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Analysis of body composition and survival in head and neck cancer patients receiving regular nutritional counseling during radiotherapy

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ABSTRACT

Background: To investigate the changes in body composition and treatment outcomes in patients with locally advanced head and neck cancer who receive regular and continuous nutritional counseling during radiotherapy.

Methods: Medical records of 26 patients who received regular weekly nutritional and dietary counseling during radiotherapy were retrospectively analyzed. Anthropometric parameters—including weight (kg), body mass index (BMI), muscle mass (MM, kg), fat-free mass (FFM, kg), body fat mass (BFM, kg), visceral fat rate (VFR), and basal metabolic rate (BMR, kcal/day)—were measured at baseline and at the end of radiotherapy by a registered dietitian using bioelectrical impedance analysis (BIA). Measurements were compared from the start to the end of radiotherapy. Survival analysis was conducted using Kaplan-Meier curves.

Results: By week 5, weight decreased by 7.3% and BMI by 6.2%. Losses in MM and FFM were also significant (MM: 4.7%, FFM: 4.4%), with the most significant decrease observed in VFR (-8.0% at week 5). BMR decreased by 4.7%, aligning with overall weight and muscle mass loss. Severe weight loss (≥5%) was associated with higher rates of problems related to oral intake, including taste changes, nausea/vomiting, dental issues, low ONS tolerance and adherence, and aspiration. Median follow-up was 8 months (range, 6 to 42 months). Two-year local control (LC) and progression-free survival (PFS) were 56.2% and 54.9%, respectively. Survival rates were significantly lower in patients with severe weight loss (LC, p=0.041; PFS, p=0.027).

Conclusion: Radiotherapy results in a decrease in weight, muscle mass, and fat over weeks. Survival outcomes are significantly worse in patients who experience severe weight loss. Since radiotherapy itself is a risk factor for malnutrition, early, regular, and proactive nutritional intervention may be recommended to prevent and manage malnutrition and maintain function in head and neck cancer patients undergoing radiotherapy.

Keywords: body composition, regular dietary counseling, head and neck cancer, malnutrition, radiotherapy

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Introduction

Nutrition is critically important for patients with head and neck cancer (HNC) because it significantly impacts both treatment tolerance, outcomes, and quality of life.[1,2] In this patient group, comorbidities, tumor location, stage, and cancer treatments such as surgery, radiotherapy, and chemotherapy can increase the risk of malnutrition.[3-5] A major challenge in managing these patients is unintentional weight loss, which is often present at diagnosis and may worsen during treatment. A decline in nutritional status results in reduced treatment adherence and poorer cancer outcomes.[6-10]

Nutritional counseling throughout radiotherapy is recognized as an essential component of care for patients with head and neck cancer (HNC), given the rapid and dynamic changes in nutritional status these patients experience during treatment.[9,11-14] The risk of malnutrition increases as radiotherapy advances, mainly due to side effects such as mucositis, dysphagia, and taste changes, which can lead to significant weekly declines in dietary intake and nutritional status.[3-5,11-14] Regular, personalized counseling sessions provided by trained dietitians have been shown to improve nutritional care and outcomes for patients at risk of malnutrition.[15]

Nevertheless, despite widespread recognition of these risks, significant gaps remain in the prevention and management of malnutrition among HNC patients. Recent roadmap statements and systematic reviews emphasize the urgent need for data-driven studies that evaluate practical aspects of nutritional interventions, including the optimal frequency, timing, and specific effects of personalized counseling and monitoring during radiotherapy.[16] The current literature also highlights barriers such as limited access to professional nutrition care and unclear guidance on which nutritional strategies most effectively preserve body composition and support favorable treatment outcomes for this patient group.[15,16]

Main Points

- Nutrition is critically important for patients with head and neck cancer because it dramatically impacts treatment outcomes.
- Radiotherapy results in a decrease in weight, muscle mass, and fat over weeks. Survival outcomes are significantly worse in patients who experience severe weight loss.
- Dietary counseling may enhance nutritional quality and patient awareness, but it cannot fully prevent treatment-related weight loss, as therapy-induced toxicities remain a predominant factor.
- Future clinical practice and research should prioritize multidisciplinary interventions that combine dietary counseling, physical activity, and metabolic monitoring to optimize body composition.

Body composition changes during radiotherapy in HNC patients are characterized by significant losses in lean body mass, skeletal muscle, fat-free mass, and body fat.[17] Severe loss of body composition during radiotherapy increases the risk of postoperative complications, reduces quality of life, worsens functional outcomes, and may decrease survival rates.[18]Therefore, regular assessment and intervention focused on maintaining healthy body composition may improve outcomes in HNC patients receiving radiotherapy.[17]

Systemic inflammatory markers such as NLR (Neutrophil-to-Lymphocyte Ratio), PLR (Platelet-to-Lymphocyte Ratio), and SII (Systemic Immune-Inflammation Index) are increasingly used to evaluate the systemic inflammatory response and predict outcomes in HNC patients undergoing radiotherapy.[19,20] Higher levels of these markers are also associated with an increased risk of severe side effects such as mucositis and impaired nutritional status, which may further lead to unfavorable outcomes.[20,21]

The present study aims to prospectively assess week-by-week changes in body composition and systemic inflammatory markers in patients with HNC who receive regular, scheduled nutritional counseling during radiotherapy. To our knowledge, few studies have examined this approach in routine clinical practice.[14] Therefore, our research aims to enhance understanding of how structured nutritional advice affects both nutritional and oncologic outcomes during radiotherapy in this high-risk group.

Materials and Methods

Study population and design

This retrospective study analyzed 26 patients who completed regular weekly nutritional counseling and intervention by a registered dietitian during radiotherapy. Seventy-two patients were initially eligible; only those who completed the intervention for all weeks were included in the final analysis, thereby minimizing loss

to follow-up and selection bias. All patients continued regular follow-up in the head and neck cancer outpatient clinic in our radiotherapy center; individual demographics, disease, and treatment characteristics are provided in Table 1.

Radiotherapy and chemotherapy

Radiotherapy treatment planning used Volumetric Modulated Arc Therapy (VMAT, Monaco Treatment Planning System v5.11), delivered with a linear accelerator (Elekta Synergy, 6 MV photons), with a median radiotherapy dose of 60 Gy. All but two patients received concurrent weekly cisplatin (40 mg/m²) according to standard protocols.

Nutritional intervention

A registered dietitian provided standardized, face-to-face nutritional counseling sessions (~30 min) for each patient weekly during radiotherapy. These sessions documented current dietary intake, food records, socioeconomic status, and nutrition-related toxicities. Adherence to dietary recommendations was monitored each week. The Subjective Global Assessment (SGA) was performed at both baseline and the end of treatment.[22] A weekly dietary recall was collected before each counseling session. During weekly interviews, patients' adherence to the prescribed counseling was monitored based on the previous week. Daily energy requirements were calculated using the Harris-Benedict formula and protein intake (1.2 g/kg/day), and oral nutrition supplements (ONS) were provided to patients who did not meet targets.[23,24] ONS intolerance was defined as the inability to meet the daily recommended intake. In our study, physical activity status was assessed through direct interview at baseline during dietitian counseling sessions. Patients were asked about their typical daily routines, work status, and engagement in structured exercise. Based on these self-reports, all patients were classified as either inactive or engaged only in light physical activities. The energy and protein requirements were calculated using the sedentary (inactive) or light activity factors since no patient reported regular activity exceeding these levels.

Table 1. Baseline characteristics of the study population at the initiation of radiotherapy (n = 26)

	n (%)
Tumor location	
Larynx	11 (42.3)
Nasopharynx	5 (19.2)
Oral cavity	3 (11.5)
Sinonasal	3 (11.5)
Oropharyngeal	3 (11.5)
Salivary gland	1 (3.8)
Gender	
Male	20 (76.9)
Female	6 (32.1)
	Median (range)
Age (years)	61 (28-89)

Measurement and data collection

Anthropometric and body composition parameters—including weight (kg), body mass index (BMI), muscle mass (MM, kg), fat-free mass (FFM, kg), body fat mass (BFM, kg), visceral fat rate (VFR), and basal metabolic rate (BMR, kcal/day)—were measured using bioelectrical impedance analysis (BIA) with the TANITA BC-420MA device. The Densi GL-150 automatic system was used for height (cm) and weight (kg).

The mean and SD of inflammatory parameters, including NLR, PLR, and SII, were calculated.[25-27] The parameters collected at the beginning and end of radiotherapy were compared.

Side-effect evaluation was performed by radiation oncologists, and the Common Toxicity Criteria v5.0 was used to assess the severity of various side effects.[28] Standard medications, like antiemetics and analgesics, mouthwash, and, in case of antibiotics, were administered for pain and nausea/vomiting caused by mucositis and painful swallowing.

Statistical analyses and visualization

Inclusion criteria limit the analysis to patients who completed all intervention weeks, reducing information bias. Outcome assessment included weekly monitoring and standardized data collection to optimize reliability. Repeated measures data were analyzed using descriptive statistics. Mean ± SD trends for each variable were plotted to assess intra-individual changes over time. Weekly percentage changes were derived as:

$$\text{Percent Change} = \frac{\text{Value}_{\text{week n}} - \text{Value}_{\text{week 1}}}{\text{Value}_{\text{week 1}}} \times 100$$

Significance testing (e.g., repeated-measures ANOVA or the Friedman test) was performed as appropriate for continuous, repeated-measures data. For the longitudinal trend analysis (Figure 1), mean values with standard deviation (SD) for each parameter were plotted across five consecutive weeks. Weekly percentage changes in body composition metrics were calculated relative to baseline (week 1) and visualized as a heatmap (Figure 2) to illustrate the temporal progression and magnitude of change for each parameter. Figure 1 and Figure 2 were generated with coding and analytic assistance using Python (version 3.x) with packages including pandas, matplotlib, and seaborn in Perplexity AI (Pro version, September 2025), an artificial intelligence platform, using user-supplied data, prompts, and post-analysis parameter review. The code and figure design were reviewed and finalized by the authors. The correlation analysis was performed using Spearman's correlation.

Group comparisons, outcome analyses, and survival analyses were performed using the Kaplan-Meier curves. Progression-free survival (PFS) was defined as local or distant failure, whereas local control (LC) was defined as local and/or regional progression without any systemic progression. Survival outcomes were calculated from the beginning of radiotherapy till the last follow-up or death. A p-value < 0.05 was considered statistically significant.

Results

All patients completed radiotherapy, and no disease progression was observed during and at the end of concurrent treatment. Patients began radiotherapy after losing a mean of 12 kg following surgery. The mean weight loss was 5.27±3.89 kg (7.01%,1.36% to 18.75%). Weekly changes of the study measurements during radiotherapy are shown in Table 2 and Figure 1. Weight decreased gradually over the weeks, with a minor increase in week 4, followed by the lowest value in week 5. BMI closely mirrored the weight trajectory, declining steadily except

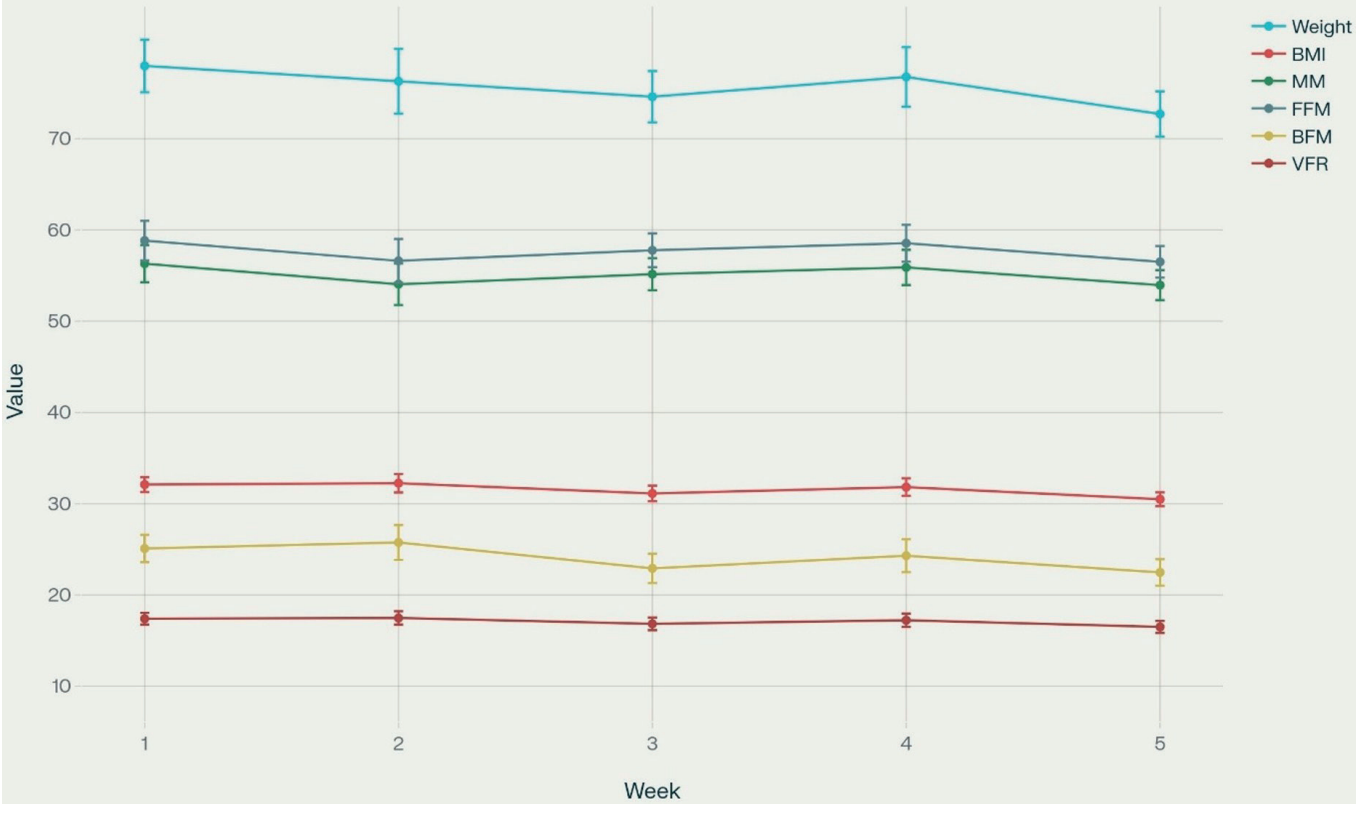

Figure 1. The mean values (±SD) of study variables—weight (kg), body mass index (BMI, kg/m^2), muscle mass (MM, kg), fat-free mass (FFM, kg), body fat mass (BFM, kg), and visceral fat rating (VFR)—were calculated weekly over five weeks. Each colored line represents the trend of one variable, with values on the Y-axis and the week number on the X-axis.

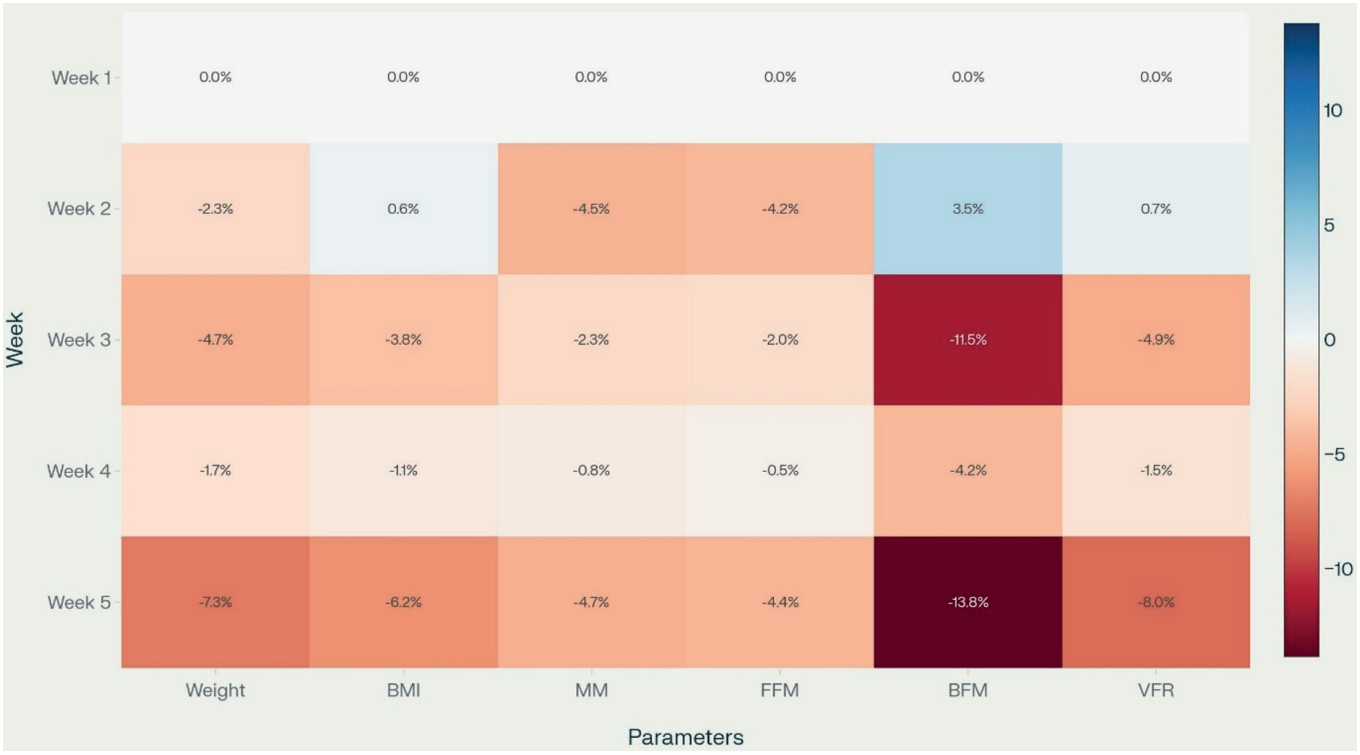

Figure 2. Weekly changes in body composition (%) during radiotherapy. The heatmap displays the percentage change in weight (kg), body mass index (BMI, kg/m^2), muscle mass (MM, kg), fat-free mass (FFM, kg), body fat mass (BFM, kg), and visceral fat rating (VFR) for each week, expressed relative to baseline (Week 1). Negative values indicate a decrease, and positive values an increase, in the given parameter relative to the starting point. Color intensity corresponds to the magnitude of change, with deeper red indicating greater loss and blue for relative gain.

