically significant.

RESULTS

Malnourished patients vs. control subjects aged younger (mean(SD) 67.0(46.5) vs. 95.3(53.92) months, $p<0.001$) and associated with higher likelihood of having a birth weight >3001 g (75.6% vs. 63.0%, $p=0.012$), shorter duration of breastfeeding (mean(SD) 12.54(4.14) vs. 13.9(3.88) months, $p=0.009$), lower number of siblings (<2 in 28.8% vs. 19.2%, $p=0.004$), family with lower monthly income (US$428 in 68.1 vs. 21.9%, $p<0.001$) and illiterate mothers (32.8 vs. 21.9%, $p=0.035$) (Table 1).

In malnourished group, height ($p<0.05$ for each), weight ($p<0.05$ for each), BMI ($p<0.05$ for each) and HFA ($p<0.001$ for each) and WFA ($p<0.001$ for each) Z scores improved significantly during 3rd month and 6th month as compared with baseline scores, whereas all anthropometric scores remained poorer than those in the control group regardless of the study visit (Table 2).

No significant difference was noted in baseline, 3rd month and 6th month WFA and HFA Z scores in malnourished and control groups with respect to gender, as well as between boys and girls in malnourished vs. control groups (Table 3).

Apart from better 6th month HFA Z scores in control subjects with higher vs. lower number of siblings ($p=0.017$), no significant difference was noted in baseline, 3rd month and 6th month WFA and HFA Z scores in malnourished and control groups with respect to number of siblings, as well as between subjects with the same sibling number in malnourished vs. control groups (Table 3).

No significant difference was noted in baseline, 3rd month and 6th month WFA and HFA Z scores in malnourished and control groups with respect to maternal education and monthly income level, as well as between subjects with similar maternal education and monthly income in malnourished vs. control groups (Table 3).

Table 1. Baseline characteristics of malnourished patients and healthy controls

		Malnourished (n=229)	Control (n=73)	p value
Age (month), mean (SD, min-max)		67.0 (46.5, 12.0-195.0)	95.3 (53.92, 13.0-202.0)	<0.001
Gender, n(%)	Boy	123 (53.7)	39 (53.4)	0.966
	Girl	106 (46.3)	34 (46.6)	
Birth weight (g), n(%)	<1000	1 (0.4)	-	0.012[a]
	1000-2000	6 (2.6)	-	
	2001-3000	49 (21.4)	27 (37.0)	
	3001-4000	171 (74.7)	44 (60.3)	
	>4000	2 (0.9)	2 (2.7)	
Duration of breastfeeding (month), mean(SD)		12.54(4.14)	13.9 (3.88)	0.009
Sibling number, n(%)	0	9 (3.9)	0 (0)	0.004
	1	57 (24.9)	14 (19.2)	
	2	107 (46.7)	36 (49.3)	
	≥3	56 (24.5)	23 (31.5)	
Monthly income (US$), n(%)	<428	156 (68.1)	16 (21.9)	<0.001
	428-1070	63 (27.5)	50 (68.5)	
	>1070	10 (4.4)	7 (9.6)	
Maternal education, n(%)	Illiterate	75 (32.8)	16 (21.9)	0.035
	Primary school	80 (34.9)	24 (32.9)	
	Secondary school	54(23.6)	19 (26.0)	
	High school	17 (7.4)	9 (12.3)	
	University	3 (1.3)	5 (6.8)	
Nationality, n(%)	Turkish	191 (83.4)	61 (83.6)	0.975
	Syrian refugee	38 (16.6)	12 (16.4)	

χ^2test, Student's t test; [a]≤2000 vs. 2001-3000 vs. ≥3001 g groups

Table 2. Change in anthropometrics during study period in malnourished patients with nutritional support and control subjects

