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Effects of Hypercaloric Enteral Feed on Malnutrition between Immigrants and Turkish Children

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Abstract

Aim: Malnutrition is a serious condition that causes many clinical consequences and causes diseases seen in adulthood. An early prevention of malnutrition is crucial and is widely applied via enteral or parenteral formula. Migration results in very low living standards that affect children more than adults and are considered a risk factor for malnutrition. This study separately investigates the effects of a hypercaloric enteral feed on malnourished immigrant and Turkish children in terms of body mass index (BMI), weight, and height scores alongside micronutrient deficiencies.

Methods: This case-control study was conducted in an outpatient clinic with patients who were diagnosed with malnutrition and aged 1-18 years, between January 1, 2019 and January 31, 2020. A total of 157 patients consisting of 111 Turkish and 47 immigrant children with primary malnutrition (<-2 SD) were included in the study. Anthropometric data recorded at baseline, 3rd and 6th months were retrospectively analyzed. All patient records were obtained from the Pediatric Outpatient Clinic of Esenler Children Hospital, Istanbul, Turkey.

Results: Both patient groups significantly benefited from the nutritional intervention in terms of weight for age or BMI, weight and height z-scores ($p<0.001$). Despite that improvement, baseline weight and BMI scores were lower in immigrant patients. The number of patients with iron deficiency anemia, B12 deficiency, and 25-hydroxy vitamin D3 was also diminished through enteral intervention ($p<0.001$).

Conclusion: The hypercaloric enteral intervention was well tolerated by both populations and has caused significant anthropometrical improvements during 6 months of duration alongside with the reduction in the number of patients with micronutrient deficiency.

Keywords: Malnutrition, body mass index, micronutrient deficiency, enteral feed

Introduction

Malnutrition is a serious condition that negatively influences the prognosis of other diseases (1). Malnutrition-based disturbed energy metabolism and immune system cause the body to be less responsive to medical care and more susceptible to side effects of the treatment, this is related to the poor clinical outcomes (2). Malnutrition occurs particularly in the case of highly stressful treatments like chemotherapy and radiotherapy. Additionally, malnourishment in children causes long-term effects that may appear in the future as various diseases (3). Moreover, even after adequate improvement in malnutrition status, they may still have persistent or long-lasting disturbances in metabolism that may adversely affect the clinical outcome (4). Nutritional interventions have developed rapidly because malnutrition is common and has severe clinical manifestations (1). The worldwide usage of enteral supplements is increasing alongside the personalized administration of these supplements according to patients' insufficiencies (5). Thus, all knowledge about tolerability, indications and side effects of these enteral supplements should be used to present the most beneficial intervention.

Studies have shown that malnutrition is affected by many factors and that some conditions are associated with malnutrition. In particular, sociodemographic

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characteristics such as family income, mother's education level, number of siblings, duration of breastfeeding, additional food intake and protein-rich food, and the number of members in the household are direct reasons for malnutrition (6-8). In addition to these, causes such as premature birth, neuromotor retardation, swallowing dysfunction, anatomical disorders, previous surgery and food allergies can be shown as patient-induced risk factors for malnutrition (9,10).

The migration causes very low living standards, which affects children more than adults. It has been observed that 20% of the immigrant refugees' children in Turkey have a chronic malnutrition disorder and %50 of the immigrant refugees who were involved in blood analysis have anemia (11). Additionally, it is known that the prevalence of malnutrition in the Middle East is more than 15% (12). Thus, comparing the efficiency of enteral supplementation among immigrants and native Turkish children diagnosed with malnutrition may present different baseline measurements such as initial blood biochemistry, metabolism, and initial weight for age (WFA) or body mass index (BMI) score. This may provide important knowledge about the effectiveness of nutritional interventions in different conditions.

This study compares the level of malnutrition among immigrant and Turkish children during their first admission to the hospital as well as to compare the effects of 1.5 kcal/mL enteral supplementation on weight, height, and BMI as well as iron, vitamin B12 and 25-25-hydroxy vitamin D3 levels (25D3).

Materials and Methods

Our study is a case-control study in which the malnutrition in Turkish and immigrant children aged 1-18 years who were followed and treated in the outpatient clinic between January 1, 2019 and January 31, 2020 was evaluated.

Compliance with Ethical Standards

The authors state that they obtained ethical approval, which was obtained from the Ethics Committee of University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital on 21/04/2021 with session number 06-2021. All patients and families were informed in detail about the study, and after giving consent enrolled on the study.