Table 2. Weekly changes in body composition and metabolic parameters during radiotherapy (mean ± standard deviation, n = 26)

Week	Weight (kg)	BMI (kg/m^2)	MM (kg)	FFM (kg)	BFM (kg)	VFR (%)	BMR (kcal)
1	71.92 ± 14.70	26.03±4.15	50.24 ± 10.41	52.77 ± 11.12	19.02 ± 7.64	11.32 ± 3.28	1455.25±292.80
2	70.30 ± 18.10	26.18±5.15	47.99 ± 11.65	50.55 ± 12.22	19.68 ± 9.77	11.40 ± 3.70	1413.73±351.41
3	68.54 ± 14.34	25.05±4.32	49.09 ± 8.96	51.71 ± 9.40	16.84 ± 8.20	10.76 ± 3.56	1396.82±277.97
4	70.71 ± 16.70	25.75±4.87	49.83 ± 9.81	52.48 ± 10.29	18.23 ± 9.15	11.15 ± 3.72	1453.25±357.32
5	66.65 ± 12.61	24.42±3.86	47.89 ± 8.40	50.44 ± 8.82	16.40 ± 7.41	10.42 ± 3.36	1386.57±258.79

BMI: body mass index; MM: muscle mass; FFM: fat-free mass; BFM: body fat mass; VFR: visceral fat rate; BMR: basal metabolic rate.

for a slight increase in week 4, then reaching the lowest point in week 5. Both MM and FFM followed a similar pattern—reduction from week 1 to week 3, a modest rebound in week 4, and then another decline by week 5. VFR was fairly stable, with only slight fluctuations and a subtle downward trend, and BMR tracked overall body composition trends with minor changes week to week, reflecting the combined influence of the other parameters.

The heatmap shows the percentage change in weekly body composition and metabolic variables relative to baseline (week 1) for patients undergoing radiotherapy (Figure 2). There is a progressive decline in almost all parameters except for a transient increase in BFM in week 2. By week 5, nearly all measures show meaningful reductions from baseline, indicating a cumulative loss in both fat and lean tissue. Both weight and BMI decrease steadily, with weight dropping by -7.3% and BMI by -6.2%

by week 5. Losses in MM and FFM are also significant (MM: -4.7%; FFM: -4.4% by week 5), with the largest decrease observed in VFR (-8.0% by week 5). BMR decreases by -4.7% in week 5, matching the overall weight loss and MM. BFM is unique in showing a transient increase (+3.5%) in week 2. From week 3 onward, there is a sharp decline, reaching -13.8% in week 5.

The differences in body composition and inflammatory markers from the start to the end of radiotherapy were statistically significant (Table 3). The mean NLR, PLR, and SI were significantly high at the end of radiotherapy ($p < 0.0001$). No significant correlation was found between the increase in inflammatory factors (NLR, PLR, SII) during radiotherapy and the percentage of weight loss in patients (ΔNLR and % weight loss: Spearman's rho ≈ 0.07, $p = 0.76$, ΔPLR and % weight loss: Spearman's rho ≈ 0.04, $p = 0.84$, ΔSII and % weight loss: Spearman's rho ≈ -0.19, $p = 0.36$).

The most significant ≥ grade 2 toxicities that could affect food and calorie intake included dysphagia (n = 20), nausea/vomiting (n = 11), and taste alterations (n = 10). Aspiration and dental prosthesis issues occur more frequently in patients with severe weight loss. Low ONS tolerance and adherence were frequently observed (n = 18) due to depression, taste intolerance, stomach fullness/early satiety, nausea, and dislike of the tastes of ONS (Table 4).

Four patients had local and/or distant progression at the time of analysis. Median follow-up was 8 months (range, 6 to 42 months). Two-year LC and PFS rates were 56.2% and 54.9%, respectively (Figure 3 and Figure 4). Patients with severe weight loss showed lower progression-free survival at the end of the follow-up (LC, $p = 0.041$; PFS, $p = 0.027$).

Discussion

There are limited studies on how frequent and consistent dietitian supervision and personalized counseling affect body composition and related clinical outcomes in head and neck cancer patients receiving radiotherapy. Key strengths of our study include providing weekly, face-to-face dietary counseling for all patients throughout radiotherapy, along with the systematic assessment of body composition parameters. This approach may highlight the importance of evaluating body composition rather than relying solely on body weight, thereby providing clinically relevant insights into the mechanisms underlying malnutrition and its potential impact on patient outcomes.[16,29]

Table 3. Pre- and post-radiotherapy values of body composition and inflammatory markers in the overall study cohort (n = 26)

	Mean ± SD		
	RT-beginning	**RT-end**	***p***
Weight (kg)	71.92 ±14.69	66.65 ±12.60	**< 0.0001**
BMI (kg/m^2)	26.03±4.15	24.42±3.86	**< 0.0001**
MM (kg)	50.24±10.40	47.89±8.39	**0.002**
FFM (kg)	52.77±11.12	50.44±8.82	**0.003**
BFM (kg)	19.02±7.63	16.39±7.41	**< 0.0001**
VFM (kg)	11.32±3.27	10.43±3.36	**0.008**
BMR (kcal)	1455.25±292.80	1386.57±258.79	**< 0.0001**
NLR	2.98±2.80	5.99±4.05	**< 0.0001**
PLR	155.51±66.91	363.55±205.94	**< 0.0001**
SII	773.01±578.55	1308.36±1118.55	**< 0.0001**

Data are shown as mean ± standard deviation at the beginning and end of radiotherapy. P-values indicate the statistical significance of differences between time points using paired tests. RT: radiotherapy; BMI: body mass index; MM: muscle mass; FFM: fat-free mass; BFM: body fat mass; BMR: basal metabolic rate.

Table 4. Frequency of side effects contributing to weight loss, stratified by mild-moderate (<5%) and severe (≥5%) weight loss groups (n=26).

Cause	**<5% Weight Loss (%)**	**≥5% Weight Loss (%)**
Pain and dysphagia	76.9	76.9
Xerostomia	30.7	30.7
Smell intolerance	–	7.1
Appetite loss	30.7	15.3
Fullness/early satiety	23.0	7.1
Taste alteration	30.7	46.1
Nausea/vomiting	38.4	46.1
Dental prosthesis problems	7.7	46.1
Aspiration	0	7.1
ONS intolerance	61.5	76.9

Values represent the percentage of patients in each group who experienced the listed side effect during the study period. Mild-moderate weight loss is defined as a <5% reduction from baseline body weight, and severe weight loss as a ≥5% reduction.

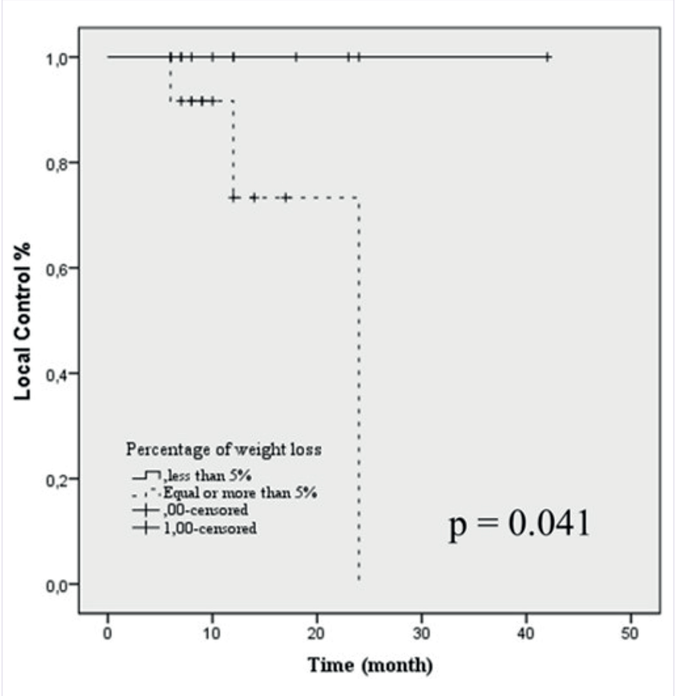

Figure 3. Kaplan-Meier curves show the 2-year local control rate for patients who lost ≥5% or <5% of weight

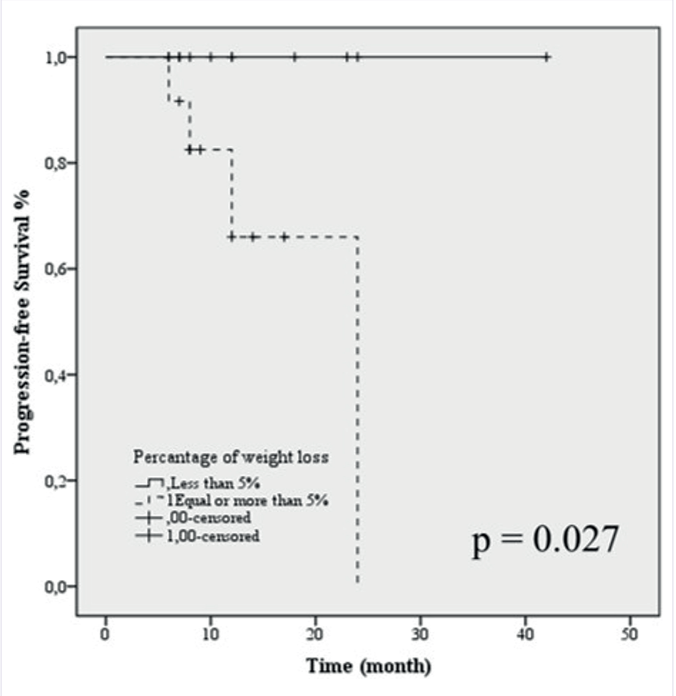

Figure 4. Kaplan-Meier curves show two-year progression-free survival rates for patients who lost≥5% or <5% of weight

During radiotherapy, the frequency and intensity of side effects increase as cumulative radiation doses accumulate week by week. In our study, the most significant decrease occurred in the last week compared with the first. This indicated clinically significant weight loss, and this information was correlated with the dose-dependent side effect. The most significant decrease was observed in VFR. BMR decline paralleled the overall loss of weight and muscle mass, which may impair physical function and recovery potential.

The study measures showed a temporary increase in weeks 3 and 4. This might indicate a recovery in this period. Between weeks 4 and 5, all variables decreased sharply, especially VFR and weight. Changing directions may highlight the dynamic nature of these measurements and may indicate the response to intervention. The positive period in weeks 3 and 4 may suggest partial stabilization, as the most significant declines occurred in weeks 4 and 5 for most variables, possibly indicating a cumulative effect of radiation therapy. BFM is showing a transient increase in week 2, possibly due to fluid shifts or measurement variability. The transient increase in body fat mass (BFM) observed in week 2 may likely reflect short-term physiological changes rather than true fat gain.[30] Radiation therapy and nutritional interventions can cause temporary fluid shifts—such as edema or changes in hydration status—which may be detected by bioelectrical impedance analysis (BIA) as an elevation in measured fat mass. Additionally, measurement variability may impact hydration and body composition readings, especially early in treatment. Therefore, this temporary BFM increase may reflect a short-lived change in fluid balance rather than a sustained accumulation of body fat.

From week 3 onward, there is a sharp decline, reaching week 5, indicating substantial fat loss. Only BMI and VFR display slight positive changes in week 2, which are short-lived and followed by further declines. The VFR remains almost unchanged in the early weeks, with minor increases, but decreases notably in week 5. This may suggest that not only subcutaneous fat, but also visceral fat was lost over the course of radiotherapy.[31] A decline in basal metabolic rate may be associated with muscle mass loss, as muscle tissue is metabolically active.[32,33] Skeletal muscle consumes the highest amount of energy among organ systems, and BMR reduction is associated with sarcopenia and muscle wasting.[32]

All three biomarkers (NLR, PLR, SII) increased by more than 2-fold during radiotherapy. No significant link was found between changes in inflammatory markers and

body weight loss in the patient group. Since no disease progression was observed at the end of radiotherapy, this may suggest increased immune-inflammatory activation due to unavoidable cumulative side effects. These effects, like mucositis and dysphagia, may lead to catabolic stress related to muscle degradation and cachexia, which may be linked to inflammation.

Table 4 summarizes the main causes of weight loss in cancer patients, comparing those with <5% versus ≥5% weight loss, and presents the frequency (number and percentage) of each cause within both groups. Dysphagia pain is the most common reason in both groups, affecting more than 75% of patients with both <5% and ≥5% weight loss. Patients were advised to have a dental examination at the beginning of treatment to assess oral health. Despite that, dental issues, especially prosthesis-related problems, were among the major eating difficulties. Low ONS tolerance and adherence may be essential in preventing severe weight loss in this population. These findings highlight which side effects are most strongly associated with more significant weight loss and provide targets for nutritional interventions in cancer patients. Although prescribed based on dietary habits and taste preferences, ONS demonstrated notable low tolerance issues, often due to treatment-related side effects or declining tolerance over time.

In the survival analysis, both local control and progression-free survival were better in patients who had less weight loss. As mentioned previously, a body weight change of more than 5% during radiotherapy may be critical for survival outcomes.[11] The weight loss due to cumulative side effects cannot be completely prevented for head and neck cancer patients in radiotherapy. Hence, we may say that it is better to start nutritional assessment and intervention at the beginning of radiotherapy, before the visible changes start. Patients may also receive dietary counseling during the postoperative period before radiotherapy. Dietary counseling may also be requested by cancer patients.[34]

Previous studies consistently identified weight loss as an independent prognostic indicator of survival in patients with HNC, highlighting its significant impact beyond traditional clinicopathological factors.[8,18] However, later research showed that more comprehensive and multimodal approaches may be necessary to prevent significant weight loss.[12,14] Therefore, in high-risk patients, proactive enteral nutrition strategies such as PEG or NG tube placement, the use of multimodal interventions including ONS and exercise, and closer monitoring may be needed.[35-37] According to guidelines, patients who consume 75-80% of the recommended amount of ONS are considered to tolerate it well.[36] Additionally, recent meta-analyses have confirmed that over 50% of patients experience critical weight loss, especially among those undergoing concurrent chemoradiotherapy, individuals with higher body mass index, and those with poor baseline performance status.[38]These findings emphasize the importance of systematically identifying high-risk subgroups and integrating proactive, personalized nutritional interventions into routine cancer care to reduce the negative effects of treatment-related weight loss on prognosis.

Although dietary support can enhance nutritional quality and patient awareness, it cannot fully prevent treatment-related weight loss, as therapy-induced toxicities remain a predominant factor. Nutritional counseling is undeniably valuable and should be regarded as an essential component of supportive care; however, maintaining body weight is rarely achievable during definitive chemoradiotherapy.[39] While dietary interventions may improve oral intake, they are insufficient on their own to counter the profound metabolic catabolism induced by therapy. Preventing skeletal muscle depletion appears to require strategies beyond dietary modification. Therefore, integration of structured exercise programs with individualized nutritional support should be strongly recommended as part of a multimodal supportive care pathway.[35,40] Future clinical practice and research should prioritize multidisciplinary interventions that combine dietary counseling, physical activity, and metabolic monitoring to optimize body composition, may reduce treatment-related toxicity, and ultimately improve survival outcomes in patients with HNC.

This study has several limitations. The retrospective, single-center design and the relatively small sample size may limit the generalizability of our findings. Additionally, there was variability in the use of oral nutritional supplements (ONS) among participants, and the short median follow-up period may restrict the assessment of survival outcomes related to nutritional factors.

Conclusion

These results reflect the effects of radiotherapy on body composition, with notable decreases in weight, muscle mass, fat mass, and metabolic rate over 5 weeks. Survival outcomes are significantly worse in patients who experience severe weight loss. Since radiotherapy itself is a risk factor for malnutrition, weekly dietitian monitoring

and counseling may help ensure timely assessment of body composition changes. They may help to decrease weight and muscle loss in HNC patients undergoing radiotherapy.

Ethical approval

This study has been approved by the Ethics Committee for Research on Non-Drug and Medical Device Research of Marmara University (approval date 10.10.2024, number 10.2024).

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: DG, SBÇ, BD, BMA; data collection: DG, SBÇ; analysis and interpretation of results: DG, SBÇ, BD, BMA; draft manuscript preparation: DG, SBÇ, BD, BMA. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Evaluation of the relationship between preoperative nutritional status and postoperative outcome in children

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ABSTRACT

Background: To evaluate the relation between preoperative nutritional status and postoperative outcome in children.

Methods: Children aged between 6 months and 18 years, who underwent surgery were included. Preoperative anthropometric measurements (BMI: body mass index, HFA: Height for age, MUAC: mid upper arm circumference; z-scores) and serum albumin/prealbumin levels and STRONGkids Nutrition Screening Test were evaluated in preoperative assessment. Children with and without preoperative malnutrition were compared for postoperative complications and outcomes.

Results: Among 57 invited patients, 51 of them with complete preoperative nutritional assessment and postoperative follow-up were included. The median age was 6.8 years (IQR: 11.2). Male to female ratio was 1.4. According to BMI z-scores, 35.3% of the cases (n=18) had acute malnutrition and 29.4% of them (n=15) had chronic malnutrition. Prealbumin levels were not different between acute and/or chronic malnourished and non-malnourished patients (p=0.744) but albumin levels were lower in malnutrition group (p=0.025). Duration of hospitalization was significantly longer in cases with malnutrition (9.0 vs 4.0 days, p=0.025). There was a significant relationship between the frequency of medium-high risk patients according STRONGkids and the frequency of malnutrition according to z-scores of MUAC (68.4% vs 32.3%; p=0.013) and HFA (93.3% vs 27.8%; p<0.001).

Conclusion: Preoperative assessment of nutritional status should be considered as essential part of preoperative work-up in children. Malnutrition significantly increases the duration of hospitalization. STRONGkids is an easy and reliable screening tool to assess the nutritional status of children and help to define the surgical patients who are at risk for malnutrition.

Keywords: malnutrition, postoperative complication, duration of hospitalization, acute malnutrition, chronic malnutrition

Introduction

The surgical mortality has been significantly reduced by the understanding of perioperative physio-pathological changes in children and the identification of nutrition-related risk factors. Malnutrition is a common morbidity observed in hospitalized children and those undergoing planned surgical treatment.[1] Cooper et al have demonstrated that 54% of children undergoing surgery suffer from protein-energy malnutrition (PEM) and it might raise up to 63% in premature infants and children under three months of age.[2] Preoperative malnutrition in

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children has been shown to result in prolonged hospital stay, increased frequency of surgical site infections, and elevated healthcare-associated costs.[3] Moreover, malnutrition is considered a preventable risk factor for postoperative complications. Although several guidelines focus on the relation between nutritional status and surgical outcomes in adult patients, there is limited evidence-based data for preoperative assessment nutrition in children.[4]

Studies in adults have demonstrated a cause-and-effect relationship between nutritional status and outcomes of surgical treatment.[4] Preoperative assessment of nutrition allows not only the identification of risk factors, but also the development of appropriate nutritional strategies to prevent potential complications after surgery and shorten hospital stays. A comprehensive nutritional assessment requires the combined use of anthropometric and biochemical parameters as well as objective and subjective evaluation tools.[5] To date, there have been limited studies evaluating the relationship between nutrition and surgical complications in children and none of the existing studies examine all parameters including anthropometric measures, serum biomarkers and screening tools in children. Therefore, we aimed to evaluate the relationship between preoperative nutritional status and surgical outcomes and complications in children.