		Malnourished (n=229)			Control (n=73)		
		Baseline	3rd month	6th month	Baseline	3rd month	6th month
Anthropometrics							
Height (cm)	Mean(SD)	101.83(22.14)	104.07(21.81)[a]	106.34(21.4)[a]	122.88(26.24)[b]	124.29(25.89)[b]	125.58(25.51)[b]
	% change from baseline		2.20	4.43	-	1.15	2.20
Weight (kg)	Mean(SD)	15.8(7.45)	17.03(7.76)[a]	18.04(8.05)[a]	27.25(14.49)[b]	27.92(14.56)[b]	28.35(14.75)[b]
	% change from baseline		7.78	14.18	-	2.46	4.04
BMI (kg/m^2)	Mean(SD)	14.56(1.22)	15.62(8.42)[a]	15.31(1.29)[a]	16.66(1.97)[b]	16.72(1.92)[b]	16.64(2.09)[b]
Height for age Z score	Mean(SD)	-1.72(0.86)	-1.64(0.82)[aa]	-1.51(0.79)[aa]	-0.39(0.48)[bb]	-0.44(0.42)[bb]	-0.44(0.45)[bb]
	% change from baseline		4.87	13.9	-	-12.8	-12.8
Weight for age Z score	Mean(SD)	-1.97(0.56)	-1.57(0.59)[aa]	-1.36(0.59)[aa]	-0.26(0.34)[bb]	-0.28(0.3)[bb]	-0.3(0.33)[bb]
	% change from baseline		25.5	44.8	-	-7.7	-15.7

[a]p<0.05 and [aa]p<0.001; compared to baseline visit in malnourished group; [b]p<0.05 and [bb]p<0.001; compared to the same visit values in the malnourished group

Table 3. Weight for age and height for age z scores in malnourished and control groups according to sociodemographic variables