Sample

Our cohort includes 157 pediatric patients diagnosed with pediatric malnutrition by a pediatrician. Hypercaloric (1.5 kcal/mL) enteral supplementation was prescribed to the patients after diet adjustment was made at the first examination. Children with ages lower than 12 months and higher than 19 years were excluded from the study. The enteral nutrition product to be chosen for those younger than 12 months with malnutrition should not be hypercaloric (1.5 kcal/1 cc). Because the renal solute loads of hypercaloric enteral products may cause secondary conditions such as dehydration and prerenal acute renal failure in this age group (9). Therefore, children under 12 months were excluded from the study. Additionally, patients who were exposed to tube feeding as the nutritional intervention and patients with acute infections were also excluded from the study. All patient records were retrospectively obtained from the Pediatric Outpatient Clinic of Esenler Children Hospital, Istanbul, Turkey.

Observation

A retrospective analysis of the effects of nutritionally complete MF6-enriched hypercaloric (1.5 kcal/mL) enteral supplement, which contains 9% protein, 40% fat, 49% carbohydrates, and 2% dietary fiber. Our cohort included 157 pediatric patients aged 1-18 years who were diagnosed with malnutrition by a pediatrician, based on WFA <-2 SD under 2 years and BMI <-2 SD for over 2 years of age. The cohort included 47 immigrants and 111 Turkish children who were used to observe any probable variation of improvement provided by nutritional intervention. Patients with infectious diseases and patients undergoing tube feed were excluded from the study. Additionally, patients who were absent in follow-ups, as well as patients with irregular usage of the prescribed hypercaloric supplement, were also excluded from the study. Retrospective analyses were based on anthropometrical and biochemical data formed from the baseline dataset alongside the analysis made at the third month and six months followed by nutritional intervention. Each analysis includes the weight percentile, height percentile, related z-scores and WFA or BMI scores, which are calculated according to the traditional database of the World Health Organization, and deficient micronutrients of Turkish and immigrant children who are unable to gain weight or grow taller (13). Indications and contraindications were separately investigated among immigrant and Turkish children to observe any differences in incompatibility and tolerability between the two ethnicities.

Anthropometric measurements of all patients were taken with the same scale by 2 different observers (TBS model, scale and height meter, Tartımsan, Istanbul, Turkey). After the anthropometric measurements, weight percentile, height percentile, related z-scores and WFA or BMI scores were calculated using the auxology program developed by Turkish Pediatric Endocrinology and Diabetes Society.

Ferritin, vitamin B12, and vitamin D values, which evaluate micronutrients from the examinations taken at the time of arrival and 3rd and 6th months follow-up via the hospital information management system, and hemoglobin and hematocrit values for evaluating the presence of anemia were noted. Vitamin D deficiency was determined with levels of 25D3. A 25D3 level of 20 ng/mL indicated 25D3 deficiency (14). Iron deficiency anemia was defined as a hemoglobin value below -2SD, suitable for age groups, and a serum ferritin level below 12 microgram/L in children (15). Vitamin B12 deficiency was defined as a measured serum vitamin B12 level below 200 pg/mL (16).

Statistical Analysis

Statistical analysis of the data was maintained by IBM SPSS (Statistical Package for the Social Sciences) Statistics program (IBM Corporation, United States). The normality test was tested according to Shapiro-Wilk. In the case of the non-parametric dataset, the Friedman test was used, which was followed by the Wilcoxon signed-rank test to compare each layer of improvement. In the case of the parametric dataset, Repeated Measures ANOVA was used alongside the multivariate test of Wilks' lambda. During the Repeated Measures ANOVA analysis of pairwise significance, Bonferroni correction with significance $p<0.05$ was used. To analyze the probable difference in the effectiveness of 1.5 kcal/mL enteral supplement on immigrant and Turkish children via weight gain, height gain and BMI z-score improvement; the Mann-Whitney U test was used. In 2x2 categorical variable comparisons, when the expected result is below 5 in more than 20% of the cells with the chi-square test, Fisher's exact test was used. Otherwise, the chi-square test was preferred in all categorical comparisons. To analyze the number of patients who improved from micronutrient deficiency over 6 months of duration, the Cochran Q test was used. Significance was evaluated with $p<0.05$ level.