Patients and Methods

Between 2021-2023, children between 6 months to 18 years-of-age who were scheduled for elective surgery with complete preoperative nutrition assessment on admission and 1 to 3 days prior to surgery were included. In addition to demographic characteristics, medical reports and nursing care forms were investigated for anthropometric measurements [weight, height (or length for children under 2 years old), body mass index (BMI), mid-upper arm circumference (MUAC), triceps skinfold thickness (TSFT)] and biochemical markers (serum albumin/prealbumin levels) if obtained during routine evaluation.

Main Points

- Preoperative acute and/or chronic malnutrition was present in 49% of pediatric surgical patients.
- Malnutrition was associated with prolonged hospitalization (9.0 vs. 4.0 days, p=0.025), especially in chronically malnourished children.
- STRONGkids demonstrated 68% sensitivity and 73.1% specificity for detecting malnutrition risk in this cohort.
- Routine preoperative nutritional assessment combining anthropometric, biochemical, and screening parameters is essential in pediatric surgical practice.

The inclusion criteria of the patients were;

1. Patients aged between 6 months to 18 years-of-age
2. Patients who undergo surgical interventions that require hospitalization including abdominal, thoracic, genito-urinary and oncologic surgery.
3. Patients with complete preoperative nutritional assessment and postoperative follow-up.

The exclusion criteria were;

1. Patients less than 6 months of age and older than 18 years-of-age.
2. Patients with surgical intervention that did not require hospitalization, outpatient surgical interventions.
3. Patients undergo cardiac, neurologic and orthopedic interventions and emergency operations.
4. Patients with incomplete nutritional assessment and postoperative follow-up.

Anthropometric measurements

The body weight, height/length and body mass index (BMI) were noted on admission. World health organization (WHO) Anthro and WHO AnthroPlus programs were used for the calculating the z scores.[6] In order to avoid missing data in patients older than 5 years old, the z scores for weight-for-age and height-for-weight parameters were not used in this study.

Although overweight and obesity (overnutrition) may theoretically be expressed under the definition of malnutrition,[7] since the aim of this study is to assess the association of undernutrition and surgical outcomes, we used the term of 'malnutrition' instead of protein-energy malnutrition (underweight, stunting and wasting) in line with previous articles.

The definitions of acute and chronic malnutrition were defined based on z scores of BMI and HFA, respectively.

According to WHO definitions, acute or chronic malnourished patients were classified under groups of moderate and severe malnutrition.[8] Mehta et al.[9] and Becker et al.[5] added -2 SD < BMI z-score ≤ -1 SD as mild malnutrition or 'at malnutrition risk' under the definition of acute malnutrition.[5,9] As in daily practice, children with mild malnutrition and related complications can easily be unnoticed, the morbidity and mortality risk increase. For that reason, to see the effect of any undernutrition conditions on surgery outcomes, the malnutrition group was enhanced as covering mild malnutrition/ at malnutrition risk group in order. Stunting reflecting chronic malnutrition is defined by WHO as HFA below -2SD: We also added -2SD< HFA z-score ≤ -1 SD to more robustly demonstrate the consequences of malnutrition and surgery in children at risk for chronic malnutrition. The nutritional definition of the study group was classified as shown in Table 1.

The MUAC was measured in millimeters using non-stretchable tape on the left arm. The midpoint of the distance between the tip of shoulder and the tip of elbow was determined while the arm was flexed at elbow. Afterwards, the arms were placed in a relaxed position and the tape was placed tightly and circularly around the arm, passing through this midpoint. The MUAC was recorded to the nearest 1mm. Z-scores for MUAC were assessed by using WHO Anthro program (< 5 years old)[6,10] and PediTools Electronic Growth Chart Calculators (≥5 years old).[11] Triceps skinfold thickness measurement was obtained by using caliper. Z-scores for TSFT were assessed by WHO Anthro program (< 5 years old)[6] and PediTools Electronic Growth Chart Calculators (≥5 years old).[11] Albumin (normal: 3.5-5.2 gr/dl) as well as prealbumin levels (normal: 18-38 mg/dL) were noted.

Table 1. Definitions used in the assessment of malnutrition severity[5,9,17]

Nutritional Assessment Tool	Malnutrition Severity
Z-scores for BMI:	
BMI z-score ≤ -3 SD	Severe Acute Malnutrition
-3SD ≤ BMI z-score < -2 SD	Moderate Acute Malnutrition
-2SD < BMI z-score ≤ -1 SD	Mild Acute Malnutrition
- 1SD < BMI z-score ≤ +1 SD	Normal
+1SD < BMI z-score ≤ +2 SD	Overweight
BMI z-score > +2 SD	Obese
Z-score for HFA:	
HFA z-score ≤ -3 SD	Severe Chronic Malnutrition
-3SD ≤ HFA z-score < -2 SD	Moderate Chronic Malnutrition
-2SD < HFA z-score ≤ -1 SD	Mild Chronic Malnutrition
- 1SD < HFA z-score ≤ +1 SD	Normal
HFA z-score > +1 SD	Tall Stature
Z-scores for Mid-upper Arm Circumference	
MUAC z-score ≤ -1 SD	Low MUAC z-score group
MUAC z-score > - 1 SD	Normal MUAC z-score group

BMI; body mass index, HFA: Height-for-Age, MUAC: mid-upper arm circumference, SD: standard deviation

Screening tools

The Screening Tool for Risk of Impaired Nutritional status and Growth (STRONGkids), which is an objective tool for nutritional assessment, was used for the assessment of malnutrition risk in patients, with its Turkish validation.[12] Table 2 demonstrates the parameters of STRONGkids and definitions for the risk assessment. Patients with '0' score was considered as 'low risk', whereas scores with 1-3 is 'moderate risk' and 4-5 points is 'high risk'. Outside the study, as a part of routine practice, patients with low risk underwent regular weight monitoring and no nutritional intervention is required. Moderate risk patients closely followed-up for weight monitoring and malnutrition assessment while high-risk patients consulted to nutrition support team as suggested in the STRONGkids.[12]

The demographic features, clinical findings, surgical treatments, surgical outcomes, perioperative and postoperative complications (surgical site infection, deep tissue infection, respiratory tract infection, bloodstream infection, catheter-related infection), and length of hospital stay were monitored and recorded for patients who underwent preoperative nutritional assessment. According to the nutritional status, patients were categorized as 'malnutrition group' and 'non-malnourished group'. Malnutrition group consists of patients with acute, chronic or acute plus chronic malnutrition. According to the aim of this study mentioned before, small number of overweight / obese patients or patients with tall stature included in 'non-malnourished group'. Demographic features, surgical outcomes and complications were compared between these two groups.

Statistical analysis and ethics

Statistical calculations were performed using SPSS 23.0 software (SPSS, Inc., Chicago, IL, USA). Descriptive statistics were presented as mean, standard deviation, median, minimum, and maximum values for continuous variables. Qualitative data were described using frequency and percentage values. Non-parametric independent numerical variables were compared using the Mann-Whitney U test, and parametric numerical variables were compared using the Student's t-test. The Pearson chi-square test and Fisher's exact test were used for the comparison of categorical variables. Sensitivity and specificity were calculated for each parameter. Results with a p-value less than 0.05 were considered statistically significant.

The Local Ethical Committee was approved the study (HU-GO-2022) and informed consent was obtained from the patients, parents and care-givers.

Results

Fifty-one patients who had complete preoperative assessment and follow-up were included. The median age of the patients was 6.8 years (IQR: 11.2 years, min: 6 months –max: 18 years). The male-to-female ratio was 1.4. Overall, 25 patients (49%) had acute and/or chronic malnutrition. Acute malnutrition, based on BMI z-scores, was observed in 35.3% (n=18) while chronic malnutrition, based on HFA z-scores, was detected in 29.4% (n=15) of the patients.

The demographic characteristics, nutritional status, and distribution of surgical procedures for the patients are presented in Table 3. Eighteen patients (35.3%) reported loss of appetite, whereas 7 patients (13.7%) reported vomiting±diarrhea and weight loss before surgery was noted in 8 patients (15.7%).

Table 2. STRONGkids Screening Tool for Malnutrition Risk in Children Under 18 years of age[12]

Malnutrition Risk Screening (Once a week for children aged 1 month to 18 years, at the first visit)		**Scoring**	
1	Does the patient at risk of malnutrition have an underlying illness or an expected major surgical intervention?	**NO**	**YES→2 points**
2	Does the patient show sign of poor nutrition based on subjective clinical evaluation? (decreased subcutaneous fat and/or muscle mass and/or vacant stare)	**NO**	**YES→1 point**
3	Is any of the following present? *Excessive diarrhea (>5 days) and/or vomiting (>3 days) *Decreased food intake in the past few days *Previous nutritional intervention *Inadequate food intake due to pain	**NO**	**YES→1 point**
4	Is there weight loss or lack of weight gain in the past week/month (<1 year of age)?	**NO**	**YES→1 point**

Malnutrition Risk and Treatment Needs		
Score	**Risk**	**Treatment**
4-5 points	High Risk	*Consultation with the nutrition support team is requested from the primary doctor for a definitive diagnosis and individualized nutritional recommendations. *Weight monitoring is conducted twice a week, and nutritional recommendations are evaluated. *Weekly nutritional risk assessment is performed.
1-3 points	Moderate Risk	*Nutritional intervention is taken into consideration. *Weight monitoring should be conducted twice a week. *Weekly malnutrition risk assessment is performed.
0 Points	Low Risk	* Nutritional intervention is not required. *Regular weight monitoring is conducted according to hospital policy. *Weekly nutritional risk assessment is performed.

Table 3. Demographic characteristics, surgical interventions and anthropometric assessment of patients

Characteristics of the Patients	n, %
Gender	
Female	21 (41.2%)
Male	30 (58.8%)
Age	
<6 years	22 (43.1%)
6-12 years	11 (21.6%)
>12 years	18 (35.3%)
Localization of surgical interventions	
Thoracic Surgery	4 (7.8%)
Abdominal Surgery	17 (33.3%)
Urological Surgery	10 (19.6%)
Oncological Surgery	10 (19.6%)
Other	10 (19.6%)
History of previous surgical procedure	
Yes	24 (47.1%)
No	27 (52.9%)
Duration of surgical procedure	
0-60 minutes	12 (23.5%)
61-90 minutes	15 (29.4%)
91-120 minutes	13 (25.5%)
121-150 minutes	6 (11.8%)
151 minutes and above	5 (9.8%)
Duration of hospital stay	
0-5 days	9 (17.6%)
6-10 days	31 (60.8%)
>10 days	11 (21.6%)
Body Mass Index Z-scores	
Severe Acute Malnutrition	4 (7.8%)
Moderate Acute Malnutrition	5 (9.8%)
Mild Acute Malnutrition	9 (17.6%)
Normal	19 (37.3%)
Overweight or Obese	14 (27.5%)
Height-for-Age Z-scores	
Severe Chronic Malnutrition	2 (3.9%)
Moderate Chronic Malnutrition	4 (7.8%)
Mild Chronic Malnutrition	9 (17,7%)
Normal	26 (51%)
Tall Stature	10 (19.6%)
Mid-upper Arm Circumference Z-scores	
Malnutrition	19 (37.3%)
No Malnutrition	32 (62.7%)
Triceps skinfold thickness Z-scores	
TSFT z-score ≤ -1 SD	6 (11.8%)
TSFT z-score > - 1 SD	45 (88.2%)
Malnutrition Risk According to the STRONGkids[11]	
Low Risk	27 (52.9%)
Moderate Risk	19 (37.3%)
High Risk	5 (9.8%)

SD: standard deviation, TSFT: Triceps skinfold thickness.

Patients were grouped under the 'malnutrition group' (acute, chronic, acute plus chronic malnutrition) and the 'non-malnourished group' (normal, overweight/obese and tall stature). There were no significant differences between these groups in terms of gender distribution and previous surgical history (p=0.332 and p=0.322, respectively). The ratio of malnutrition was similar in abdominal and non-abdominal surgeries (p=0.322). However, when patients with acute and chronic malnutrition were evaluated separately, acute malnutrition was more frequent in the abdominal surgery group (n=13/27, 48.1% vs. n=5/24, 20.8%) (p=0.042). Chronic malnutrition ratio was not different between abdominal (8/27, 29.6%) and non-abdominal surgery group (n=7/24, 29.2%). The ratios of abdominal and non-abdominal surgeries were also similar in groups of low MUAC z-score (≤ -1 SD) and normal MUAC z-score (> -1 SD) (p=0.514). Besides, the ratio of normal and low TSFT z-score (≤ -1 SD) patients did not show any difference in abdominal and non-abdominal surgery groups (p=1.0). According to the STRONGkids risk classification, 16 out of 27 patients (59.3%) having abdominal surgery were

Table 4. Comparison of demographic features, surgical complications and duration of hospitalization in patients with malnutrition and non-malnourished ones (*p values less than 0.05 is considered as statistically significant)

Patient Characteristics	Malnutrition (n=25)	Non-malnourished (n=26)	p-value
Gender			
Female	12 (48%)	9 (34.6%)	0.332
Male	13 (52%)	17 (65.4%)	
Surgical site			
Abdominal Surgery	15 (60%)	12 (46.2%)	0.322
Non-abdominal Surgeries	10 (40%)	14 (53.8%)	
Previous surgical procedure			
Yes	10 (40%)	14 (53.8%)	0.322
No	15 (60%)	12 (46.2%)	
Serum albumin level (g/dL)			
Mean ± SD	4.15±0.39	4.42±0.40	**0.025***
Minimum-maximum	3.37-4.69	3.76-5.71	
Serum prealbumin level (mg/dL)			
Median (IQR)	16,5(3.5)	16.9 (7.8)	0.744
Minimum-maximum	9-21.1	15.1-35.3	
Median hospital stay (days)			
Median (IQR)	9 (6)	4 (6)	**0.025***
Minimum-maximum	3-32	3-15	
STRONGkids classification[11]			
Low Risk	8 (%32)	19 (%73.1)	**0.003***
Moderate-high Risk	17 (%68)	7 (%26.9)	

IQR: interquartile range, SD: standard deviation.

in the moderate/high malnutrition risk group. The ratio was 33.3% (n=8/24) in the non-abdominal surgery group and no statistical significance was shown (p=0.064) (Table 4). The number of patients with moderate/high risk according to STRONGkids was higher in 'malnutrition group' compared to 'non-malnourished group' (68% vs 26.9%; p=0.003). In the chronic malnutrition group, moderate/high malnutrition risk was more frequent than low risk (93.3% vs. 27.8%, p<0.001). However, acute malnutrition group did not show any difference (61.1% vs. 39.4%, p=0.138). Based on MUAC z scores classification, there were significantly more patients at moderate/high risk in low MUAC z-score group (68.4%) than patients with normal MUAC (32.3%) (p=0.013). The sensitivity of STRONGkids (moderate to high risk) to detect malnutrition was 68% and specificity was 73.1%.

The mean albumin and median prealbumin preoperative values for the study population were 4.29 ± 0.42 g/dL (minimum: 3.37 and maximum: 5.71) and 16.9 mg/dL (IQR: 3.9, minimum: 9, maximum: 35.5), respectively. Only one case in the study group had an albumin level <3.5 g/dL. Prealbumin levels were evaluated in 19 patients, and 13 of them (68.4%) had low levels than normal limits (Table 3). Despite clinical insignificance, the albumin levels were lower in 'malnutrition' group (4.15±0.39 vs. 4.42±0.4; p=0.025), but prealbumin levels were similar (p=0.744) (Table 4).

Patients in malnutrition group showed a longer hospital stay (9.0 vs. 4.0 days) (p=0.025) (Table 4). While duration of hospital stay in patients with acute malnutrition and non-malnourished group was similar (p=0.238), chronic

malnutrition was associated with a slightly longer hospital stays (9.0 vs 7.5 days) (p=0.05). The ratio of patients stayed in the hospital longer than 10 days was higher in the malnutrition group than the non-malnourished group (36% vs 7.7%, p=0.014). There was no difference in abdominal surgery and non-abdominal surgery group based on hospital stay duration (p=1.0).

Forty-two patients (82.4%) were given prophylactic antibiotics before surgery. Only 2 patients (3.9%) showed bloodstream infection but no catheter related infection. Postoperative complications and Clavien-Dindo classification grades for each complication is listed in Table 5. At least one postoperative complication was seen in 12 patients (23.5%); surgical site infections (SSI) (n=9, 17.6%), pulmonary complications (n=3, 5.9%), late enterocutaneous fistula (n=1, 2.0%), late anastomotic stricture (n=1, 2.0%), and urethrocutaneous fistula after hypospadias repair (n=2, 3.9%). Despite the rate of postoperative complication was higher in the malnutrition group (72,7% vs. 27.2%), there were no significant difference between the malnutrition and non-malnourished group (p=0.076). The acute malnutrition group did not show higher complication rate than patients with BMI >-1 SD (p=0.726). The postoperative complications were higher but not statistically significant in chronic malnutrition group with HFA≤ -1 SD (54.5% vs. 22.5%, p=0.061). Among the cases with complications, a patient with enterocutaneous fistula had acute malnutrition and a patient with anastomotic stricture had chronic malnutrition, while the nutritional status of the other cases with complications was normal. While 66.7% (n=6) of patients with SSI had acute and/or chronic malnutrition (chronic malnutrition in 5 patients and acute malnutrition in 1 patient), 45.2% of patients with no SSI showed malnutrition (p=0.291). Six of nine patients with SSI had TSFT z-score ≤ -1SD, but MUAC z-score were lower than normal limits in 3 patients. There was no significant difference between malnutrition and non-malnourished groups based on MUAC z -score and TSFT z-scores. (p=0.446, p=0.576, respectively). The site of the operation was not different in patients with SSI (p=0.464).

Discussion

Malnutrition is considered as a preventable risk factor for the development of postoperative complications in surgical patients.[4] Several studies showed that malnutrition has a negative impact on surgical outcomes in adult patients and is associated with longer hospital stays and increased healthcare costs.[4] Nutrition health is an important factor not only for preparing but also for recovery from the surgery.[13] Since children who require surgical intervention are exposed to physiological stress, their nutritional needs may change during the pre and postoperative period. Hence, providing optimal nutritional support is an integral part surgical care to minimize surgical morbidity. In children, malnutrition not only causes imbalance of weight and height but also impairs the cognitive and neurodevelopment of a child. The nutritional guidelines for surgical patients are mostly based on adult data and include recommendations for adult population. There is insufficient information about the relationship between nutritional status and surgical outcomes in children. Moreover, there is no consensus on how and when to assess the preoperative nutrition in children and which treatment strategies can be apply in the presence of malnutrition. In this study, we aimed to evaluate the role of preoperative nutrition status on surgical outcomes and complications in children who underwent surgical intervention. In this context, we evaluated the relationship between nutritional status

Table 5. Postoperative complications and Clavien-Dindo classification grades for each type of surgical interventions.