	Weight for age								Height for age					
	Malnourished				Control				Malnourished			Control		
	N	Baseline	3rd month	6th month	N	Baseline	3rd month	6th month	Baseline	3rd month	6th month	Baseline	3rd month	6th month
Gender														
Boy	123	-1.95(0.55)	-1.55(0.6)	-1.35(0.62)	39	-0.24(0.35)	-0.26(0.32)	-0.3(0.34)	-1.74(0.89)	-1.67(0.85)	-1.53(0.83)	-1.72(0.86)	-1.64(0.82)	-1.51(0.79)
Girl	106	-1.99(0.57)	-1.58(0.57)	-1.38(0.56)	34	-0.28(0.34)	-0.29(0.27)	-0.3(0.31)	-1.71(0.84)	-1.61(0.78)	-1.5(0.74)	-0.4(0.51)	-0.44(0.45)	-0.48(0.42)
p value		0.696	0.652	0.444		0.561	0.445	0.599	0.798	0.575	0.839	0.611	0.493	0.951
Sibling#														
0	9	-1.6(0.6)	-1.22(0.6)	-1.06(0.7)	-	-	-	-	-1.19(1.21)	-1.21(1.24)	-1.11(1.19)	-	-	-
1	57	-1.96(0.44)	-1.52(0.47)	-1.32(0.52)	14	-0.24(0.34)	-0.27(0.23)	-0.28(0.27)	-1.74(0.83)	-1.64(0.84)	-1.48(0.78)	-0.49(0.39)	-0.47(0.3)	-0.44(0.3)
2	107	-2.05(0.55)	-1.65(0.57)	-1.38(0.61)	36	-0.28(0.33)	-0.31(0.31)	-0.35(0.31)	-1.79(0.79)	-1.71(0.77)	-1.55(0.8)	-0.37(0.37)	-0.45(0.33)	-0.53(0.3)
3	38	-1.94(0.71)	-1.59(0.78)	-1.48(0.7)	23	-0.24(0.38)	-0.23(0.32)	-0.23(0.38)	-1.7(1.0)	-1.61(0.89)	-1.63(0.77)	-0.38(0.66)	-0.4(0.6)	-0.3(0.65)
≥4	18	-1.8(0.44)	-1.4(0.42)	-1.25(0.36)	-	-	-	-	-1.61(0.92)	-1.55(0.57)	-1.36(0.55)	-	-	-
p value		0.016	0.055	0.400		0.776	0.505	0.294	0.315	0.366	0.176	0.518	0.337	0.017
Maternal education														
Illiterate	75	-2.06(0.58)	-1.7(0.61)	-1.44(0.65)	16	-0.13(0.27)	-0.18(0.26)	-0.18(0.29)	-1.85(0.84)	-1.77(0.82)	-1.6(0.87)	-0.21(0.44)	-0.28(0.47)	-0.27(0.47)
Primary school	80	-1.95(0.52)	-1.49(0.57)	-1.34(0.54)	24	-0.21(0.36)	-0.23(0.31)	-0.26(0.32)	-1.6(0.94)	-1.54(0.84)	-1.45(0.73)	-0.33(0.37)	-0.41(0.29)	-0.45(0.28)
Secondary school	54	-1.85(0.51)	-1.44(0.55)	-1.19(0.56)	19	-0.37(0.36)	-0.37(0.3)	-0.39(0.36)	-1.73(0.8)	-1.62(0.8)	-1.49(0.81)	-0.53(0.59)	-0.59(0.53)	-0.61(0.51)
High school	17	-2.04(0.72)	-1.7(0.59)	-1.65(0.59)	9	-0.29(0.35)	-0.3(0.31)	-0.33(0.29)	-1.83(0.74)	-1.74(0.66)	-1.56(0.7)	-0.43(0.55)	-0.41(0.45)	-0.3(0.61)
University	3	-2.15(0.55)	-1.88(0.38)	-1.49(0.43)	5	-0.45(0.3)	-0.41(0.28)	-0.49(0.31)	-1.14(1.08)	-1.07(0.7)	-1.32(0.42)	-0.66(0.33)	-0.56(0.14)	-0.56(0.25)
p value		.226	.113	.079		.212	.476	.337	.419	.295	.568	.281	.349	.284
Monthly income (US$)														
<428	156	-1.96(0.55)	-1.54(0.6)	-1.32(0.6)	16	-0.21(0.39)	-0.17(0.28)	-0.19(0.33)	-1.72(0.87)	-1.64(0.81)	-1.5(0.8)	-0.33(0.54)	-0.31(0.45)	-0.29(0.49)
428-1070	63	-2.01(0.58)	-1.62(0.57)	-1.45(0.6)	50	-0.29(0.33)	-0.31(0.31)	-0.35(0.32)	-1.79(0.89)	-1.69(0.88)	-1.59(0.82)	-0.39(0.49)	-0.47(0.44)	-0.49(0.45)
>1070	10	-1.92(0.54)	-1.65(0.45)	-1.4(0.47)	7	-0.14(0.36)	-0.24(0.26)	-0.23(0.34)	-1.38(0.59)	-1.37(0.42	-1.22(0.35)	-0.53(0.28)	-0.49(0.13)	-0.45(0.25)
p value		.817	.497	.142		.486	.308	.318	.304	.354	.179	.415	.388	.459

Poor weight gain, short stature and loss of appetite were concomitantly evident on admission in most (62.0%) of malnourished patients. Poor weight gain was the sole symptom on admission in only 6.6% of malnourished patients, while it was accompanied by loss of appetite or short statute in 23.1% and 6.1% of patients, respectively (Table 4).

When compared to baseline, serum levels for folate, iron, ferritin, Vit B12 and 25-OH Vit D improved at 6th month of nutritional support, while Hb, hematocrit and platelet levels increased and CRP levels decreased significantly starting from the 3rd month of nutritional support (p values ranged from 0.021 to <0.001) (Table 4).