Results

From the total cohort of 157 malnourished outpatients, 70,3% (n=111) are Turkish and remaining 29.7% (n=47) are immigrants. The ages of the patients ranged from 1 year (12 months) to 17.3 years (208 months). There are 53 females (47.7%), 58 males (52.2%) in the Turkish group and 20 females (42.6%), and 27 males (57.5%) in the immigrant group. The major symptoms of our patients with malnutrition are 76.6% (n=121) not gaining weight and 23.4% (n=37) not gaining height.

As shown in Figure 1 and Table 1, a significant improvement in weight z-scores was seen in both immigrant and Turkish children with a feeding intervention of 1.5 kcal/mL ($p<0.001$). This overall improvement in weight z-scores of both malnourished immigrant and Turkish children was also observable during pairwise analysis between baseline, 3rd, and 6th months ($p<0.001$). Additionally, Turkish children had worse weight z-score status when they first applied to the hospital ($p=0.007$) (Table 2). The improvement trend of height z-scores was also similar to weight z-scores as significant overall and pairwise improvement was observed in both Turkish and immigrant children ($p<0.001$ and $p<0.001$ respectively). Moreover, there was no difference in the baseline height z-scores between the two groups ($p=0.681$) (Table 2). Similarly, significant overall and pairwise improvements in BMI z-scores were also observed in both populations ($p<0.001$). Like weight z-scores, the initial condition of BMI z-scores of Turkish children are worse than immigrant children ($p=0.036$) (Table 2). There was not a significant difference in the improvement rate of height, weight, and BMI z-scores between the two ethnic populations ($p=0.629$, 0.115, and 0.839 respectively). As seen in Table 3, the prevalence of iron deficiency anemia, B12 deficiency and 25-D3 deficiency in immigrant and Turkish patients decreased significantly to one-fifth of the initial prevalence. Thus, the number of patients without any micronutrient deficiency was significantly increased in both groups over 6 months of duration after 1.5 kcal/mL nutritional intervention ($p<0.001$).

Discussion

Our study is a retrospective observational study investigating the effects of oral nutritional supplements in children of two different ethnicities diagnosed with malnutrition according to a pediatrician, WFA or BMI <-2 SD for the appropriate age group. Malnutrition is a frequent condition affecting every population worldwide, with a prevalence of >900 million individuals worldwide (1). Malnutrition negatively affects energy metabolism, alters the wound-healing process and weakens the immune system. Early intervention is critical in children because of the serious consequences of malnutrition. Its negative effects on clinical prognosis cause complications such as the increased risk of infectious disease, slowing of mental development, delayed wound healing, decreased muscle strength, and impaired renal function (1,17). However, low-income countries suffer the consequences of undernourishment more often compared to high-income countries. Contrary to this, obesity and diabetes are more prevalent in high-income countries because of an unhealthy diet (18). Enteral nutrition interventions are preferred in patients with malnutrition but a normally functioning gastrointestinal tract. These interventions consist of artificially prepared formulas with different calorie amounts and additional ingredients (19).

Table 1. P-values of overall height, weight and BMI improvements along with patients with different ethnicity and different major symptoms over 6 months of nutritional intervention