Type of surgical intervention	Surgical site infection (n, Grade)	Pulmonary complications (n, Grade)	Postoperative complications (n, Grade)
Thoracic	1, II	1, II	-
Abdominal	2, II	1, II	Enterocutaneous fistula (n=1), IIIb Anastomotic stricture (n=1), IIIb
Urologic	5, II	-	Uretrocutenous fistula (n=2), IIIb
Oncological	-	-	-
Others	1, II	1, II	Blood stream infections (n=2), II

Clavien-Dindo Grade II; Complication requires pharmacological treatment; Clavien- Dindo Grade IIIb; Complication requires surgical treatment under general anesthesia.

and surgery outcome by using a wide spectrum of preoperative nutritional assessment tools including anthropometric measures, biochemical markers, and screen tools.

Malnutrition can be observed in children who require hospitalization for various reasons. In the pediatric surgery practice, gastrointestinal (GI) tract anomalies may cause decreased appetite, refusal to eat, and also the GI tract surgery may worsen the nutritional status. Although current pediatric data concentrated in patients undergoing cardiac surgery, abdominal and oncologic surgery may have obvious impact on nutrition in children.[14] Firstly, Durakbaşa et al reported that the overall malnutrition was 13.4% in pediatric surgical patients.[15] The American and European Societies for Pediatric Gastroenterology, Hepatology, and Nutrition have emphasized that identifying the risk of malnutrition in pediatric patients is a preventive measure against malnutrition-related complications and prolonged hospital stays, recommending its routine implementation.[5] For this reason, the nutritional status of all patients should be evaluated preoperatively and patients with malnutrition should be defined and treated before surgery. In our study, we used both anthropometric measurements and biochemical investigations. As recommended in previous consensus reports anthropometric measurements such as body weight for height (BWH) and BMI were used to define acute malnutrition, while HFA is considered as an indicator of chronic malnutrition.[16] In our study, only BMI z-scores were used to assess acute malnutrition as BWH z-scores cannot be calculated for children over 5 years old. In the preoperative assessment 49 % of our patients had acute and/or chronic malnutrition. In subgroups, acute and chronic malnutrition was determined in 35.3% and 29.4%, respectively. However, we could not make subgroup analysis for mild, moderate and severe malnutrition due to small sample size in each group. We also evaluated other anthropometric parameters such as z-scores of MUAC and TSFT. An indirect method for malnutrition assessment, the MUAC z-scores, which can be determined by a non-stretchable tape has the advantages of being correlated with BMI, high sensitivity of catching mild and moderate malnutrition, detecting malnutrition in non-ambulatory children.[17] We found that 37.3% of the patients showed low MUAC z-scores (≤ -1 SD) that was compatible with malnutrition. Triceps skinfold thickness measurement is recommended to detect fat stores in children.[18] To reveal the relationship of decreased fat stores and malnutrition, we evaluated TSFT z-scores and found that 11.8% patients had TSFT z-scores ≤ -1 SD.

Patients grouped under the malnutrition and non-malnourished groups according to BMI and/or HFA z-scores were compared. Gender and previous surgery history were similar in two groups. The abdominal surgery was higher in only acute malnutrition group (48.1%) when compared to patients with normal nutritional status (20.8%), but not in chronic malnutrition. Therefore, we conclude that patients, especially those undergoing abdominal surgery, may require more comprehensive evaluation of nutritional status before surgery to avoid missing acute malnutrition which may resolve in a relatively short time if the surgery is elective.

Serum albumin level, which has a half-life of 18-20 days compared to the 2-day half-life of prealbumin, can be used for evaluating nutritional status over a longer period. Low albumin levels are associated with chronic loss, while low prealbumin levels shows acute protein loss.[19] However, albumin levels are commonly used in some of the screening tools, albumin and prealbumin levels cannot be considered as only indicator for malnutrition. Although, hypoalbuminemia is considered as an independent risk factor for surgical site infections, serum protein levels should be evaluated together with the other parameters.[2] In our study, only one of the patients had low albumin levels whereas 13 of 19 patients (68.4%) had low prealbumin levels. Also, while evaluating the serum proteins, it should be kept in mind that serum levels of albumin and prealbumin might be affected by inflammation and metabolic disorders and prolonged hospitalization is an important risk factor for low albumin levels.[2] In our study group despite clinically insignificant differences, patients with malnutrition showed statistically lower albumin levels. Prealbumin levels were similar in two groups, but the sample number is small. Since prealbumin levels is not the sole criteria for assessing the preoperative malnutrition, we suggest that they did not affect our results. Furthermore, due to the retrospective design of the study, prealbumin levels may have been assessed in a selected group of patients with short-term insufficient preoperative nutrition. Although its use in pediatric surgical population is not clear, it can be monitored in patients with evident preoperative malnutrition.

Up to now, various screening tools have been identified to determine the risk of malnutrition in children. Subjective Global Nutritional Assessment (SGNA) and Screening Tool for Risk on Nutritional Status and Growth (STRONGkids) are common tools used in children to have a standardized assessment of nutrition.[15,20,21] STRONGkids is a nutritional risk screening tool for hospitalized children

and it is different from SGNA in purpose, methodology, complexity and time to administer. It is an easy and simply applicable tool and does not require training and physical examination like SGNA.[20,21] STRONGkids provides a structured, standardized screening framework, which reduces variability in nutritional risk recognition between clinicians. Many hospitals adopt a ≥1 point threshold for at least a dietitian review, since even "moderate risk" can progress quickly in hospitalized children. It is particularly useful in toddlers younger than 3 years-of age, children with chronic disease and surgical treatment.[22] Omar et al reported that STRONGkids exhibited the best accuracy in detecting acute and chronic malnutrition in children when compared to other tools.[23] It has also been utilized as a reliable assessment tool in pediatric surgery patients.[15] We used the Turkish version of STRONGkids in our study.[12] The sensitivity and specificity of the STRONGkids to define malnutrition in our study was 68% vs 73.1%, respectively. Chronic malnutrition group showed significantly high number of patients in moderate/high malnutrition risk than lower risk. Therefore, we suggest that STRONGkids can be used to define malnutrition risk, especially in chronic malnourished surgical patients and it can easily be applied preoperatively in surgical clinics and can be used repeatedly during hospitalization in children. Although there was no significant difference, the higher ratio moderate/high STRONGkids risk scores (59.3% vs. 33.3%) in patients undergone abdominal surgery may support the need for clinicians to focus on nutrition before elective abdominal surgery. Moreover, presence of moderate/high risk score was more frequent in the low MUAC z-score group. Hence, an easy tool to detect for malnutrition (MUAC) can be used even in the absence of scale and stadiometer in a surgery department.

Children undergoing surgical intervention also face surgical stress and cause metabolic response similar to that in adults. However, they are more fragile and due to their limited energy sources, development of acute and chronic malnutrition is more likely. This risk is reported to be particularly high after prolonged and serious surgeries and during long hospital stays.[2] Similar to our results, Secker et al. demonstrate a significant relationship between height-for-age and prolonged hospital stay.[20] Also, El-Regibi et al found higher complication rates and prolonged hospital stays in children who underwent hepatobiliary and GI surgery.[24] However, Toole et al. found similar results in children who underwent cardiac surgery, they did not define a similar relation between prolonged hospital stay and acute malnutrition.[14] In our study, we found that patients with malnutrition, especially chronic malnutrition had slightly longer hospital stay than normal nourished children but not in children with acute malnutrition. These results suggest that having a malnutrition associated with longer hospital stays and worse outcomes. Therefore, we suggest that patients with malnutrition, especially chronic malnutrition, requires a comprehensive preoperative assessment and special attention for postoperative complications.

In our study, 9 of 12 patients (75%) with postoperative complications had malnutrition. While the complication rate was high in the chronic malnutrition group (54.5% vs. 22.5%), the difference was not significantly significant due to limited number of patients. Malnutrition is considered as a risk factor for development of surgical site infections (SSI).[25] In a meta-analysis, it has been shown that undernutrition is predictive for postoperative infectious complications in children.[26] However, authors reported no high-quality data confirming a relation between undernutrition and SSI.[25] Since, development of SSI is multifactorial, malnutrition can be considered as one of the risk factors for developing postoperative infections. In our study group 17.6% of cases (n=9) develop SSI in the postoperative period and six of them had either acute or chronic malnutrition. The rate of SSI was similar in malnutrition and non-malnourished group. Interestingly, a recent and a big cohort study from Saxena et al, showed that even in younger ages, there were no relationship between anthropometric measurements and surgical complications.[27] Prolonged surgery was only risk factor in patients with complications.[27] The variation in different studies may be related to the use of different tools to assess nutrition and to the characteristics of the patient groups selected in each study.

The nutritional guidelines on surgery recommend assessment of nutritional status in all surgical patients preoperatively.[4] Although the aim of preoperative assessment is to define patients who are at risk for complications, the prevention of these complications with appropriate nutritional treatment is also recommended. In elective surgical procedures, 7 to 10 days enteral or parenteral nutritional treatment is recommended prior surgery.[28] In pediatric population, the optimum time of nutritional treatment and the best formula to overcome acute nutrition is not clear. Therefore, nutritional treatment strategy should be developed in pediatric surgical patients.

Our study has limitations such as small sample size and heterogenous group of patients with different surgical interventions. The effect of different types of surgery could not be evaluated because of small

amount of data in subgroup analysis. Larger cohort of studies are needed to define the role of preoperative malnutrition on surgical outcomes and complications in different surgical interventions. Although it is difficult to have a firm conclusion about a strong correlation between malnutrition and postoperative complications / outcomes, we suggest patients with chronic malnutrition at higher risk for developing complications and associated with longer hospital stays. Despite these limitations, we firstly used all preoperative nutritional assessment tools to define malnutrition in children before surgery and showed that STRONGkids is easy and reliable screening tool in children. Studies including large cohort of pediatric surgical patients are needed to define the best assessment method and principles of nutrition treatment to prevent malnutrition related complications. High quality evidence-based data in pediatric population may contribute to publish pediatric guidelines instead of following recommendations adapted from adult results.

In conclusion, preoperative assessment of nutritional status should be considered as integral part of preoperative work-up in children undergoing surgical treatment. STRONGkids is an easy and reliable screening tool to assess the nutritional status of children and help to define the surgical patients who are at risk for malnutrition. Chronic malnutrition significantly increases the duration of hospitalization. Nutritional treatment and optimizing the nutritional status are mainstay of preventive measures for malnutrition related postoperative complications in children.

Ethical approval

The study was approved by Hacettepe University Ethics Committee (date: 01.01.2024, number: HU-GO-2022). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: TS, OB; data collection: TT, DY; analysis and interpretation of results: TT, TS, HHG; draft manuscript preparation: TT, TS, HHG. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Enhancing patient outcomes in home enteral nutrition through checklist-based discharge education

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ABSTRACT

Objective: This study evaluated the effectiveness of checklist-guided discharge education in reducing post-discharge complications and emergency department visits among patients receiving home enteral nutrition (HEN), and assessed its impact on caregiver competence and patient safety.

Methods: A prospective, quasi-experimental, pre-post test controlled study was conducted between November 2024 and July 2025 with 52 HEN patients and their caregivers. Participants were randomly allocated to an intervention group, which received structured, hands-on training using the *Home Enteral Nutrition Caregiver Task Checklist*, or a control group that followed routine discharge procedures. Demographic and clinical data, feeding methods, complications, and emergency department visits were tracked over three months.

Results: Baseline demographics and comorbidities were comparable between groups. The intervention group showed significantly fewer mechanical complications, including tube obstruction, dislodgement, and replacement ($p<0.05$). Gastrointestinal complications such as diarrhea, constipation, bloating, and vomiting were also reduced ($p<0.05$). Nasogastric tube users experienced more mechanical events, whereas intermittent feeding was associated with greater gastrointestinal complications. Emergency department visits were significantly lower in the intervention group ($p<0.001$), while hospital readmissions did not differ significantly. Effect size analyses revealed large effects for mechanical complications and emergency department visits, and moderate effects for gastrointestinal complications outcomes.

Conclusion: Checklist-guided discharge education is a practical and effective strategy to improve HEN management. By reducing mechanical and gastrointestinal complications and lowering emergency department visits, structured education enhances caregiver competence, strengthens patient safety, and promotes more sustainable home care.

Keywords: enteral nutrition, home care services, gastrostomy, discharge education, caregivers, patient safety

Introduction

Enteral tube feeding (ETF) is recognized as an effective and reliable method of treatment for patients with a functional gastrointestinal system who are unable to meet their nutritional needs orally.[1] Conditions such as stroke, motor neuron disease, multiple sclerosis, dementia, head and neck cancers, cardiovascular diseases, burns, and trauma impair swallowing function and place patients at significant risk of malnutrition. In this context, ETF plays both a preventive and therapeutic role in the management of malnutrition.[2]

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Advances in medical technology and the expansion of home healthcare services have transformed ETF from a hospital-based intervention into a practice increasingly maintained in patients' homes with the support of caregivers. In the United States, approximately 344,000 individuals across all age groups receive ETF annually, while in Europe, 35.5% of individuals over 65 years of age are reported to be managed with HEN.[3,4]Home-based ETF contributes to reduced hospital readmissions, lower healthcare costs, improved patient independence, and enhanced quality of life.[5,6] However, it is also associated with mechanical and gastrointestinal complications such as diarrhea, constipation, nausea, vomiting, tube obstruction, tube dislodgement, aspiration, and electrolyte imbalances, which may compromise patient safety and clinical outcomes.[7]

In home ETF, caregiving responsibilities are primarily assumed by family members. The knowledge, attitudes, and practices of caregivers are closely linked to patient safety. Yet, the literature highlights frequent knowledge gaps among caregivers in managing complications such as tube obstruction, leakage, and displacement.[8-10] Furthermore, insufficient time allocated for appropriate discharge planning often leave caregivers insufficiently prepared to manage ETF at home, leading to preventable complications and unnecessary healthcare utilization.[11]

Evidence-based discharge education has been shown to enhance caregiver knowledge and skills, reduce anxiety, and lower complication rates.[12-14] In enterally fed populations, these programs have been shown to lower complication rates, enhance recovery, and prevent unplanned hospital readmissions. For instance, systematic nursing interventions reduced the incidence of diarrhea, abdominal distension, and constipation in children receiving ETF compared with control groups.[15] Similarly, comprehensive educational tools, such as brochures and instructional videos, have been shown to significantly improve caregivers' competence in managing nasogastric feeding, resulting in lower complication rates.[15,16] Studies conducted in Taiwan and the United Kingdom further demonstrate that standardized discharge education leads to fewer complications after gastrostomy placement, underscoring the importance of sustained and structured training programs in preventing adverse outcomes.[13,16] Multivariate analyses also confirm that participation in hospital–community–family education programs serves as a protective factor for patient prognosis.[12] Beyond clinical outcomes, standardized education has been shown to ease caregiver burden by reducing stress and anxiety, thereby supporting the continuity of home care.[13]

In Türkiye, studies on home ETF have largely focused on identifying the educational needs of patients and caregivers.[17] However, the potential impact of discharge education supported by structured tools—such as checklists—on patient outcomes, complication rates, and hospital readmissions remains insufficiently explored. This gap underscores the necessity of generating locally relevant, evidence-based data to guide clinical practice.

Accordingly, the present study aims to evaluate the effects of checklist-guided discharge education on the outcomes of patients receiving home ETF. We hypothesize that the use of standardized checklists will enhance caregiver competence, reduce preventable complications, improve patient safety, and minimize unnecessary hospital readmissions.

Main Points

- Checklist-guided discharge education significantly reduces post-discharge mechanical and gastrointestinal complications in home enteral nutrition patients.
- Structured, hands-on caregiver training enhances caregiver competence and strengthens patient safety during the early post-discharge period.
- Systematic discharge education markedly decreases enteral feeding–related emergency department visits.
- Percutaneous endoscopic gastrostomy (PEG) feeding is associated with fewer mechanical complications than nasogastric tubes, while intermittent feeding increases gastrointestinal risks, highlighting the need for tailored feeding strategies.

Materials and Methods

This quasi-experimental, pre-post test controlled study was conducted between November 2024 and July 2025 with patients receiving HEN and their caregivers at the Palliative Care Unit of Sabuncuoğlu Training and Research Hospital in Amasya, Turkey. Inclusion criteria included patients aged ≥18 years receiving HEN along with their family caregivers, whereas healthcare professionals providing care were excluded. Collected data included patient and caregiver characteristics, feeding methods, and clinical outcomes such as gastrointestinal symptoms, tube-related complications, and unplanned emergency admissions.

Data collection tools

In this study, data were collected using a Data Collection Form designed by the researcher based on a review of the literature. This form included the sociodemographic characteristics of patients and caregivers, as well as the clinical outcomes of patients receiving enteral nutrition.[17,18] For discharge education, the Home Enteral Nutrition Caregiver Task Checklist was used. This scale was originally developed by Silver et al. (2004), with a reported Cronbach's alpha of 0.94. In the Turkish adaptation, the Cronbach's alpha was 0.75.[17,19] The checklist consists of 33 items in four subdimensions: technical tasks, nutrition-related tasks, care management tasks, and functional tasks.

Intervention and control groups

Participants were randomly assigned to an intervention or control group. Randomization was performed using a simple random allocation table, and patients were assigned to groups based on this table. Group homogeneity was ensured with respect to age. The intervention group received standardized, hands-on discharge education, with the Home Enteral Nutrition Caregiver Task Checklist used as one of the tools within this structured training. The control group received routine discharge education, which included guidance on the type and amount of food and fluids to be provided, methods for measuring these amounts, and the regulation of feeding frequency and timing throughout the day. Instructions also covered maintaining the patient's head in an elevated position during feeding and pausing the administration if oral intake occurred. Additionally, caregivers were given the opportunity to practice the feeding procedures. Post-discharge follow-up was conducted via telephone for three months, with outcomes systematically recorded. The study was completed with 52 patients (26 per group), excluding 15 participants due to intensive care unit (ICU) transfer, discontinuation of enteral feeding, or death.

Education and follow-up process

Data were collected through face-to-face interviews conducted by the researcher. All patients and caregivers were provided with verbal and written information regarding the purpose and procedures of the study, and written informed consent was obtained from those who agreed to participate. Caregivers in the intervention group received standardized, hands-on training using the checklist, delivered by the same researcher. Training sessions were repeated at least three times in the hospital prior to discharge, with the number of repetitions increased based on the caregivers' learning needs.

During the post-discharge period, communication with patients and caregivers was maintained via telephone, and they were provided with the opportunity to consult the researcher if needed. The researcher monitored and recorded patient outcomes over the three-month follow-up period through weekly phone calls.For patients and caregivers in the control group, only home visits were conducted, and subsequent follow-up was performed through telephone calls. The study was completed with a total of 52 patients, 26 in the intervention group and 26 in the control group. During the follow-up period, 7 patients in the intervention group and 8 patients in the control group were excluded due to ICU readmission, discontinuation of enteral feeding, or death.

Ethical considerations of the study

Ethical approval was obtained from the Amasya University Non-Interventional Ethics Committee (ID: E-76988455-050.04-228910), and institutional permissions were secured. All participants provided written informed consent, and no interventions beyond standard care were applied.