Gastrointestinal intolerance symptoms were note evident in majority of patients at 3rd month and 6th month of nutritional support (96.9% and 98.7%, respectively) with significantly lower likelihood of intolerance symptoms from 3rd month to 6th month of nutritional support (p=0.002) (Table 4).

Table 4. Clinical characteristics, laboratory findings and gastrointestinal intolerance in malnourished patients (n=229)

Clinical Characteristics						
Major symptoms on admission, n(%)	Poor weight gain		15 (6.6)			
	Poor weight gain + short stature		14 (6.1)			
	Poor weight gain + loss of appetite		53 (23.1)			
	Short stature + loss of appetite		5 (2.2)			
	Poor weight gain + short stature + loss of appetite		142 (62.0)			
Energy need (kcal), mean(SD)			1344.67(323.45)			
Daily dosing frequency, n(%)	2x1		134 (58.5)			
	3x1		88 (38.4)			
	4x1		5 (2.2)			
	5x1		2 (0.9)			
Laboratory Findings						
Mean(SD)	Baseline	3rd month	6th month	p value		
				Base vs. 3rd mo	Base vs. 6th mo	3rd vs. 6th month
WBC	9021.57 (2576.2)	8789.12 (1877.94)	8825.98 (1841.46)	0.393	0.355	0.966
Hb (g/dL)	12.40 (1.25)	12.47 (1.11)	12.61 (1.13)	0.045	<0.001	<0.001
Hematocrit (%)	36.81 (3.16)	37.21 (2.98)	37.58 (3.08)	<0.001	<0.001	<0.001
Platelet	332860.26 (83999.88)	356735.68 (83823.56)	366054.15 (84427.78)	<0.001	<0.001	0.214
Vit B12 (pg/mL)	373 (171.48)	379.66 (141.78)	388.14 (160.42)	0.366	<0.001	0.072
Folate (ng/ml)	8.33 (2.73)	8.86 (2.8)	8.49 (2.59)	0.329	0.023	0.021
Iron (µg/dL)	66.25 (26.34)	66.13 (19.81)	70.6 (23.09)	0.878	0.007	<0.001
Ferritin (ng/mL)	27.11 (21.66)	27.09 (20.33)	28.18 (18.13)	0.879	<0.001	<0.001
25-OH Vit D (ng/mL)	24.65 (9.11)	23.29 (9.49)	26.79 (8.76)	0.106	<0.001	0.001
CRP (mg/dL)	0.1 (0.63)	0.03 (0.07)	0.02 (0.03)	0.003	0.001	0.439
Gastrointestinal Tolerability						
Intolerance symptoms, n(%)	3rd month		6th month			
None	222(96.9)		226(98.7)			
Nausea	6(2.6)		3(1.3)			
Constipation	1(0.4)		0(0.0)			
Distention or vomiting	0(0.0)		0(0.0)			
	6th month intolerance			p value		
3rd month intolerance, n	No	Yes	Total	0.002		
No	221	1	222			
Yes	5	2	7			
Total	226	3	229			

Duration of breastfeeding was significantly shorter in Syrian refugees vs. Turkish patients (mean(SD) 10.32(4.16) vs. 12.98(4.00) months, p=0.001), in case of lower vs. higher maternal educational attainment (<12 months vs. >14 months, p<0.005), ≥3 vs. lower number of siblings (p=0.008) and lower vs. higher monthly income (p<0.016) (Table 5).

Having no siblings was associated with lower energy need and lower baseline, 3rd month and 6th month weight and height values (p<0.008) (Table 5). No significant difference was noted in energy need and baseline, 3rd month and 6th month weight and height values with respect to gender, nationality, birth weight, maternal education or symptoms on admission (Table 5).