Sub-groups	Height Z-scores			Weight Z-scores			BMI Z-scores		
	Baseline - 3rd Month	**Baseline - 6th Month**	**3rd Month - 6th Month**	**Baseline - 3rd Month**	**Baseline - 6th Month**	**3rd Month - 6th Month**	**Baseline - 3rd Month**	**Baseline - 6th Month**	**3rd Month - 6th Month**
Immigrant children n=47, 29.7% (Mean±SD)	<0.001* (-1.79±0.9) (-1.65±0.8)	0.001* (-1.79±0.9) (-1.35±1.0)	0.016* (-1.65±0.8) (-1.35±1.0)	<0.001* (-2.26±0.6) (-1.74±0.8)	<0.001* (-2.26±0.6) (-1.47±0.7)	<0.001* (-1.74±0.8) (-1.47±0.7)	<0.001† (-2.02±1.3) (-1.21±1.1)	<0.001† (-2.02±1.3) (-0.85±1.0)	<0.001† (-1.21±1.1) (-0.85±1.0)
Overall improvement (0-6 months)	<0.001**			<0.001**			<0.001†		
Turkish children n=111, 70.3% (Mean±SD)	0.004* (-1.91±0.9) (-1.77±0.9)	<0.001* (-1.91±0.9) (-1.59±0.8)	<0.001* (-1.77±0.9) (-1.59±0.8)	<0.001* (-2.02±0.6) (-1.49±0.6)	<0.001* (-2.02±0.6) (-1.06±0.7)	<0.001* (-1.49±0.6) (-1.06±0.7)	0.004† (-1.51±1.6) (-0.84±0.9)	<0.001† (-1.51±1.6) (-0.42±0.8)	<0.001† (-0.84±0.9) (-0.42±0.8)
Overall improvement (0-6 months)	<0.001**			<0.001**			<0.001†		
Inability to gain weight n=121, 76.6% (Mean±SD)	<0.001* (-2.43±0.6) (-2.18±0.6)	<0.001* (-2.43±0.6) (-1.82±0.9)	<0.001* (-2.18±0.6) (-1.82±0.9)	<0.001* (-1.96±0.6) (-1.45±1.0)	<0.001* (-1.96±0.6) (-1.28±08)	<0.001* (-1.45±1.0) (-1.28±08)	0.163† (-0.83±1.0) (-0.60±0.8)	<0.001† (-0.83±1.0) (-0.28±0.7)	0.098† (-0.60±0.8) (-0.28±0.7)
Overall improvement (0-6 months)	<0.001**			<0.001**			0.001†		
Inability to gain height n=37, 23.4% (Mean±SD)	<0.001* (-1.64±1.0) (-1.54±0.8)	<0.001* (-1.64±1.0) (-1.30±0.9)	<0.001* (-1.54±0.8) (-1.30±0.9)	<0.001* (-2.26±0.6) (-1.73±0.6)	<0.001* (-2.26±0.6) (-1.37±0.7)	<0.001* (-1.73±0.6) (-1.37±0.7)	<0.001† (-2.18±1.4) (-1.25±1.0)	<0.001† (-2.18±1.4) (-0.86±1.0)	<0.001† (-1.25±1.0) (-0.86±1.0)
Overall improvement (0-6 months)	<0.001**			<0.001**			<0.001†		
Total (Mean±SD)	<0.001* (-1.82±0.9) (-1.69±0.8)	<0.001* (-1.82±0.9) (-1.42±0.9)	<0.001* (-1.69±0.8) (-1.42±0.9)	<0.001* (-2.19±0.6) (-1.67±0.7)	<0.001* (-2.19±0.6) (-1.35±0.7)	<0.001* (-1.67±0.7) (-1.35±0.7)	<0.001† (-1.87±1.4) (1.10±1.0)	<0.001† (-1.87±1.4) (-0.7±0.9)	<0.001† (-1.10±1.0) (-0.7±0.9)
Overall improvement (0-6 months)	<0.001**			<0.001**			<0.001†		

*: Wilcoxon signed-rank test, **: Friedman test, †: Repeated measures ANOVA, SD: Standard deviation, Mean±SD values were written as two lines according to the order defined in the table [e.g. Baseline (0) - 3rd Month]

Oral nutritional interventions are widely used to treat malnutrition. Thus, the efficacy and compatibility of different ethnic populations should also be evaluated to choose the appropriate nutritional intervention and to prevent food insecurity (20). Despite many studies demonstrating the benefits of complementary feeding, information on the differentiating effects of oral nutrition supplements (ONS) is lacking. Compared with dietary advice (73%), ONS has shown a greater benefit (89%) upon regaining the disrupted energy metabolism in patients with malnutrition in a more cost-effective way. Despite numerous flavors of ONS products, the general downside of ONS intervention is adherence to the treatment, which has been found to be lower compared to dietary advice (21). Additionally, nausea and constipation may be encountered in ONS treatment, and it has been indicated that usage of ONS along with synbiotics prevents constipation compared to the group solely taking ONS. In our study, we selected our cohort based on patients who fully adhered to the given treatment to prevent results from irregular ONS usage and evaluated the sole effects of the intervention of two ethnic populations. Despite our hypercaloric intervention, none of our patients complained of nausea or constipation over 6 months of intervention. A greater number of patients may be required to test the compatibility of our ONS treatment.

Weight for age and BMI form the backbone of our study as they have been shown to be reliable and budget-friendly measurements in terms of evaluating the state of malnutrition (22,23). Our findings showed that 1.5 kcal/mL enteral intervention provided to both immigrant and Turkish children significantly restored weight and height z-scores during 6 months of duration. Similarly, the number of patients with vitamin B12, 25-D3, and iron micronutrient deficiency was also diminished through enteral intervention. Our findings also showed that major symptoms of the inability to gain weight or height caused no significant difference in terms of anthropological improvement, which underlines the similar potential of hypercaloric ONS treatment on both wasted and stunted children due to undernourishment. Additionally, children from both ethnicities showed similar improvements in the case of weight, height, and BMI z-scores as well as micronutrient concentrations. This indicates that equal benefits were provided via hypercaloric intervention to both populations despite significantly different initial weight and BMI z-scores. Our study showed that treating malnutrition with hypercaloric ONS is a cost-effective choice with high tolerability in Turkish and immigrant children with the inability to gain weight or height as well as with micronutrient deficiencies.