Statistical analysis of the data

All data were analyzed using SPSS version 26.0. Continuous variables were summarized as mean ± SD, and categorical variables as frequencies and percentages. Group comparisons were conducted using the Mann–Whitney U test for continuous variables and the Chi-square test for categorical variables. Post-discharge mechanical and gastrointestinal (GI) complications at one and three months, as well as emergency visits, were analyzed with the Mann–Whitney U test. Associations between complications and patient or caregiver characteristics were evaluated using non-parametric tests. Effect sizes were calculated with Cohen's d for continuous outcomes and effect size r for non-parametric comparisons, interpreted as small (d = 0.2), moderate (d = 0.5), and large (d ≥ 0.8).

Results

Sociodemographic and clinical characteristics

The demographic and clinical characteristics of the participants are presented in Table 1. In the intervention group, 65.4% of patients were female, compared with 61.5% in the control group ($p > 0.05$). The mean age was 79.46 ± 13.97 years in the intervention group and 76.73 ± 21.12 years in the control group. Hypertension, diabetes, and cardiovascular diseases were the most common comorbidities, each present in 50% of participants. Stroke and dysphagia were the leading indications for ETF, accounting for 50% and 46.2% of cases in the intervention and control groups, respectively. All patients in the intervention group were fed via percutaneous endoscopic gastrostomy (PEG), whereas 69.2% of control patients used PEG and 30.8% used nasogastric tubes.

Post-discharge mechanical complications

During the three-month follow-up, the most frequent mechanical complications were tube replacement (59.6%), tube obstruction (53.8%), and tube dislodgement (25%). Comparison between groups demonstrated significant differences in tube obstruction (Month 1: $Z = -5.761$, $p<0.001$; Month 3: $Z = -4.808$, $p<0.001$), tube dislodgement (Month 1: $Z = -2.693$, $p = 0.007$; Month 3: $Z = -2.161$, $p = 0.031$), tube replacement (Month 3: $Z = -4.990$, $p <0.001$), and total mechanical complications (Month 1: $Z = -5.433$, $p<0.001$; Month 3: $Z = -5.120$, $p<0.001$) (Table 2).

Post-discharge gastrointestinal complications

Gastrointestinal complications (GI) were also reduced in the intervention group compared with controls. At one month, significant differences were found in diarrhea ($Z = -3.877$, $p <0.001$) and abdominal distension ($Z = -3.045$, $p = 0.002$). At three months, constipation ($Z = -2.722$, $p = 0.006$), diarrhea ($Z = -5.664$, $p <0.001$), abdominal distension ($Z = -3.403$, $p = 0.001$), and overall GI complications ($Z = -2.778$, $p = 0.005$) were significantly lower in the intervention group (Table 3).

Association of complications with patient and caregiver characteristics

No significant differences in mechanical or GI complications were observed based on patient age,

Table 1. Sociodemographic and Clinical Characteristics of Patients and Caregivers.

	Intervention Group	**Control Group**
Patient Gender	N (%)	N (%)
Female	17 (65.4)	16 (61.5)
Male	9 (34.6)	10 (38.5)
Patient Age (Mean ± SD)	79.46±13.97	76.73±21.12
Chronic Diseases		
Hypertension, Diabetes, Cardiovascular	13 (50)	13 (50)
COPD, Cardiovascular	4 (15.4)	3 (11.5)
Parkinson, Dementia	2 (7.7)	7 (26.9)
Alzheimer	4 (15.49	3 (11.5)
Indication for Enteral Nutrition	N (%)	N (%)
Stroke, Dysphagia	13 (50)	12 (46.2)
Parkinson-Dementia	3 (11.5)	7 (26.9)
Geriatric Conditions	5 (19.2)	5 (19.2)
Alzheimer	5 (19.2)	2 (7.7)
Type of Tube		
PEG	26	18
NG	-	8
Feeding Method		
Continuous infusion	14 (53.8)	12 (46.2)
Intermittent	12 (46.2)	14 (53.8)
	Intervention Group	**Control Group**
Caregiver Gender	N (%)	N (%)
Female	19 (73.1)	21 (80.77)
Male	7 (26.9)	5 (19.23)
Caregiver Age (Mean ± SD)	**79.46±13.97**	**76.73±21.12**
Marital Status		
Married	22 (84.6)	22 (84.6)
Single	4 (15.4)	4 (15.4)
Education Level		
Illiterate	1 (3.8)	1 (3.8)
Literate	2 (7.7)	-
Primary	11 (42.3)	19 (73.1)
Secondary	9 (34.6)	6 (23.1)
University	3 (11.5)	-

Table 1. Continued

	Intervention Group	Control Group
Occupation		
Housewife	14 (53.8)	21 (80.77)
Retired	5 (19.2)	1 (3.8)
Civil Servant	4 (15.4)	3 (11.5)
Worker	3 (11.5)	1 (3.8)
Relation to Patient		
Relative	24 (92.3)	25 (96.2)
Paid caregiver	2 (7.7)	1 (3.8)
Previous Experience		
Yes	2 (7.7)	4 (15.4)
No	24 (92.3)	22 (84.6)
Sufficiency of Enteral Nutrition		
Yes	6 (23.1)	19 (73.1)
Partly	18 (69.2)	6 (23.1)
No	2 (7.7)	1 (3.8)

sex, or comorbidities (p> 0.05). However, mechanical complications were significantly higher among patients with nasogastric tubes compared with PEG (Z = –2.286, p = 0.022), and GI complications varied significantly by feeding method, with intermittent feeding associated with more GI events (Z = –2.754, p = 0.006). No significant relationship was found between the caregiver's sex, education level, occupation, and prior caregiving experience and mechanical or gastrointestinal complications (p> 0.05), whereas a significant positive correlation was observed between age and mechanical problems (p <0.05) (Table 4).

Healthcare utilization: Emergency visits and rehospitalizations

A significant difference was observed in enteral feeding–related emergency department visits between groups (Z = –5.059, p < 0.001). In the intervention group, reasons for emergency visits included tube obstruction (7.7%), tube dislodgement (7.7%), constipation (7.7%), and diarrhea (7.7%). In contrast, the control group presented more frequently with tube obstruction (50%), tube dislodgement (50%), vomiting (34.6%), and diarrhea (19.2%). No statistically significant difference was found between groups for hospital readmissions (Z = –0.730, p = 0.465) (Table 5).

Effect sizes (Cohen's d)

Cohen's d values indicated large clinical effects for mechanical complications (d = 1.788, effect size r = 0.666) and emergency visits (d = 1.548, r = 0.612), as well as a moderate effect for GI complications (d = 0.794, r = 0.368). The effect size for hospital readmissions was small (d = 0.259, r = 0.128). These findings suggest that checklist-guided discharge education produced moderate-to-large reductions in post-discharge mechanical and GI complications and emergency visits, while no meaningful effect was observed for hospital readmissions.

Table 2. Mechanical Problems After Discharge.

Problems	Intervention Group	Control Group	Z	p
1st Month				
Tube obstruction	14.54	37.02	-5.761	<0.001
Tube dislodgement	21.26	30.56	-2.693	0.007
Total mechanical problems	14.90	36.67	-5.433	<0.001
3rd Month				
Tube obstruction	16.54	35.10	-4.808	<0.001
Tube dislodgement	22.50	29.37	-2.161	0.031
Tube replacement within 3 months	15.94	35.67	-4.990	<0.001
Total mechanical problems	15.12	36.46	-5.224	<0.001

*Z, Mann–Whitney U test; p, significance level; *p < 0.05*

Table 3. Gastrointestinal Problems After Discharge.

Problems	Intervention Group	Control Group	Z	p
1st Month				
Diarrhea	18.18	33.52	-3.877	<0.001
Bloating	19.72	32.04	-3.045	0.002
3rd Month				
Constipation	20.50	31.29	-2.722	0.006
Diarrhea	15.00	36.58	-5.664	<0.001
Bloating	18.96	32.77	-3.403	0.001
Total gastrointestinal problems	20.12	31.65	-2.778	0.005

*Z, Mann–Whitney U test; p, significance level; *p < 0.05*

Table 4. Associations of Mechanical and Gastrointestinal Problems with Various Variables.

	Total Mechanical Problems		Total Gastrointestinal Problems	p
Patient Age	r=0.112	0.430*	r=0.001	0.993*
Caregiver Age	r=0.343	**0.013***	r=-.064	0.654*
Patient Gender	**Mean Rank**	**Z/p**	**Mean Rank**	**Z/p**
Female	25.79	-.455	27.29	0.495
Male	27.74	0.649*	25.13	0.620*
Type of Tube				
PEG	24.49	-2.286	25.84	-0.738
NG	37.56	**0.022***	30.13	0.461*
Feeding Method				
Continuous infusion	24.70	-1.101	21.94	-2.754
Intermittent	29.38	0.271*	33.80	**0.006***
Caregiver Gender				
Female	27.13	-0.710	27.76	-1.411
Male	23.06	0.478*	19.56	0.158*
Previous Experience				
Yes	29.00	-0.438	22.33	-0.718
No	26.17	0.662*	27.04	0.473*
Education Level	**Mean Rank**	**K/p**	**Mean Rank**	**K/p**
Illiterate	21.75	5.048	28.50	5.048
Literate	13.75	0.282*	11.50	0.074*
Primary	30.23		27.83	
Secondary	22.17		29.70	
University	22.50		5.83	
Occupation				
Housewife	29.09	6.360	27.59	1.327
Retired	17.33	0.273*	25.17	0.932*
Civil Servant	25.71		23.64	
Worker	8.50		17.50	

*r, Spearman correlation; K, Kruskal–Wallis test; Z, Mann–Whitney U test; *, significance level.

Table 5. Readmissions Related to Enteral Nutrition.

Outcomes	Intervention Group (Mean Rank)	Control Group (Mean Rank)	Z	p
Emergency department visits	15.70	35.90	-5.059	<0.001
Hospital readmissions	25.02	26.94	-0.730	0.465

*Z, Mann–Whitney U test; p, significance level; *p < 0.05*

Discussion

This study examined the effects of structured discharge education on mechanical and gastrointestinal complications and emergency visits in HEN patients. Our findings indicate that caregivers who received systematic education experienced significantly fewer post-discharge mechanical and gastrointestinal complications and reduced emergency department visits. Mechanical complications were particularly more frequent in patients using nasogastric tubes, and increased caregiver age was associated with higher risk. Effect size analyses (Cohen's d) demonstrated large effects for mechanical complications and emergency visits, and a moderate effect for gastrointestinal complications. These results underscore the critical role of structured, targeted education programs in improving HEN management and patient safety.

The mean age of our sample aligns with previous studies on home care patients.[9,20] The increasing prevalence of chronic diseases and higher disability levels with aging are key factors explaining the initiation of HEN. In our study, the most common indications were neurological disorders, oncological diseases, and elderly individuals requiring intensive care. Neurological disorders, particularly stroke, are widely reported as the primary clinical indication for HEN in the literature.[21] Gastrostomy (PEG or surgical) was used in 81.48% of patients as the enteral access method, consistent with ESPEN data showing PEG as the most frequently employed intervention (61.4%) and similar rates reported in other studies (~77%).[22,23]

Mechanical complications are common in patients receiving HEN. More than half of our patients experienced tube occlusion or replacement post-discharge, and one-quarter experienced accidental tube dislodgement. Literature reports tube occlusion rates ranging from 9% to 45%, while leakage and peristomal skin inflammation are less frequent.[7,24-26] Tube occlusion in PEG tubes is reported at 23–35%, whereas short-term NG tube use shows occlusion at 2–9% and dislodgement at 60%.[27] In our study, tube kinking and connection separations were not observed, and only one patient had peristomal infection, likely due to the three-month follow-up period. Literature indicates that 58.4% of caregivers report accidental tube dislodgement as a complications.[19,24] The first weeks post-discharge are the most challenging for caregivers, with mechanical problems most frequently reported during this period.[26,28]The implementation of a structured checklist ensures that all essential steps for safe enteral feeding are consistently communicated to caregivers, which likely contributed to the lower incidence of tube-related mechanical complications observed in the intervention group.

Mechanical complications were significantly higher in NG tube users compared to PEG users. PEG is considered the gold standard for long-term feeding due to lower complication rates and higher quality of life.[21]The findings of our study also support this information. While all patients in the intervention group were fed via PEG, approximately half of the patients in the control group used an NG tube. This situation can be considered an important reason for the higher incidence of tube dislodgement and tube replacement frequency in the control group, as well as for the statistically significant difference observed between the groups. Intermittent gravity feeding has been shown to reduce vomiting, regurgitation, constipation, diarrhea, and abdominal distension compared to bolus feeding; however, increased feeding frequency raises regurgitation risk.[29]

The most frequent GI complications in our study were bloating (69.2%), constipation (59.6%), diarrhea (48.1%), and vomiting (30.8%). Literature also reports constipation, nausea-vomiting, and diarrhea as the most common GI complications.[3,30-32] The risk of *Clostridioides difficile*-associated diarrhea is nine times higher in HEN patients compared to non-enterally fed individuals.[33] Diarrhea and vomiting associated with PEG may relate to abdominal distension and feeding volüme.[34] Enteral feeding intolerance remains common despite optimal techniques; more than 20% of patients experience nausea, vomiting, diarrhea, or bloating.[35]

No significant association was found between age or chronic diseases and mechanical or GI complications. However, patients with neurological disorders experienced more complications than those with oncological conditions.[5,36,37]

A key finding of our study is the positive effect of systematic education on unplanned emergency visits. Literature reports 20.5–37.3% readmission rates for HEN patients, primarily due to feeding intolerance, device-related problems, and sodium imbalance from dehydration.[21,38-40] Home visits and nutrition support team interventions significantly reduce readmissions and hospital stay duration.[40,41]In this context, checklist-based education provides a structured framework that enables caregivers to recognize early warning signs and respond appropriately. This approach likely contributed to the reduction in unplanned emergency visits and facilitated timely interventions at home in the intervention group.

Caregivers' knowledge and skills are critical for preventing complications and maintaining nutrition. However, advanced age may limit a caregiver's ability to acquire new knowledge and skills and apply them to complex patient care. In our study, an increase in caregiver age was associated with a higher incidence of mechanical complications in patients. This is particularly important for preventing mechanical complications that require rapid intervention. Therefore, implementing more intensive education, support, and follow-up strategies for older caregivers is crucial to reduce the risk of complications. Systematic nursing interventions effectively reduce complication rates, prevent readmissions, and decrease stress during care.[12,13,15] The home enteral tube feeding program reduced hospital and ICU stay durations and lowered annual healthcare costs.[41] Significant differences in mechanical and GI complications between the education and control groups during the first 1 and 3 months post-discharge support the effectiveness of these programs.

This study has several limitations that should be considered. First, the follow-up period was limited to the first three months after discharge, which may have restricted the observation of long-term mechanical and gastrointestinal complications. Second, the study was conducted at a single center with a relatively homogeneous sample, which may limit the generalizability of the findings to broader populations. Third, some mechanical complications were reported by caregivers rather than directly observed by researchers, introducing a potential risk of underreporting or reporting bias. Another limitation is the difference in the types of enteral feeding tubes used between the intervention and control groups. The presence of patients fed via NGT in the control group may have particularly increased the risk of mechanical complications and influenced the outcomes, representing a significant limitation of the study. Finally, although systematic education and follow-up interventions were implemented, variability in caregiver adherence and individual patient conditions could have influenced the observed outcomes. Additionally, an a priori sample size calculation was not performed, which may have affected the study's statistical power and should be considered when interpreting the results.

This study demonstrates that checklist-guided, structured discharge education significantly improves clinical outcomes and patient safety among individuals receiving HEN. Caregivers who received standardized, hands-on training experienced markedly lower post-discharge mechanical complications including tube obstruction, dislodgement, and replacement—as well as gastrointestinal complications such as diarrhea, constipation, abdominal distension, and vomiting. Moreover, enteral feeding–related emergency department visits were significantly reduced, highlighting the effectiveness of systematic education in preventing early post-discharge complications, although hospital readmissions did not differ significantly between groups. The findings underscore the critical role of caregiver competence in HEN management, as structured education enhances caregivers' ability to identify and manage potential complications, particularly during the early post-discharge period when patients are most vulnerable. The study further supports the superiority of PEG over nasogastric tubes for long-term feeding due to lower complication rates and improved quality of life. Additionally, intermittent feeding schedules were associated with an increased risk of gastrointestinal events, emphasizing the need for careful monitoring. Overall, checklist-based discharge education represents an effective strategy that should be integrated as standard practice in HEN programs. Such interventions not only improve clinical outcomes and patient safety but also enhance the efficiency of home care services and may reduce healthcare costs. Future research should investigate long-term effects, multicenter implementation, and cost-effectiveness to further validate and generalize these findings. Overall, checklist-based discharge education represents an effective strategy that should be integrated as a standard practice within HEN programs. Such interventions not only enhance clinical outcomes and patient safety but also

improve the efficiency of home care services and may contribute to reduced healthcare costs. Future research should explore the long-term effects, multicenter implementation, and cost-effectiveness of checklist-guided education to further validate and generalize these findings.

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Ethical approval

This study has been approved by the Amasya University Non-Interventional Ethics Committee (approval date 26/11/2024, number E-76988455-050.04-228910). Verbal and written consent was obtained from the patient's guardian, caregiving relative, and paid caregivers.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: AYI; data collection: AYI, BÇA; analysis and interpretation of results: AYI; draft manuscript preparation: AYI, BÇA. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Is carbohydrate consumption a risk factor for breast cancer?

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ABSTRACT

Objective: The aim of this study is to determine the association between excessive carbohydrate and simple sugar consumption and the increased risk of breast cancer.

Methods: Patients in the control group who were followed up with a diagnosis of breast cancer in our clinic between June 2021 and June 2022 and did not have breast cancer were included in the study. Demographic data of the patients (age, gender), presence of comorbid diseases, menopause status, body mass index (BMI), fat rate (body and abdominal), and average carbohydrate and simple sugar consumption rate in the daily diet were recorded.

Results: The mean age of the patients was 45.98 ± 11.53 years. 78 (24.3%) of the patients were in group 1, and 243 (75.7%) were in group 2. There was no statistically significant difference between the groups regarding age, menopausal period, presence of comorbid diseases, BMI, daily fiber consumption, and body and abdominal fat ratio ($p>0.05$). The average carbohydrate and simple sugar consumption rate in the daily diet in group 1 was statistically significantly higher than in group 2 ($p<0.002$, $p=0.005$, respectively). Consuming high amounts of carbohydrates and simple sugar in the daily diet statistically increases breast cancer ($p<0.05$).

Conclusion: In our study, a strong relationship was found between carbohydrate and simple sugar consumption in the daily diet and breast cancer risk. Considering the increasing prevalence of simple sugar and carbohydrate consumption, we expect that this specific factor will strongly contribute to reducing the incidence of breast cancer in the future.