Table 5. Breastfeeding, energy need, weight and height according to sociodemographic characteristics and admission symptoms in malnourished patients

	n	Duration of breastfeeding (mo)	Energy need (kcal)	Weight (kg)			Height (cm)		
				Baseline	3rd mo	6th mo	Baseline	3rd mo	6th mo
Gender									
Boy	123	12.96(3.95)	1347.4(320.21)	15.91(7.48)	17.1(7.72)	18.06(7.95)	101.77(22.18)	103.87(21.78)	106.15(21.37)
Girl	106	12.06(4.33)	1341.51(328.66)	15.67(7.45)	16.94(7.85)	18.02(8.2)	101.91(22.2)	104.29(21.95)	106.56(21.53)
p value		0.453	0.362	0.683	0.672	0.703	0.959	0.882	0.911
Nationality									
Turkish	191	12.98(4.00)	1342.46(326.06)	15.79(7.57)	16.99(7.88)	17.95(8.15)	101.7(22.34)	103.96(21.95)	106.16(21.54)
Syrian refugee	38	10.32(4.16)	1355.79(313.96)	15.86 (6.87)	17.21(7.27)	18.51(7.62)	102.53(21.39)	104.63(21.38)	107.24(20.94)
p value		0.001	0.754	0.755	0.745	0.561	0.709	0.783	0.709
Birth weight (gr)									
<1000	1	9	920	8.4	9.8	10.4	79	82	85
1000-2000	6	11.67(4.55)	1165 (274.5)	11.43(4.53)	12.75(4.48)	13.52(4.48)	88 (18.37)	91(17.23)	93.58(16.7)
2000-3000	49	12.65(4.08)	1425.31	17.19(7.69)	18.33(7.94)	19.38(8.15)	106.67(20.78)	108.53(20.51)	110.92(20.22)
3000-4000	171	12.5(4.16)	1330.29	15.61(7.45)	16.85(7.81)	17.86(8.12)	101.04(22.55)	103.35(22.25)	105.57(21.81)
>4000	2	17.5(2.12)	1350	14.85(0.49)	16.45(1.06)	18.1(0.99)	104(1.41)	106(1.41)	108.5(2.12)
p value		0.343	0.057	0.059	0.099	0.062	0.128	0.151	0.138
Maternal education									
Illiterate	75	11.21(3.67)	1408.8(349.34)	17.28(8.12)	18.54(8.54)	19.73(8.88)	105.73(23.25)	108.03(23.15)	110.41(22.64)
Primary school	80	11.98(4.24)	1361.25(319.32)	16.14(7.51)	17.48(7.83)	18.45(8.12)	103.56(22.2)	105.59(21.59)	107.8(21.29)
Secondary school	54	14.24(3.35)[a]	1265.37(285.37)	14.07(6.43)	15.17(6.52)	16.12(6.72)	96.09(19.96)	98.55(19.79)	100.71(19.22)
High school	17	15.24(4.51)[a]	1281.76(301.71)	14.06(6.32)	15.14(6.66)	15.72(6.69)	97.06(21.53)	99.24(21.06)	101.76(20.6)
University	3	15.00(7.81)[a]	1083.33(160.73)	10.57(2.18)	11.40(2.55)	12.43(2.79)	88.67(11.15)	91.33(11.72)	92.67(11.93)
p value		<0.001	0.179	0.090	0.080	0.061	0.092	0.098	0.081
Sibling #									
0	9	13.33(3.67) [b]	1040(171.61)[b]	9.74(2.37)[b]	10.69(2.42)[b]	11.42(2.42)[b]	81.00 (10.12)[b]	83.67(10.14)[b]	86.44(9.4[b]
1	57	12.93(4.08) [b]	1365.61(332.11)	16.29(8.12)	17.62(8.45)	18.68(8.89)	102.82(22.11)	105.16(21.77)	107.44(21.37)
2	107	13.03(4.14) [b]	1340.56(308.09)	15.47(6.63)	16.68(6.91)	17.72(7.17)	101.64(21.37)	103.81(21.08)	106.11(20.72)
≥3	56	11.09(4.05)	1380.18(342.35)	16.91(8.34)	18.11(8.71)	19.05(8.91	104.54(23.66)	106.73(23.27)	108.85(22.82)
p value		0.040	0.023	0.013	0.011	0.011	0.016	0.016	0.017
Monthly income (US$)									
<428	156	11.86(4.05)[c]	1348.91(330.04)	16.03(7.65)	17.31(7.98)	18.37(8.29)	102.38(22.69)	104.63(22.41)	106.91(21.95)
428-1070	63	13.78(3.75)	1370(315)	16(7.27)	17.18(7.52)	18.08(7.77)	102.67(21.53)	104.87(21.05)	107.06(20.79)
>1070	10	15.4(5.21)	1119(171.43)	10.89(2.44)	11.75(2.71)[c]	12.61(2.95)	88.1(11.86)	90.3(11.44)	92.9(10.91)
p value		0.003	0.059	0.068	0.047	0.054	0.148	0.136	0.143
Symptoms-admission									
Poor weight gain	15	10.6(5.78)	1198(169.42)	12.91(3.27)	14.07(3.23)	15.07(3.85)	97.2(14.5)	99(14.3)	100.87(14.56)
Poor weight gain + short stature	14	12.21(4.35)	1334.29(353)	16.45(9.48)	17.88(9.72)	19.01(9.95)	104(26.63)	106.43(25.84)	108.79(24.86)
Poor weight gain + loss of appetite	53	12.19(3.95)	1390(313.03)	16.62(7.09)	17.84(7.3)	18.76(7.44)	107.23(22.08)	109.29(21.65)	111.28(21.22)
Short stature + loss of appetite	5	13.2(5.5)	1400(176.78)	15.22(3.21)	15.82(3.78)	16.88(3.38)	98.6(12.54)	100.4(13.09)	103.2(11.84)
Poor weight gain + short stature + loss of appetite	142	12.89(3.93)	1342.32(338.55)	15.75(7.77)	17(8.15)	18.03(8.5)	100.21(22.48)	102.55(22.21)	104.94(21.84)
p value		0.453	0.362	0.557	0.659	0.640	0.287	0.275	0.307