Study Limitations

A longer period of treatment may be required to fully understand the long-term effectiveness of the hypercaloric treatment on both ethnic groups. Moreover, the immigrant cohort is limited in compared to our Turkish cohort, which may prevent healthy comparison. An equal number of participants with a higher total number may be required to demonstrate the side effects and efficacy of hypercaloric treatment on different ethnic groups. Lastly, the information about the regular dietary regimens in our patient's daily life is missing, which may pollute the exact effects of the selected nutritional intervention.

The strength of our study was that it was one of the few studies comparing and follow-up immigrant and local children's outcomes, reaching a high number of patients, and emphasizing micronutrient deficiencies in addition to anthropometric measurements.

Conclusion

Both immigrant and Turkish children tolerated the 1.5 kcal/mL enteral intervention well and significant improvements were observed in terms of BMI, weight, and height z-scores. No complaints were observed upon using hypercaloric ONS over 6 months. Additionally, nutritional intervention through hypercaloric formula has diminished the number of patients with deficient micronutrients. Rates of anthropometrical improvement were similar in both the immigrant and Turkish groups.

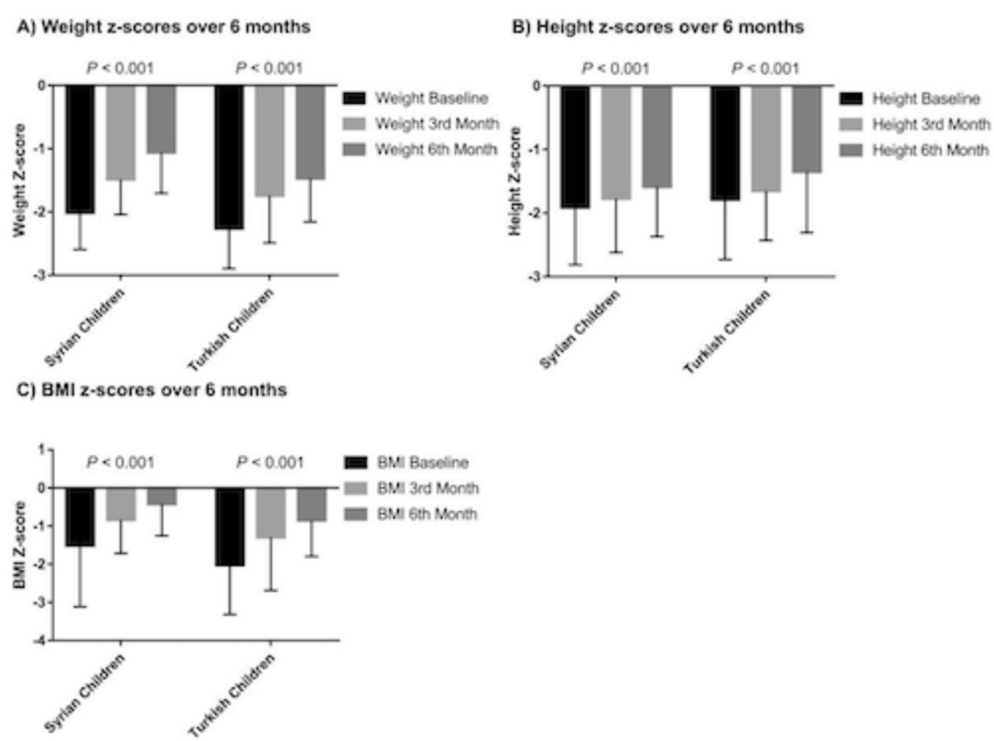

Figure 1. Weight, height and BMI z-score improvement in immigrant and Turkish children over 6 months of duration. Baseline **A)** weight, **B)** height and **C)** BMI z-scores were compared with the measurements done in the 3rd and 6th months separately in the Immigrant and Turkish cohorts. Related p-values were given inside the figure
BMI: Body mass index

Table 2. Differences of baseline anthropometrical measurements and number of micronutrient deficient between Turkish and Immigrant children along with male and female children