Keywords: breast cancer, carbohydrate, neoplasms, nutrition, risk factors

Introduction

Cancer, one of the most common diseases in the world, is one of the social health problems with a high mortality rate.[1] Today, it ranks second among the causes of death after cardiovascular diseases. It is estimated to rise to first place in the next twenty years, with approximately 29.5 million new cancer cases.[2,3] Breast cancer is the most frequently diagnosed cancer in women. The accounting for 29% of all cancers.[1]

Cancer can occur due to environmental and genetic reasons. While genetic factors have a minimal effect, it is known that cancer develops mainly due to environmental factors.[4] The most important environmental factors are cigarettes, foods, obesity, hormones, viruses, and physical and chemical agents. The relationship between cancer and nutrition varies between 10-70%, averaging 35%.[5] Alcohol consumption has been proven to be associated with cancer. The relationship between nutritional factors other than these and breast cancer is not clear.

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Epidemiological studies assessing the intake of other foods, such as meat, dairy, and soy products, have yielded inconsistent results. Dietary fat intake has also been investigated as a possible risk factor because it may increase endogenous estrogen levels, but the results obtained from the studies have been found contradictory.[6] Although the relationship between breast cancer and carbohydrates in the diet is not clear, it is stated that the effect of glucose on insulin levels may be related to the risk of cancer.[7]

High carbohydrate and simple sugar consumption is associated with cancer development through various molecular pathways. High glycemic load/carbohydrate intake may lead to postprandial hyperinsulinemia and increased bioavailability of circulating IGF-1, thereby stimulating the PI3K/AKT and MAPK pathways via IGF-1R.[8] This, in turn, may support tumorigenic processes associated with proliferation and inhibition of apoptosis. The role of the IGF-1/IGF-1R axis in breast cancer is supported by strong biological rationale, with reports indicating differential sensitivities depending on molecular subtype.[9] Large-scale meta-analyses and reviews suggest that the hyperinsulinemia–IGF-1 axis may be linked to risk, although the magnitude of this association appears to vary according to context (e.g. metabolic status, subtype).[8]

Carbohydrates are organic compounds that are among the essential nutrients, provide energy to the body, and are the most abundant in nature. Among various factors affecting the risk of breast cancer, nutrition attracts excellent attention as it is a modifiable risk factor.[10] The aim of this study is to determine the association between excessive carbohydrate and simple sugar consumption and the increased risk of breast cancer.

Main Points

- It has been found that high consumption of carbohydrates and simple sugars in the daily diet significantly increases the risk of breast cancer.
- Reducing consumption of simple sugars and refined carbohydrates in particular is important in terms of public health policies aimed at reducing the incidence of breast cancer.
- This study highlights the need to focus on carbohydrate and sugar intake in the development of nutrition-based prevention strategies.

Material and Method

The study was designed as a cross-sectional analysis. Factors influencing or associated with the development of breast cancer were examined.

Patient selection

It was examined as a prospective observational study with patients in the control group who were followed up with a diagnosis of breast cancer in the oncology clinic of our hospital between June 2021 and June 2022 and were known not to have breast cancer. Patients who were diagnosed with breast cancer, underwent surgery, underwent oncology follow-up, and agreed to participate in the study were included. The control group of the study consists of patients without a history of breast cancer who come to the general surgery outpatient clinic for routine breast check-ups. Patients whose data were incomplete and who did not agree to participate in the study were excluded. Patients who were followed up with a diagnosis of breast cancer were grouped as group 1, and control patients were grouped as group 2. High carbohydrate and simple sugar consumption was analyzed as a risk factor for breast cancer development.

Data collecting

Demographic data (age, gender), anthropometric measurements (BMI, body fat percentage, abdominal fat percentage), presence of comorbid diseases, menopausal period, and carbohydrate and simple sugar consumption data from seventy-two-hour food consumption records were recorded for the patients, including in the study.

Food consumption analysis

In the study, seventy-two-hour food consumption records of the patients were recorded. For food consumption records to be reliable, tea cups, water glasses, bowls, dessert spoons, tablespoons, serving spoons, ladles, a slice of bread, a meatball, chicken, fish, and a slice of cheese, and their quantities were shared visually. The patients were given detailed information about the amount of food consumption by looking at the samples. The patients were asked to write down the foods they consumed daily when coming to the follow-up examination. The researcher evaluated food consumption records using the BEBIS® 8.1 (Ebispro for Windows, Stuttgart, Germany; Turkish Version BEBIS®, Nutrition Information System, Version 8.1) program. The

average carbohydrate, simple sugar consumption rate, and fiber amount were noted.

Cut-off value for carbohydrates and simple sugars

According to current international guidelines, carbohydrate intake is recommended to constitute 45–60% of total energy. Intakes above this range are considered "high carbohydrate consumption." Therefore, in our study, individuals who obtained more than 60% of their total energy from carbohydrates were classified as having high carbohydrate intake.[11]

According to the recommendations of the World Health Organization (WHO) and the United States Dietary Guidelines (USDA), free or added sugars should not exceed 10% of total energy intake. This threshold has been established to reduce the risk of chronic diseases such as obesity, type 2 diabetes, and cancer. Accordingly, in our study, individuals who obtained more than 10% of their daily energy intake from simple sugars were classified as having high simple sugar consumption.[12]

Anthropometric measurements

The patients' height, body weight, waist, and hip circumference were recorded. While waist and hip circumference measurements were taken, individuals were taken standing upright and without any clothing. Measurements were taken with a tape measure. During the measurements, care was taken to ensure that the tape measure was in contact with the skin without applying too much pressure. After the measurement was taken, it was recorded in millimeters on the study form. Body mass index was calculated by dividing body weight (kg) by the square of height (m2). Body weight, total body, and abdominal area fat percentage were measured with a TANİTA TBF-300 brand scale while fasting, wearing light clothing, and without shoes.

BMI (>25 kg/m2), body fat ratio (>27%), waist/hip ratio (>0.85) and daily fiber consumption amount (>20 g/day) consumption rate cut-off values have been determined.[13-15]

Statistical analysis

While making statistics of continuous data in the scales, mean and standard deviation, minimum and maximum values of the features were used. Frequency and percentage values were used when defining categorical variables. Independent t-test was used to compare the means of two independent groups. The Chi-square test was used to evaluate the relationship between categorical variables. To evaluate the incidence of breast cancer with clinical data, logistic regression analysis was performed with backward and entered methods with statistically significant variables. The statistical significance level of the data was taken as $p<0.05$. Statistical analyses were performed using the MedCalc program and www.e-picos.com.

Ethics committee approval

Ethics committee approval for this study was obtained from a Osmaniye Korkut Ata University Science Scientific Research and Publication Ethics Board (Date: 20.10.2023, Approval Number: 2023/07/15) and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

During the study, 78 patients who were followed up with a diagnosis of breast cancer in our hospital's oncology clinic were included in the study. Five breast cancer patients with missing data and two who did not agree to participate in the study were excluded from the study. The study was conducted with a total of 321 patients, 78 of whom were diagnosed with breast cancer (group 1) and 243 of whom were in the control group (group 2) who met the inclusion criteria. The demographic and clinical characteristics of the patients in both groups are summarized in Table 1.

All patients were women. The mean age was 45.98±11.53 years. 122 (38%) of the patients were in the premenopausal period, and 199 (62%) were in the postmenopausal period. 67 (20.9%) of the patients had a history of comorbid diseases. Of these, 59 (18.4%) had diabetes mellitus and 42 (13.1%) had hypertension.

The mean BMI was 27.89±7.12 kg/m2. The average body fat ratio was 37.12±7.29. The mean abdominal fat percentage was 36.33±9.87. The average amount of fiber consumed in the daily diet was 19.23±5.43 grams.

BMI value was <25 kg/m2 in 44 (13.7%) of the patients and ≥25 kg/m2 in 277 (86.3%). Body fat ratio was ≤27 in 52 (16.2%) of the patients and >27 in 269 (83.8%). The waist/hip ratio was ≤0.85 in 105 (32.7%) of the patients

Table 1. Demographic and clinical data of patients

		Breast Cancer	Control Group	
	All patient (n=321)	**Group 1 (n=78)**	**Group 2 (n=243)**	**p value**
	x±SD	**x±SD**	**x±SD**	
Age (years)	45.98±11.53	47.07±10.09	45.36±11.27	0.24*
BMI (kg/m^2)	27.89±7.12	28.81±6.99	27.65±6.23	0.17*
Body fat percentage (%)	37.12±7.29	38.17±7.12	36.79±6.67	0.12*
Abdominal fat percentage (%)	36.33±9.87	37.29±9.43	35.99±8.71	0.26*
Waist/hip ratio	0.94±0.34	0.96±0.24	0.93±0.36	0.49*
Carbohydrate consumption	64.11±13.45	69.52±12.37	62.18±9.82	0.002*
Simple sugar consumption rate (%)	14.02±6.78	15.11±6.02	13.24±4.81	0.005*
Pulp (gr)	19.23±5.43	18.73±5.39	19.57±4.04	0.14**
	n (%)	**n (%)**	**n (%)**	
menopausal				
premenopausal	122 (38)	27 (34.7)	95 (39.1)	0.48**
postmenopausal	199 (62)	51 (65.3)	148 (60.9)	
BMI				
<25	44 (13.7)	9 (11.5)	35 (14.4)	0.52**
≥25	277 (86.3)	69 (88.5)	208(85.6)	
Fat				
High	269 (83.8)	68 (87.2)	201 (82.7)	0.35**
Normal	52 (16.2)	10 (12.8)	42 (17.3)	
Waist/hip ratio				
High	216 (67.3)	55 (70.5)	161 (66.3)	0.49**
Normal	105 (32.7)	23 (29.5)	82 (33.7)	
Comorbid disease	67 (20.9)	17 (21.8)	50 ()	0.82**
Diabetes mellitus	59 (18.4)	14 (17.9)	45 (18.5)	0.91**
Hypertension	42 (13.1)	11 (14.1)	31 (12.8)	0.76**
Carbohydrate consumption				
High	176 (54.8)	55 (70.5)	121 (49.8)	0.001**
Normal	145 (45.2)	23 (29.5)	122 (50.2)	
Simple sugar consumption				
High (>10)	196 (61.1)	63 (80.8)	133 (54.7)	<0.001**
Normal (≤10)	125 (38.9)	15 (19.2)	110 (44.3)	
Pulp				
Low (<20)	262 (83.6)	61 (78.2)	201 (82.7)	0.37
Normal (≥20)	59 (18.4)	17 (21.8)	42 (17.3)	

*Student t test. **Chi square

and >0.85 in 216 (67.3%). The carbohydrate ratio in daily energy intake was ≤60% in 176 (54.8%) of the patients and >60% in 145 (45.2%). The simple sugar consumption rate was ≤10 in 125 (38.9%) of the patients and >10 in 196 (61.1%). The daily fiber consumption amount was ≥20 g/day in 262 (83.6%) of the patients and <20 g/day in 59 (18.4%).

There was no statistically significant difference between the groups regarding age, menopausal period, presence of comorbid diseases, BMI, daily fiber consumption, and body and abdominal fat ratio (p>0.05).

The average daily carbohydrate consumption rate was 69.52±12.37 in group 1 and 62.18±9.82 in group 2. The average daily simple sugar consumption rate was 15.11±6.02 in group 1 and 13.24±4.81 in group 2. The average carbohydrate and simple sugar consumption rate in the daily diet in group 1 was statistically significantly higher than in group 2 (p<0.002, p=0.005, respectively).

The risk of developing breast cancer in those who obtain more than 60% of their daily energy intake from carbohydrates is 241% of the risk of those who obtain <60% (OR: 2.41, 95% CI 1.39 - 4.17). The risk of developing breast cancer in those whose simple sugar intake is more than 10% of the carbohydrate amount in their daily diet is 347% of the risk of those whose carbohydrate intake is ≤10% (OR: 3.47, 95% CI 1.87 - 6.44). Consuming high amounts of carbohydrates and simple sugar in the daily diet statistically increases breast cancer (p<0.05) (Table 2).

Discussion

The current study showed that high consumption of carbohydrates and simple sugars in the daily diet increased the risk of breast cancer (p<0.05). Cancer is the second leading cause of death in the world.[2] Our study is essential for public health when considering nutrition-related risk factors in breast cancer.

In recent years, the carbohydrate content in the diet has changed. The consumption of refined sugar has increased the diet's glycemic index (GI) and glycemic load (GL). High GI foods, such as simple sugars, refined carbohydrates, and starches, cause a rapid increase in blood sugar. As a result, insulin release increases. High insulin levels cause the production of Insulin-like growth factor-1 (IGF-1) and testosterone, which are considered risk factors for breast cancer. In addition, chronic hyperinsulinemia associated with insulin resistance has a vital role in the etiology of breast cancer because it induces IGF-1 production, which can cause mutagenic changes.[16] In our study, the high consumption of carbohydrates and simple sugars may be related to the mentioned mechanism. In future studies, the hypothesis related to the etiology of the disease may be supported by measuring blood insulin levels and IGF-1.

In a prospective study, the relationship between developing breast cancer and consumption of carbohydrate-containing foods was examined. After an eighteen-year follow-up period, female cases of breast cancer were observed. However, there is no relationship between breast cancer and total fiber consumption, carbohydrate intake, and GL.[17] In studies examining dietary carbohydrate intake and breast cancer risk, GL and GI of food were examined.[18]

A study of 688 pre- and postmenopausal breast cancer survivors prospectively examined various nutritional factors associated with cancer prognosis. No significant relationship was found between carbohydrate intake, GL or Gİ and breast cancer-specific mortality.[19] While only one of the studies included in a recent meta-analysis showed a modest increase in breast cancer risk in women with a high-GI or GL-related diet, two other studies also observed controversial results. The current study observed a significant difference in carbohydrate intake between Group 1 and Group 2. However, the fact that GI and GL were not evaluated is a limitation.[20]

A prospective study from Japan analyzed age-adjusted mortality from breast cancer from National Nutrition Survey data and Japan Vital Statistics. As a result, an inverse correlation was found between carbohydrate intake and death from breast cancer.[21] This may be due to the increase in fiber associated with carbohydrate

Table 2. The relationship between carbohydrate and simple sugar consumption in breast cancer formation with multivariate analysis

	Odds ratio	95% Confidence Interval	p value
Carbohydrate	2.41	1.39 – 4.17	<0.05
Simple sugar	3.47	1.87 – 6.44	<0.05

intake. Contrary to the stated opinion, our study found no relationship between fiber content and breast cancer.

There is a direct proportional relationship between carbohydrate intake and breast cancer risk. It is predicted that the relationship between breast cancer and carbohydrates is primarily caused by simple sugar intake. In the review conducted by Li et al., dietary carbohydrate intake was suggested to be associated with lower breast cancer incidence, mortality, and recurrence risk.[22]

Many prospective cohort studies have been conducted recently on dietary fiber intake and breast cancer. Most results show that the relationship between the two is not significant. Precise estimates of dietary fiber intake are conflicting due to difficulties in obtaining and limited heterogeneity of fiber intake in geographically limited populations.[23] In a random-effects meta-analysis of prospective observational studies, Farvid et al. demonstrated that higher total fiber intake was associated with a reduced risk of breast cancer. This finding was consistent for both soluble fiber and among women with premenopausal and postmenopausal breast cancer.[24]

Early exposure to environmental carcinogens, endocrine disruptors, and unhealthy foods (such as refined sugars, processed fats, and food additives) is hypothesized to promote molecular damage that increases breast cancer risk. In their review, Natarajan et al. aimed to gather information on potential exposures during adolescence and emphasized that preventing environmental exposure at this stage is challenging. The authors highlighted that young women are repeatedly exposed to media messages promoting unhealthy foods, representing a significant risk factor. Moreover, adolescents living in disadvantaged neighborhoods face additional challenges such as limited access to healthy foods and increased exposure to polluted air, water, and soil.[25]

In a study conducted in Denmark, the relationship between breast cancer and dietary carbohydrate intake in postmenopausal women was examined. No significant relationship was found between breast cancer and carbohydrate intake and fructose, which is the carbohydrate subgroup.[26]

In another prospective cohort study examining the relationship between dietary fructose intake and cancer risk, breast cancer was detected in 3.36% of women participating in the study between 1980 and 1998. As a result of statistical analysis, no relationship was found between fructose consumption and breast cancer in postmenopausal and premenopausal women.[17] A recent meta-analysis found not association between total sugar and fructose intake and breast cancer risk.[27] Contrary to the literature, our study suggests that as simple sugar consumption increases, the risk of breast cancer increases by 347% and can be considered a risk factor.

Today, most people consume foods and beverages sweetened with high-fructose corn syrup. Excessive dietary sugar intake, particularly fructose, is associated with an altered metabolic state both systemically and within specific tissues. This altered metabolism has multiple profound effects and is linked to the development of various diseases, including diabetes, cardiovascular disorders, and even cancer. In their review, Strober and Brady highlighted the association between increased dietary fructose intake, the development of metabolic dysfunctions, and the rising incidence of breast cancer.[28]

This topic also has implications across different domains. Since estrogen, progesterone, and insulin-like growth factor levels vary with menopausal status in breast cancer, the hyperinsulinemic stimuli triggered by carbohydrate consumption may elicit different biological responses in premenopausal and postmenopausal women. In their meta-analysis, Schlesinger et al. reported findings suggesting that the association between carbohydrate intake, glycemic load, and breast cancer risk was more pronounced among postmenopausal women.[27]

It is thought that the lack of a consistent relationship between dietary factors and breast cancer in epidemiological studies may be due to measurement and data errors resulting from the evaluation method of diet and insufficient dietary diversity in individual studies.

It is essential to take preventive measures against the association between high carbohydrate and simple sugar consumption and breast cancer. Concrete public health strategies should be considered. Our specific recommendations include the development of nutrition policies, clear and informative food labeling, implementation of additional taxation on such foods, and widespread community-based nutrition education programs.

The study's strengths were that the patients' daily food consumption and frequency were examined. This distribution feature has shown that carbohydrate and simple sugar consumption increases the likelihood of being a risk factor for breast cancer. In addition, the food

consumption record training given to the participants face-to-face at the beginning of the study increased the reliability of the forms taken during the control examination.

Our study has some limitations. Due to its cross-sectional descriptive design, causality between carbohydrate intake and breast cancer could not be established; the relationship was identified as an association rather than a causal effect. The study does not adequately control for possible confounding variables such as physical activity, smoking and alcohol intake, which are necessary to isolate the effect of carbohydrate intake on breast cancer risk. The patients' carbohydrate and simple sugar intake data were obtained through a 72-hour dietary recall. This method is subject to recall bias and may include inaccuracies or omissions in the recorded information.

Since the relationship between breast cancer and carbohydrate intake is largely associated with hyperinsulinemia, assessing patients' insulin and IGF-1 levels through blood tests could have provided objective evidence for future studies. Evaluating Gİ and GL in addition to carbohydrate amount in the study would have been more accurate in evaluating cumulative effects. Finally, evaluating glucose, fructose, or galactose as a simple sugar source could provide data on which type of monosaccharide has a stronger relationship.

Conclusion

High daily intake of carbohydrates and simple sugars is associated with an increased risk of breast cancer. Considering the growing prevalence of excessive sugar and carbohydrate consumption, this factor is expected to play a significant role in reducing future breast cancer incidence. Policies aimed at reducing simple sugar intake to below 10% of total energy and limiting refined carbohydrate consumption are strongly recommended.