[a]p<0.005; compared to illiterate and primary school graduate status (Mann-Whitney U test with Bonferroni correction)
[b]p<0.008; compared to patients with siblings or ≥3 siblings (for breastfeeding) (Mann-Whitney U test with Bonferroni correction)
[c]p<0.016; compared to higher monthly income values (Mann-Whitney U test with Bonferroni correction)

Table 6. Correlations between age, duration of breast feeding and anthropometrics

		Age	Duration of breast feeding	Weight		Height	
				3rd month	6th month	3rd month	6th month
Weight							
baseline	r	.988	-0.016	.995	.992	.983	.983
	p	<0.001	0.815	<0.001	<0.001	<0.001	<0.001
	N	229	229	229	229	229	229
3rd month	r	.986	-0.023	1.000	.995	.983	.982
	p	<0.001	0.724	-	<0.001	<0.001	<0.001
	N	229	229	229	229	229	229
6th month	r	.984	-0.019	.995	1.000	.980	.981
	p	<0.001	0.78	<0.001	-	<0.001	<0.001
	N	229	229	229	229	229	229
Height							
baseline	r	.984	-0.031	.983	.979	.998	.996
	p	<0.001	0.644	<0.001	<0.001	<0.001	<0.001
	N	229	229	229	229	229	229
3rd month	r	.984	-0.031	.983	.980	1.000	.997
	p	<0.001	0.636	<0.001	<0.001	-	<0.001
	N	229	229	229	229	229	229
6th month	r	.984	-0.036	.995	.981	.997	1.000
	p	<0.001	0.59	<0.001	<0.001	<0.001	-
	N	229	229	229	229	229	229

Spearman correlation analysis, r: correlation coefficient

Baseline weight and height at baseline were positively correlated with patient age (r=0.988 and r=0.984, respectively, p<0.001 for each). Weight and height values at each visit were positively correlated with each other (r ranged from 0.979 to 0.998, p<0.001 for each). No correlation was noted between duration of breastfeeding and other parameters (Table 6).