Categories	Baseline height Z-scores (Mean±SD)	Baseline weight Z-scores (Mean±SD)	Baseline BMI Z-scores (Mean±SD)	Baseline micronutrient status (N %)
P-values of immigrant (n=47, 29.7%) children vs Turkish (n=111, 70.3%) children	0.681* (-1.79±0.9) vs (-1.91±0.9)	0.007* (-2.26±0.6) vs (-2.02±0.6)	0.036† (-2.02±1.3) vs (-1.51±1.6)	0.699†† **Deficient:** (97, 87.4) vs (40, 85.1) **Non-deficient:** (14, 12.6) vs (7, 14.9)
P-values of female (n=73, 46.2%) vs male (n=85, 53.8%) children	0.792* (-1.83±0.9) vs (-1.82±0.9)	0.954* (-2.17±0.7) vs (-2.20±0.5)	0.610† (-1.81±1.4) vs (-1.92±1.5)	0.741†† **Deficient:** (64, 87.7) vs (73, 85.9) **Non-deficient:** (9, 12.3) vs (12, 14.1)
P-values of patients with the inability to gain weight (n=121, 76.6%) vs patients with the inability to gain height (n=37, 23.4%)	0.003* (-2.26±0.6) vs (-1.96±0.6)	0.000* (-1.64±1.0) vs (-2.43±0.6)	0.000† (-2.19±1.4) (-0.83±1.0)	0.165††† **Deficient:** (102, 84.3) vs (35, 94.6) **Non-deficient:** (19, 15.7) vs (2, 5.4)

*: Mann-Whitney U test, †: Student's t-test, ††: Chi-square, †††: Fisher's exact test, SD: Standard deviation, N: Number of patients, Mean and SD values were written according to the order given in "Categories" column; Percentage values were written based on sub-groups given in "Categories" column

Table 3. Number of Turkish and Immigrant patients with micronutrient deficiency over 6 months

	Number of Immigrant Children			Number of Turkish Children			Total		
	Baseline	**3rd Month**	**6th Month**	**Baseline**	**3rd Month**	**6th Month**	**Baseline**	**3rd Month**	**6th Month**
IDA N (%)	31 (66.0)	11 (23.4)	4 (8.5)	71 (64.0)	50 (45.0)	12 (10.8)	102 (64.6)	61 (38.6)	16 (10.1)
B12 deficiency, N (%)	12 (25.5)	1 (2.1)	1 (2.1)	33 (29.7)	5 (4.5)	1 (0.1)	45 (28.5)	6 (3.8)	2 (1.3)
25D3 deficiency, N (%)	17 (36.2)	7 (14.9)	4 (8.5)	46 (41.4)	18 (16.2)	3 (2.7)	63 (39.9)	25 (15.8)	7 (4.4)
Normal, N (%)	7 (14.9)	28 (59.6)	40 (85.1)	14 (12.6)	46 (41.4)	96 (86.5)	21 (13.3)	74 (46.8)	136 (86.1)
P-values according to the number of normal patients	Baseline vs 3rd Month: <0.001* Baseline vs 6th Month: <0.001* 3rd Month vs 6th Month: <0.001* Overall: <0.001**			Baseline vs 3rd Month: <0.001* Baseline vs 6th Month: <0.001* 3rd Month vs 6th Month: <0.001* Overall: <0.001**			Baseline vs 3rd Month: <0.001* Baseline vs 6th Month: <0.001* 3rd Month vs 6th Month: <0.001* Overall: <0.001**		
P-values of Turkish vs Immigrant patients in terms of elimination of micronutrient deficiency††	0.768† **Improved:** (82, 84.5) vs (33, 82.5) **Not improved:** (15, 15.5) vs (7, 17.5)								

*: McNemar test, **: Cohran's Q test, †: Chi-square, N: Number of patients, IDA: Iron deficiency anemia, 25D3: 25-Hydroxyvitamin D3, ††: N and percentage values were written according to the given order and percentage values were written based on Turkish and Immigrant sub-groups respectively after the exclusion of patients without baseline micronutrient deficiency

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital on 21/04/2021 with session number 06-2021.

Informed Consent: All patients and families were informed in detail about the study, and after giving consent enrolled on the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.A., M.C.U., Concept: E.A., M.C.U., Design: E.A., M.C.U., Data Collection or Processing: M.C.U., Analysis or Interpretation: E.A., Literature Search: E.A., M.C.U., Writing: E.A., M.C.U.

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