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Ethical approval

This study has been approved by the Osmaniye Korkut Ata University Science Scientific Research and Publication Ethics Board (approval date 20.10.2023, number 2023/07/15). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: AT; data collection: AT, EGD; analysis and interpretation of results: AT; draft manuscript preparation: AT, EGD. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Comparative analysis of nutrient contents of multi-micronutrient supplements marketed for children in Türkiye

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ABSTRACT

Objective: The market for multi-micronutrient supplements for children is expanding rapidly in Türkiye, despite national guidelines not recommending routine supplementation for healthy, well-nourished children. A critical knowledge gap exists regarding the composition of these commercially available products and their alignment with national nutritional standards. This study aimed to analyze the contents of multi-micronutrient supplements marketed for children in Türkiye and compare them with national dietary reference values (DRV) and daily maximum limits (DML).

Methods: This observational, cross-sectional study was conducted between April and May 2025. A total of 89 multi-micronutrient supplements from 27 different brands, all with specific dosage recommendations for children under 18 years old, were analyzed.. Data were collected from pharmacies in İzmir and Manisa. The declared micronutrient contents on product labels were compared with the age-specific DRVs and DMLs established by the Turkish Food Codex.

Results: The most frequently included micronutrients were Vitamin C (71.9%), Vitamin D (70.8%), and Zinc (61.8%). A significant heterogeneity was observed in the micronutrient content of the products. For the 4-10 age group, essential minerals such as calcium, magnesium, and iron were often supplied at subtherapeutic doses, meeting only 22.8%, 20.6%, and 42.0% of the mean DRV, respectively. Conversely, the maximum doses in some products for the same age group significantly exceeded safety limits, reaching 467% of the DML for Vitamin A, 300% for Vitamin D, and 200% for Zinc.

Conclusion: The Turkish market for pediatric multi-micronutrient supplements is characterized by a lack of standardization, which poses a dual risk to children: potential inefficacy due to subtherapeutic doses of key minerals and a risk of chronic toxicity from excessive intake of vitamins A, D, and zinc. These findings contradict national health guidelines and highlight an urgent need for stricter regulatory oversight of supplement composition and labeling, alongside stronger clinical guidance for parents to prevent both inadequate and excessive micronutrient intake.

Keywords: dietary supplements, pediatric, micronutrients, vitamins, nutrition policy

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Introduction

Background

The popularity of dietary supplements for children, particularly those in the form of flavored gummies and chewables, is on the rise on a global scale. The revenue of the vitamin and mineral market in Türkiye is projected to attain US$29.72 million by the year 2025, exhibiting a compound annual growth rate that is anticipated to exceed both the global rate of 6.7% and the US rate of 7.52% between the years 2025 and 2029, with a projected growth rate of 10.49%.[1,2] This increase in market growth reflects parents' growing awareness of their children's nutritional needs and the increasing importance placed on preventive health approaches. Parents commonly regard these supplements as a means of protecting their children against infections and supporting their physical and cognitive development.[3-5]

Adequate intake (AI) of micronutrients, including vitamins, minerals, and trace elements, is essential for children's optimal growth, physical and cognitive development, immune function, and overall health.[6,7] Deficiencies and excesses in these essential nutrients can result in a variety of adverse health consequences, which may have long-term consequences.[7-10] Therefore, nutritional supplements intended for children must provide these essential components within appropriate amounts.[11]

Main Points

- The composition of pediatric multi-micronutrient supplements in the Turkish market is characterized by significant heterogeneity and a lack of standardization.
- This market poses a dual risk: subtherapeutic doses of essential minerals, such as calcium and magnesium, which can lead to inefficacy, and excessive doses of vitamins A, D, and zinc that exceed daily maximum limits, potentially leading to chronic toxicity.
- The widespread availability and marketing of these products contradict national health guidelines, which do not recommend routine supplementation for healthy, well-nourished children.
- Stricter regulatory oversight of supplement composition and stronger clinical guidance for parents are urgently needed to prevent both inadequate and excessive micronutrient intake.

In Türkiye, the Ministry of Health has established a national policy that stipulates the administration of vitamin K at birth, vitamin D in the first year of life, and iron supplementation between 4-12 months of age (2-12 months in cases of prematurity).[12,13] However, beyond these national recommendations, additional vitamin and mineral supplementation for healthy children who consume a normal and balanced diet is not recommended.[12-15]

Aim

Given the expanding market and its potential effects on child health, there is a clear need for data specific to the Turkish context to understand the characteristics of available supplements and their alignment with relevant nutritional guidelines. This study aims to address this gap by analyzing the multi-micronutrient content of dietary supplements marketed for children in Türkiye and comparing it with established national daily nutritional reference values.

Material and Methods

Study design and settings

This was an observational, cross-sectional, descriptive study conducted between April and May 2025. The study was reported in accordance with The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines (Supplementary Material).[16]

The study was conducted in the provinces of Manisa and İzmir to reflect the demographic and socioeconomic diversity of the Aegean Region. These locations were selected based on logistical feasibility and resource constraints. In each province, three districts representing low, middle, and high socioeconomic levels were selected via purposive sampling. Within these selected districts, convenience sampling was utilized to access centrally located pharmacies with high foot traffic. A total of 18 different pharmacies were visited, comprising a minimum of one and a maximum of five pharmacies from each district. This sampling strategy was chosen for its practicality in reaching the maximum number of products within a limited time frame. Since manufacturer formulations are standardized nationally, data from locations were pooled to analyze the widest possible

range of unique product brands available in the Turkish market.

The study included all multi-micronutrient supplements that were sold with or without a prescription in the visited pharmacies and had a specific dosage recommendation for children under 18 years of age on their packaging. Products sold online were excluded from the scope of the study due to the difficulty of price standardization and the inability to verify regional availability. Products containing a single micronutrient were excluded from the study. For the purpose of this analysis, multi-micronutrient supplements were defined as any product containing at least two distinct micronutrients or active ingredients in a single formulation, regardless of the total count.

Dietary reference intakes and values

In this field, two main reference value systems stand out globally: the Dietary Reference Intakes (DRI) framework [17], developed by the Food and Nutrition Board (FNB) of the National Academies of Sciences, Engineering, and Medicine for the United States (US) and Canada, and the Dietary Reference Values (DRV) framework[18], established by the European Food Safety Authority (EFSA) for the European Union. In Türkiye, two different frameworks are used: the Turkish Food Codex (TFC)[19] and the Turkey Dietary Guidelines (TDG).[15] A comparative summary of the dietary reference value terminologies, definitions, and primary areas of application used by the FNB, EFSA, and Türkiye is presented in Table S2 (Supplementary Material). A comparison of the TFC and international DRV is presented as an interactive website at https://onurdersan.github.io/micronutrients/.[20]

Variables, measurement and procedure

For each product, the name, brand, supplement type, pharmaceutical form (e.g., syrup, capsule, chewable), flavor, the presence of a figure and a child figure on the packaging, the total package quantity, the recommended daily dosages according to age, and the content and amounts of micronutrients (vitamins, minerals) and other active ingredients (e.g., fish oil/fatty acids, herbal extracts) in these dosages were recorded. The products and their contents were verified using the official lists of the Republic of Türkiye Ministry of Agriculture and Forestry and the Ministry of Health, as well as the manufacturers' official websites. To ensure a homogeneous market analysis, the study specifically included products legally classified as dietary supplements, which are regulated and licensed by the Ministry of Agriculture and Forestry. Products registered as pharmaceuticals under the Ministry of Health were used for exclusion verification and were not included in the final analysis, as they are subject to different regulatory standards regarding labeling and composition.

The number of days a product would last was calculated as [total quantity ÷ daily dose], and the cost per day of use was calculated as [product price ÷ (total quantity × daily dose)]. To ensure international comparability given currency fluctuations of Turkish Liras (TRY), all cost data were also converted to Euros (EUR) based on the average exchange rate during the study period (1 EUR = 43.28 TRY), obtained from the Central Bank of the Republic of Türkiye.

For each micronutrient, product contents were compared with the age- and gender-specific DRVs[21] and Daily Maximum Limits (DMLs)[22] as reported by the TFC[19] (Supplementary Table S2).

Statistical analysis and data visualization

Data analysis and visualizations were performed using the jamovi software (The jamovi project. Sydney, Australia. version 2.3) and IBM SPSS Statistics for Windows (IBM Corp. Released 2021. Version 28.0. Armonk, NY).

The distribution of the data was assessed using histograms, Q-Q plots, and the Kolmogorov-Smirnov test. Continuous variables were summarized as mean ± standard deviation (SD) or median and interquartile range (IQR). Categorical variables were presented as absolute numbers and percentages (n [%]).

Ethical considerations

This study did not require institutional ethics committee approval, as all data was compiled from publicly available sources and it did not involve any human or animal subjects.

Results

A total of 93 products from 28 brands were included in the study. Four products were excluded due to content discrepancies and missing data. Analyses were performed on a total of 89 products from 27 brands (mean, 3.3±3.6; range, 1-13).

Of the products, 48.3% (n=43) were in syrup form, 14.6% (n=13) were chewable tablets, and 12.4% (n=11) were chewable gels. In terms of flavor, 35.96% (n=32) of the products contained orange, 13.48% (n=12) contained mixed fruit, and 13.48% (n=12) contained lemon.

A total of 51.7% (n=46) of the products featured at least one figure on the packaging. Of the 17 different figures, the most common type was an animal (n=33, 37.1%). The most frequently used figure was fish (17 products from 6 brands, 19.1%). A child figure or picture was included on 25.9% (n=23) of the products.

The products contained a supply sufficient for an average of 25.9±12.7 days (range, 10-70) for the 4-10 age group and 23.6±10.2 days (range, 10-60) for the 11-18 age group. The average retail price of the products was 491±216 TRY (11.3±4.99 EUR) (range, 101-1149 TRY, 2.33-26.5 EUR). The average daily cost was 23.3±17.7 TRY (0.54±0.4 EUR) (range, 5.0-100 TRY, 0.12-2.3 EUR) for children aged 4-10 years and 26.6±12.9 TRY (0.61±0.3 EUR) (range, 5.5-53.3 TRY, 0.13-1.23 EUR) for those aged 11-18 years.

The three most common micronutrients found in the products were vitamin C (n=64, 71.91%), vitamin D (n=63, 70.79%), and zinc (n=55, 61.8%). The micronutrient contents and their proportions are presented in Table 1.

The micronutrient amounts in the products were compared with the DRVs established by the TFC for various age groups, and the results are presented as a percentage of the DRV in Table 2, Table 3, and Table 4. The mean ratios of micronutrient levels to the DRV varied widely, ranging from 15% to 1250% for vitamin C, 50% to 750% for vitamin D, and 28% to 40000% for vitamin B12. For the 4-10 age group, the mean daily dose met only 22.8% (±9.9) of the DRV for calcium, 20.6% (±9.1) for magnesium, 41.6% (±10.6) for iodine, and 42.0% (±31.2) for iron. For the 11-18 age group, the mean daily dose met only 24.1% (±4.0) of the DRV for magnesium and 37.1% (±22.5) for vitamin K.

For the 4-10 age group, the mean DRV ratio was less than 100% for 21 micronutrients, whereas the mean DRV ratio for vitamin D was 196%. For the 11-18 age group, the mean DRV ratio was below 100% for 8 micronutrients and above 100% for 14 micronutrients. Regarding other active ingredients, the mean DRV ratio for DHA (Docosahexaenoic acid) was above 100% in all age groups. The mean daily dose of DHA met 326.8% (±206.1) of the DRV for children aged 4-8 years, 245.1% (±154.5) for those aged 9-11 years, and 297.0% (±172.4) for those aged 12-13 years.

A comparison of the ratios of product contents to the DMLs established by the TFC and UL (Upper level of intake) for EFSA is presented in Table 4. In the 4-10 age group, the maximum dose was found to correspond to 467% of the DML for vitamin A, 300% of the DML for vitamin D, 200% of the DML for iron, and 200% of the DML for zinc. In the 11-18 age group, the maximum dose was found to correspond to 125% of the DML for vitamin A and 100% of the DML for both zinc and iodine.

Discussion

To our knowledge, this is the first study to analyze the contents and marketing features of multi-micronutrient supplements for children in Türkiye. The primary finding of the study is the notable heterogeneity in the multi-micronutrient content of food supplements marketed for children in Türkiye. This heterogeneity raises serious concerns regarding the consistency and predictability of nutrient intake when these products are used, as some supplements provide adequate amounts of micronutrients while others fall below or significantly exceed reference values.

National and international guidelines clearly state that healthy children who consume a balanced and varied diet do not require additional multi-micronutrient supplementation. In contrast, our study reveals the existence of a market aimed at the general pediatric population, offering a wide range of products that go beyond the principle of *complementing, not replacing, a diet*. The significant variation in nutrient content, even among products targeting the same age group, poses a challenge for parents and caregivers attempting to make informed choices. The absence of standardized formulations complicates the selection of an appropriate supplement and may lead to either insufficient or excessive intake, depending on the chosen product. This underscores the need for stronger clinical guidance to bridge the gap between parental purchasing behaviors and the actual health requirements of children.

Table 1. Content and distribution of micronutrients and other active ingredients in the products

Micronutrient	Unit	n (%)	Mean±SD (95% CI mean lower-upper)	Median (IQR, 25th-75th p)	Minimum-Maximum
Vitamin C	mg/d	64 (71.91%)	102±183 (55.8-147)	60 (45, 35-80)	12-1000
Vitamin D	U/d	63 (70.79%)	375±194 (326-424)	400 (200, 200-400)	100-1000
Zinc	mg/d	55 (61.8%)	5.9±3.21 (5.03-6.76)	5 (3.62, 3.88-7.5)	2-15
Vitamin B6	mg/d	50 (56.18%)	1.48±1.83 (0.96-2)	1 (0.837, 0.563-1.4)	0.25-8.23
Vitamin A	µg/d	47 (52.81%)	514±413 (393-635)	400 (200, 300-500)	125-2333
Niacin	mg/d	44 (49.44%)	10.9±7.62 (8.58-13.2)	10 (4.25, 8-12.3)	0.6-50
Vitamin B12	µg/d	43 (48.31%)	29.7±152 (17.2-76.6)	2.5 (2.75, 1.25-4)	0.7-1000
Folate	µg/d	42 (47.19%)	176±93.4 (147-206)	155 (100, 100-200)	50-400
Riboflavin	mg/d	42 (47.19%)	1.5±2.22 (0.80-2.2)	1 (0.6, 0.8-1.4)	0.3-15
Vitamin E	mg/d	41 (46.06%)	7.74±4.61 (6.28-9.19)	6 (5, 5-10)	1.5-24
Thiamin	mg/d	40 (44.94%)	1.46±2.04 (0.80-2.11)	1 (0.4, 0.7-1.1)	0.25-11.8
Pantothenic Acid	mg/d	39 (43.82%)	4.62±3.47 (3.49-5.74)	4 (3, 3-6)	1-23
Iodine	µg/d	31 (34.83%)	67.0±25.7 (57.6-76.4)	75 (25, 50-75)	25-150
Selenium	µg/d	31 (34.83%)	35.6±23.6 (26.9-44.2)	45 (37.5, 17.5-55)	0.1-100
Omega3	mg/d	27 (30.34%)	617±612 (375-859)	444 (480, 255-735)	33.2-2931
DHA	mg/d	22 (24.72%)	266±172 (189-342)	245 (185, 116-302)	80-740
EPA	mg/d	21 (23.6%)	275±247 (162-387)	180 (300, 90-390)	24-873
Manganese	mg/d	18 (20.22%)	0.91±0.46 (0.68-1.15)	0.92 (0.41, 0.59-1)	0.3-2
Chromium	µg/d	17 (19.1%)	35.2±27.7 (20.9-49.4)	15 (50, 10-60)	6-80
Vitamin K	µg/d	14 (15.73%)	26.4±9.3 (21-31.7)	30 (10, 20-30)	20-37.5
Iron	mg/d	14 (15.73%)	6.7±3.74 (4.54-8.86)	6.13 (3.13, 5-8.13)	1.05-14
Molybdenum	µg/d	12 (13.48%)	42.7±20.3 (29.8-55.6)	42.5 (15, 35-50)	10-75
Copper	µg/d	11 (12.36%)	458±316 (246-670)	300 (350, 275-625)	150-1000
L-Arginine	mg/d	11 (12.36%)	205±128 (119-290)	250 (163, 87.5-250)	25-450
Magnesium	mg/d	10 (11.24%)	95.7±43.5 (64.6-127)	94 (33.3, 66.8-100)	45-200
Phosphatidylserine	mg/d	7 (7.87%)	48.6±48.1 (4.08-93.1)	10 (90, 10-100)	10-100
Sambucus nigra	mg/d	7 (7.87%)	116±72.3 (48.8-183)	100 (100, 75-175)	10-200
Beta Glucan	mg/d	6 (6.74%)	60±34.6 (23.6-96.4)	50 (37.5, 50-87.5)	10-100
Choline	mg/d	6 (6.74%)	252±420 (269-773)	100 (59, 41-100)	20-1000
Calcium	mg/d	5 (5.62%)	176±70.2 (88.4-263)	150 (0, 150-150)	128-300
Citrus Bioflavonoids	mg/d	5 (5.62%)	274±546 (-404-952)	46 (33, 17-50)	6.9-1250

* Micronutrients and other active ingredients found in at least five products are presented in the table.
/d: per recommended daily dose (represents the amount of nutrient consumed when the product is taken at the daily dosage recommended by the manufacturer on the label).
Basil Extract: Ocimum basilicum L, CI: Confidence interval, IQR: Interquartile range, NC: Not Calculated, SD: Standard Deviation, 25th - 75th p: 25th - 75th percentile.
IQR=[75th percentile-25th percentile]

Table 2. Distribution of DRV percentages for micronutrient content for the 4-10 age group according to the TFC

Micronutrient	Mean (±SD)	Median (IQR)	Minimum-Maximum
Biotin, %	71.5 (±67.7)	40.0 (70.0)	18.8 - 300
Calcium, %	22.8 (±9.92)	18.8 (5.38)	16.0 - 37.5
Vitamin B12, %	97.5 (±72.9)	80.0 (50.0)	28.0 - 400
Copper, %	33.8 (±18.7)	30 (9.00)	15 - 75
Folate, %	83.6 (±38.9)	75.0 (50.0)	25.0 - 209
Iodine, %	41.6 (±10.6)	46.7 (16.7)	20.0 - 50.0
Iron, %	42.0 (±31.2)	39.3 (19.6)	7.50 - 121
Magnesium, %	20.6 (±9.11)	18.5 (7.53)	12.0 - 33.3
Manganese, %	39.1 (±13.1)	42.5 (25.0)	15.0 - 50.0
Niacin, %	63.6 (±33.4)	62.5 (15.6)	18.8 - 200
Pantothenic Acid, %	71.2 (±35.3)	66.7 (33.3)	16.7 - 200
Phosphorus, %	17.1 (±NC)	17.1 (0.00)	17.1 - 17.1
Riboflavin, %	76.5 (±35.0)	64.3 (42.9)	21.4 - 200
Selenium, %	83.4 (±48.7)	90.9 (50.0)	9.09 - 200
Thiamin, %	89.8 (±39.5)	90.9 (36.4)	22.7 - 200
Vitamin A, %	69.2 (±55.2)	50.0 (56.3)	11.4 - 292
Vitamin B6, %	71.5 (±35.7)	71.4 (48.2)	17.9 - 200
Vitamin C, %	87.8 (±88.0)	75.0 (50.0)	15.0 - 625
Vitamin D, %	196 (±108)	200 (100)	50 - 750
Vitamin E, %	63.8 (±32.0)	50.0 (41.7)	16.7 - 167
Vitamin K, %	35.1 (±12.4)	40.0 (13.3)	13.3 - 50.0
Zinc, %	56.5 (±29.7)	50.0 (35.0)	20.0 - 150