DISCUSSION

Our findings in a retrospective cohort of malnourished and control children revealed poor weight gain accompanied with short stature and loss of appetite as the leading symptom profile on admission in malnourished patients, while higher likelihood of younger age, shorter duration of breastfeeding, lower family monthly income and poorer maternal education in malnourished vs. control children. Notably, data from a recent study in Turkish children indicated lower birth weight and shorter breast-feeding duration in children with stunting and underweight than those with normal or taller height and normal weight or overweight/obesity, respectively[18]. In addition, data from Eastern Turkey revealed association of low monthly family income and educational level, prematurity and unemployed father with increased risk of malnutrition, with no significant relationship between malnutrition and gender[12].

Indeed, inadequate and inappropriate food intake due to poverty is considered to be the main underlying cause of malnutrition along with close correlation of level of education and sanitation, production and cultural food traditions, the availability and quality of health services and monthly income of family with prevalence of malnutrition[12,13,19,20].

Higher maternal educational attainment and higher monthly income, as the two factors decreasing the likelihood of pediatric malnutrition, were also associated with longer duration of breastfeeding in current study. Nonetheless, baseline WFA and HFA Z scores were similar in our malnourished patients with different maternal education and family income background along with lack of correlation between duration of breastfeeding and baseline weight or height values in malnourished children. This seems to indicate potential role of these factors in development but not severity of malnutrition in pediatric age.

In addition, lack of a sibling was associated with higher risk of malnutrition along with lower weight and height values at baseline as well as under nutritional support in malnourished patients in our

study, despite longer duration of breastfeeding with decreasing sibling number.

Nonetheless, sibling status had no significant impact on baseline, 3rd month and 6th month WFA and HFA Z scores similar to maternal educational attainment and family income.

Overall, 6-month high-calorie enteral nutritional support was associated with significantly improved anthropometrics (weight, height, BMI, WFA Z and HFA Z scores) with favorable gastrointestinal tolerability. Accordingly, significantly improved anthropometric status as well as laboratory parameters such as hemoglobin, Vit D and iron after a short-term high-energy enteral nutrition in the present cohort of malnourished children from a province located in Southeastern Turkey with high risk of poverty indicate the importance of early nutritional screening and appropriate provision of clinical nutrition to timely overcome the potential disparities in children's development living in this geography as driven by risks associated with poverty that include inadequate nutrition, low maternal education and low levels of maternal well-being[3].

Achievement of improved laboratory findings (folate, iron, ferritin, Vit B12, 25-OH Vit D levels, Hb, hematocrit, platelet and CRP levels) along with anthropometrics via 6-month nutritional support in the current study seems also notable given the association of malnutrition in children ages five to nine years with increased risk of underweight, anemia, and illness all of which are conditions that decrease attendance, performance, and years in primary school[3,21].

Administration of 6-month high calorie enteral feeding was associated with significantly improved height, weight, BMI values as well as HFA and WFA Z scores in malnourished children starting from the 3rd month of clinical nutrition regardless of the symptoms on admission, whereas all anthropometric scores remained poorer than those in the control group regardless of the study visit.

In addition, although the likelihood of malnutrition was more likely in children with younger age, shorter duration of breastfeeding and lower monthly income and lower maternal educational levels, our findings indicate significantly improved anthropometrics in malnourished children with implementation of clinical nutrition, regardless of the gender, birth weight, duration of breastfeeding, sibling number, maternal education or monthly income level. Hence, provision of high-calorie enteral nutritional support achieved improved anthropometrics in malnourished children overall independent of the risk factor status.

Nonetheless, given that all anthropometric scores remained poorer in malnourished patients than those in the control group during 6-month study period, our findings seem to emphasize the positive correlation of anthropometric improvement with the duration of enteric feeding and the likelihood of ongoing adequate nutrient intake to enable recovery and catch up growth via weight gain velocity exceeding normal rates[1,2,17,22-24]. In fact, the positive correlation of weight and height values at baseline and those achieved under 3rd month and 6th month nutritional support with each other seems also support the likelihood of increased efficacy of a longer term clinical nutrition.

Baseline, 3rd month and 6th month WFA or HFA Z scores in malnourished or control groups as well as between malnourished vs. control groups were similar with respect to gender, sibling number, maternal education and monthly income level.

Interventions to improve nutrition in each of the early lifecycle stages including preschool ages, schooling ages, and later adolescence is considered likely to achieve returns in later stages such as decreased risk of anemia and poor performance in school as well as nutrition-related chronic diseases that greatly exceed their costs[3,25]. The success of short-term nutritional support in our cohort of children with primary malnutrition seems notable in this regard, emphasizing the crucial role of early nutritional screening and timely diagnosis and management of malnutrition in the pediatric age group. This seems also notable given the association of malnutrition with increased risk of mortality, particularly in the first year of life among children younger than age five years and thus importance of addressing catch-up by concern of mortality risk within the first year and by concerns relating to later-life consequences for survivors beyond the 1,000-day window[3,4].

Our findings also revealed favorable gastrointestinal tolerability with decrease in the frequency of symptom-free patients from 3rd month to 6th month of high-calorie fiber-containing enteral nutrition. This seems notable given the association of high-energy formula with higher likelihood of intolerance as compared with standard formula, whereas consideration of fibre-free vs. fibre-containing

formula with higher likelihood of gastrointestinal intolerance symptoms in a range of medical conditions[17,26-28].

According to our findings, being a Syrian refugee was not associated with increased risk of malnutrition and apart from shorter duration of breastfeeding in Syrian refugees, no significant difference was noted in baseline and follow up data on weight and height scores between Turkish and Syrian children with malnutrition. Notably, data from a past study on nutritional profile of 14,552 Syrian refugee children aged 6 to 59 months (7% from Turkey) before resettlement also revealed an overall low prevalence of undernutrition whereas high prevalence of overweight or obese among Syrian children (5.1% and 7.8%, respectively for Turkey), as considered likely to indicate effectiveness, in addition to expose possible gaps, of refugee nutrition programs in countries of asylum[29].

Study' certain limitations should be considered. First, due to retrospective single-center study design, establishing the temporality between cause and effect as well as generalizing our findings to overall pediatric malnourished patient population is not possible. Second, high-calorie enteric feeding regimen was used as a supplement in all of our patients and thus lack of data on calorie value of the normal diet of the children is another limitation which otherwise would extend the knowledge achieved in the current study. Nevertheless, despite these certain limitations, given the restricted amount of data available on nutritional support in early and middle childhood and adolescence age in nutrition rehabilitation of malnourished children Turkey, our findings represent a valuable contribution to the literature.

In conclusion, our findings indicate efficacy and tolerability of 6-month high-calorie enteral nutritional support in malnourished children with growth faltering in terms of improved anthropometrics, laboratory markers of nutritional status and gastrointestinal tolerance. Findings in our cohort suggest the potential utility of high-calorie enteral formula as a first-line nutritional support to meet the nutrient needs and to promote catch-up growth or maintain growth among malnourished children, regardless of initial symptoms and socio-economic risk factors for poor nutritional status. Representing efficacy of nutritional support in a population of malnourished children living in a region specifically associated with poor nutritional status driven by poverty-related risks, our findings indicate importance of early nutritional screening and appropriate provision of clinical nutrition to overcome the disparities in children's growth and development. Future prospective large-scale and long-term studies are needed to address the impact of high-calorie enteral feeding on the potential for catch-up growth in relation to risk factors and severity of malnutrition among pediatric patients in both the outpatient and inpatient settings.

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