Values represent the percentage of the DRV met by the product when consumed at the manufacturer's recommended daily dosage.
DRV: Dietary Reference Values, IQR: Interquartile Range, NC: Not Calculated, SD: Standard Deviation, TFC: Turkish Food Codex

Table 3. Distribution of DRV percentages for micronutrient content for the 11-17 age group according to the TFC

Micronutrient	Mean (±SD)	Median (IQR)	Minimum-Maximum
Biotin, %	154 (±194)	100 (110)	20 - 800
Calcium, %	16.0 (±NC)	16 (0.00)	16 - 16
Vitamin B12, %	2318 (±8676)	120 (300)	40 - 40000
Copper, %	106 (±31.5)	100 (18.8)	75 - 150
Folate, %	135 (±45.4)	150 (50.0)	75 - 200
Iodine, %	64.4 (±24.7)	50.0 (43.3)	30.0 - 100
Iron, %	67.0 (±31.5)	78.6 (53.6)	31.4 - 100
Magnesium, %	24.1 (±4.02)	25.1 (1.60)	17.1 - 26.7
Manganese, %	64.4 (±25.0)	50.0 (35.0)	25.0 - 100
Niacin, %	103 (±58.4)	100 (56.3)	37.5 - 313
Pantothenic Acid, %	116 (±78.2)	100 (66.7)	41.7 - 383
Riboflavin, %	173 (±229)	111 (28.6)	64.3 - 1071
Selenium, %	113 (±53.4)	100 (100)	9.09 - 200
Thiamin, %	234 (±268)	132 (81.8)	72.7 - 1073
Vitamin A, %	68.4 (±34.7)	60.0 (39.6)	31.3 - 156
Vitamin B6, %	157 (±175)	100 (64.3)	35.7 - 588
Vitamin C, %	214 (±304)	106 (87.5)	31.3 - 1250
Vitamin D, %	295 (±135)	225 (200)	60.0 - 500
Vitamin E, %	107 (±62.3)	100 (33.3)	25.0 - 250
Vitamin K, %	37.1 (±22.5)	30.0 (11.7)	16.0 - 80.0
Zinc, %	86.1 (±36.4)	75.0 (50.0)	30 - 150

Values represent the percentage of the DRV met by the product when consumed at the manufacturer's recommended daily dosage.
DRV: Dietary Reference Values, NC: Not Calculated, SD: Standard Deviation, TFC: Turkish Food Codex

Table 4. Distribution of DRV percentages for DHA content according to the TFC

	Mean	SD	Median	25th p	75th p	Minimum	Maximum
DHA, for 4-8 years, %	326.83	206.05	272.22	133.33	510.46	88.89	822.22
DHA, for 9-11 years, %	245.12	154.54	204.17	100.0	382.84	66.67	616.67
DHA, for 12-13 years, %	297.03	172.40	212.50	166.43	425.0	95.83	645.83

DHA: Docosahexaenoic acid, DRV: Dietary Reference Values, SD: Standard Deviation , TFC: Turkish Food Codex, 25th p: 25th percentile, 75th p: 75th percentile.

Parental anxiety and the power of persuasion in marketing

Our study revealed that more than half of the products (51.7%) featured a character or figure on their packaging, and a quarter (25.9%) included a child figure. The fact that the most commonly used figure was a fish (19.1%) is likely a marketing strategy to associate the products with the perceived cognitive benefits of omega-3 fatty acids. Research has shown that cartoon characters on packaging significantly influence children's taste perceptions and product preferences, creating *pester power*.[23]

This trend is not unique to Türkiye. Studies conducted in the US, China, and other developed countries show that approximately one-third of children use dietary supplements and that multivitamins are the most common type. [24,25] Parents' reasons for using dietary supplements are to improve general health, strengthen immunity, and support appetite and diet.[3,4,24,26] Consistent with the parental perception of immune support, the most frequent micronutrients in the products in our study included popular ones such as zinc and vitamins C and D. Similarly, studies analyzing the content of multivitamins and multiminerals in Peru and the US reported that the most common ingredients were vitamins C, D, A, and zinc.[27,28]

This marketing approach medicalizes normal dietary diversity and replaces nuanced clinical judgment with a simple consumer choice, which shifts the burden of risk assessment onto parents who lack the necessary tools (such as UL information on labels) to make an informed decision.

The double-edged sword of dosage: Risks of insufficiency and excess

The most central finding of this study is the variability in micronutrient content among the products. This variability creates a dual-risk profile for the consumer: on one hand, the risk of receiving subtherapeutic doses that provide a false sense of security, and on the other, the more concerning risk of chronic exposure to excessive doses that approach or exceed established safety limits.

Our analysis showed that in products formulated for the 4-11 age group, the average content of 21 different micronutrients fell below the TFC DRV. Essential minerals critical for child development, such as calcium, magnesium, and iron for bone health and neurological development, were offered at levels meeting approximately 20-40% of the DRV. While these amounts align with the regulatory definition of a supplement intended to complement a varied diet, they may be considered subtherapeutic in the context of parental reliance. Parents often use these products to address perceived dietary inadequacies, yet these dosages may be insufficient to correct actual deficits, creating a gap between consumer expectation and physiological impact. This finding of our study was consistent with other research. A study in the US found that while many vitamins were provided at or above the Recommended Dietary Allowance (RDA), calcium, magnesium, and phosphorus were consistently labeled below the RDA.[29] A market analysis in Canada revealed that the median doses of calcium and iron in pediatric supplements were similarly low.[30]

Although product labels technically declare these amounts in compliance with regulations, the marketing of these products as comprehensive 'multivitamin/ multimineral' formulations can create a paradox. Parents who purchase these supplements may believe they are meeting their children's nutritional needs under the perceived illusion of *comprehensive nutritional support*, while in reality, the subtherapeutic doses of essential minerals mean their children may still be at risk for essential mineral deficiencies. This false assurance can deter parents from seeking dietary solutions or using appropriate, single-ingredient supplements when clinically indicated.

Conversely, the prolonged use of such supplements, especially when combined with dietary intake, may lead to exceeding safe upper limits and potentially result in adverse health effects.[31,32] Table 5 illustrates the potential risk by comparing it with the safety thresholds established by the TFC. Our findings align with research from Canada, where median doses of vitamins A, B6, B12, and C, as well as other B vitamins, were found to significantly exceed the AI recommendations.[30] Another study in Danish children found that a significant proportion of those using multivitamin and mineral supplements exceeded the ULs for micronutrients such as vitamin A, zinc, iodine, and iron.[33] Similarly, Saavedra-Garcia et al. reported that vitamin A and folate most frequently exceeded the recommended UL.[27] In their study evaluating the micronutrient content for children aged 1-3 years, Samuel et al. reported that more than one-third of the products contained Vitamin A that exceeded the UL, and one-fifth contained niacin that also exceeded the UL.[34]

Table 5. Distribution of DML percentages for micronutrient content according to the TFC

	4-10 Years			11-18 Years		
	Mean (SD)	**Median (IQR)**	**Min (Max)**	**Mean (SD)**	**Median (IQR)**	**Min (Max)**
Biotin	2.86 (2.71)	1.60 (2.80)	0.75 (12.0)	1.54 (1.94)	1.00 (1.10)	0.20 (8.0)
Calcium	24.3 (10.6)	20.0 (5.73)	17.1 (40.0)	8.53 (NC)	8.53 (0.00)	8.53 (8.53)
Choline	82.5 (138)	36.4 (16.0)	7.27 (364)	60.1 (82.1)	25.7 (59.7)	7.27 (182)
Vitamin B12	0.16 (0.12)	0.13 (0.08)	0.05 (0.67)	18.33 (21.2)	18.33 (15)	3.33 (33.3)
Copper	33.8 (18.7)	30 (9.0)	15 (75)	53.1 (15.7)	50.0 (9.38)	37.5 (75.0)
Folate	55.7 (25.9)	50.0 (33.3)	16.7(139)	44.9 (15.1)	50.0 (16.7)	25.0 (66.7)
Iodine	83.2 (21.1)	93.3 (33.3)	40.0 (100)	64.4 (24.7)	50.0 (43.3)	30.0 (100)
Iron	69.1 (51.4)	64.7 (32.4)	12.3 (200)	55.2 (25.9)	64.7 (44.1)	25.9 (82.4)
Magnesium	61.8 (27.3)	55.6 (22.6)	36.0 (100)	36.2 (6.02)	37.6 (2.40)	25.6 (40.0)
Manganese	78.1 (26.3)	85.0 (50.0)	30 (100)	64.4 (25.0)	50.0 (35.0)	25.0 (100)
Molybdenum	24.4 (11.6)	24.3 (8.57)	5.71 (42.9)	17.3 (4.13)	20.0 (5.71)	10.0 (21.4)
Niacin	4.07 (2.14)	4.00 (1.0)	1.20 (12.8)	3.28 (1.87)	3.20 (1.80)	1.20 (10.0)
Pantothenic Acid	0.85 (0.42)	0.80 (0.40)	0.20 (2.40)	0.69 (0.46)	0.60 (0.40)	0.25 (2.30)
Phosphorus	34.3 (NC)	34.3 (0.00)	34.3 (34.3)			
Riboflavin	1.07 (0.49)	0.9 (0.60)	0.30 (2.80)	1.21 (1.60)	0.775 (0.20)	0.45 (7.50)
Selenium	46.3 (26.3)	50.0 (27.5)	5.00 (110)	31.1 (14.7)	27.5 (27.5)	2.50 (55.0)
Thiamin	1.98 (870)	2.00 (800)	500 (4.40)	2.58 (2.95)	1.45 (0.900)	0.80 (11.8)
Vitamin A	111 (88.2)	80.0 (90.0)	18.3 (467)	54.8 (27.8)	48.0 (31.7)	25.0 (125)
Vitamin B6	20.0 (9.99)	20.0 (13.5)	5.0 (56.0)	22.0 (24.5)	14.0 (9.00)	5.00 (82.3)
Vitamin C	14.0 (14.1)	12.0 (8.00)	2.4 (100)	17.1 (24.3)	8.50 (7.00)	2.50 (100)
Vitamin D	78.5 (43.1)	80.0 (40.0)	20.0 (300)	59.0 (27.0)	45.0 (40.0)	12.0 (100)
Vitamin E	5.67 (2.84)	4.44 (3.70)	1.48 (14.8)	4.76 (2.77)	4.44 (1.48)	1.11 (11.1)
Vitamin K	26.4 (9.30)	30.0 (10.0)	10.0 (37.5)	13.9 (8.43)	11.3 (4.38)	6.00 (30.0)
Zinc	75.3 (39.6)	66.7 (46.7)	26.7 (200)	57.4 (24.3)	50.0 (33.3)	20.0 (100)
Beta Glucan	7.50 (4.33)	6.25 (4.69)	1.25 (12.5)	15.0 (7.13)	12.5 (6.25)	6.25 (25.0)
L-Arginine	17.0 (10.7)	20.8(13.5)	2.08 (37.5)	7.67 (3.61)	9.50 (3.25)	1 (10)
Chromium	19.4 (16.3)	8.33 (27.6)	3.33 (44.4)	19.3 (11.8)	19.4 (16.7)	1.67 (33.3)
L-Carnitine	10.0 (NC)	10 (0.00)	10 (10)	5.00 (4.33)	2.50 (3.75)	2.50 (10.0)
Caffeine				24.3 (NC)	24.3 (0.00)	24.3 (24.3)
Coenzyme Q10				1.00 (0.00)	1.00 (0.00)	1 (1)
L-Tyrosine	10.0 (NC)	10 (0.00)	10 (10)			
Citicoline	12.0 (NC)	12 (0.00)	12 (12)	18.7 (11.0)	25 (9.50)	6 (25)
Uridine				28.6 (NC)	28.6 (0.00)	28.6 (28.6)

DML: Daily Maximum Limits, IQR: Interquartile Range, NC: Not Calculated, SD: Standard Deviation, TFC: Turkish Food Codex

Therefore, the study's findings have important implications for clinicians. Clinicians should proactively inquire about all supplement use and document brand names and dosages. As physicians are the most frequent source of information, they have a critical role in educating parents about the lack of evidence for routine multivitamins, specific national recommendations for vitamin D and iron, and the dangers of toxicity from over-the-counter products.[5] This critical role is further reinforced by the finding in the study by Koç et al. that "72% of families believe that excessive use of nutritional supplements is not harmful".[5]

Study Limitations

This study has several limitations. First, it was conducted within a specific time frame and a limited geographical area using a convenience sampling method; therefore, while it captures nationally distributed brands, the findings may not be generalizable to the entire national market. The study provides a snapshot of the market, a limitation that should guide future research, as formulations and product availability can change rapidly. This cross-sectional design may introduce seasonality bias, as certain formulations predominantly marketed for winter use (e.g., specific immune boosters) might be underrepresented compared to peak-season availability. Licensed products that were unavailable on the market could not be included in the study. The exclusion of online marketplaces restricts our findings to the traditional retail pharmacy sector, where parents typically seek professional face-to-face guidance, potentially missing online-exclusive brands. Furthermore, the analyses are based solely on the nutritional content declared on product labels and manufacturers' official websites and do not include independent chemical analysis. However, significant research shows that the actual content of nutritional supplements often deviates from label declarations.[29,35,36] We acknowledge that web-based data may lag behind physical labeling updates. Therefore, our findings reflect the declared safety profile presented to the consumer rather than the analytically confirmed composition. A major limitation of our study is the lack of separate DRV data for age and gender in the TFC.

In light of these findings, future research could focus on conducting laboratory analyses to verify label claims, investigating the impact of pediatric nutritional supplement use on children's overall nutrient intake and micronutrient status, examining the knowledge and attitudes of parents in Türkiye regarding these products, and evaluating the long-term health outcomes associated with their use.

Conclusion

The market for multi-micronutrient supplements marketed for children in Türkiye is characterized by remarkable heterogeneity and a lack of standardization in product content. This situation creates a dual-risk profile for children. On one hand, the provision of subtherapeutic doses of essential minerals such as calcium, magnesium, and iron may create a false sense of security in parents, thereby failing to address existing nutritional deficiencies. On the other hand, the presence of micronutrients, particularly vitamins A and D and zinc, in doses exceeding the nationally established DML, carries a risk of chronic toxicity and excessive intake.

The current market structure contradicts national and international health guidelines that do not recommend such supplements for healthy, well-nourished children. Marketing strategies, such as figures on packaging, create a market shaped by consumer demand, targeting parental anxiety rather than evidence-based medical necessity. In light of these findings, clinicians should counsel families on the non-necessity of routine use of these supplements, actively inquire about the products and dosages being used, and educate them on the potential risks of toxicity. Policymakers should more strictly regulate the content and labeling standards of supplements for children, incorporate safety limits such as the UL into legislation, and oversee misleading marketing practices. Future research should verify label claims with chemical analyses and evaluate the long-term health outcomes of these products.

In conclusion, the multi-micronutrient supplement market for children in Türkiye presents a picture that carries risks of both insufficient and excessive dosages and requires public health regulation. Urgent regulatory measures and strong clinical guidance are imperative to protect children's health.

Ethical approval

This study did not require institutional ethics committee approval, as all data were compiled from publicly available sources and it did not involve any human or animal subjects.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: DO; data collection: DO, IO; analysis and interpretation of results: DO; draft manuscript preparation: DO, IO. All authors reviewed the results and approved the final version of the article.

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The authors declare that there is no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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IDDSI flow characteristics of paediatric formulas prepared with a maltodextrin/carob gum thickener in Türkiye

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ABSTRACT

Objective: This study evaluated IDDSI syringe-flow behaviour of paediatric formulas in Türkiye under laboratory conditions when prepared with a maltodextrin/carob-gum thickener commonly used locally and is marketed for reflux. Findings concern IDDSI flow under laboratory conditions and do not constitute clinical recommendations.

Methods: Fifteen commercial paediatric formulas (5 powdered, 10 liquid) were prepared with the thickener at 1.7 g/100 mL using a 7-minute rest protocol. The IDDSI syringe flow test (10 mL, 10 s) was performed at 0, 7, 15, 30, and 45 minutes. Two independent researchers assessed flow; inter-rater reliability was evaluated. Preparation water was 37–38 °C; testing occurred under standard room conditions; samples were covered between timepoints. Linear regression examined potential associations between thickening success, formula type, and macronutrient content.

Results: At baseline, all formulas were classified as IDDSI Level 0. After 45 minutes, 8 of the 15 formulas (53%) reached IDDSI Level 1 or higher. A higher percentage of liquid formulas (60%) thickened successfully compared to powdered formulas (40%), although this difference was not statistically significant. The thickness level increased significantly over time ($p < 0.001$), but the regression model revealed no significant associations between thickening success and formula type or macronutrient composition ($p > 0.05$).

Conclusion: Under these standardised laboratory conditions, fewer than half of tested formulas reached IDDSI Level 1 with this maltodextrin/carob-gum thickener. Outcomes varied by product and were not predictable from nutritional content or formula type. Product-specific testing is warranted, and clinical studies are required before informing practice.

Keywords: IDDSI, infant formula, thickener, viscosity, formula consistency

Introduction

Paediatric feeding disorders (PFDs), defined as the inability to consume an age-appropriate diet orally, are a common clinical diagnosis. The prevalence of PFDs is known to be higher in children with a history of premature birth, neuromuscular disorders, cardiopulmonary disorders, upper respiratory-digestive system anomalies, and gastrointestinal system disorders.[1] A frequent underlying contributor to PFD is dysphagia-a swallowing disorder that compromises the safety, efficiency, or adequacy of food or fluid intake.[2]

Dysphagia affects approximately 590 million people (8%) worldwide, with a prevalence of around 0.9% in the paediatric population.[3,4] Considering that approximately

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25% of children with dysphagia have otherwise typical development, the problem is more widespread than is often assumed.[1,4,5] Dysphagia is classically categorised as oropharyngeal or oesophageal, arising from structural or motility disorders.[6] Oropharyngeal dysphagia (OD) refers to any abnormality in the physiology of swallowing within the upper gastrointestinal tract. This can include an imbalance in the coordination between respiratory and feeding functions, leading to clinical complications such as malnutrition, aspiration pneumonia, and premature death.[7,8] OD can severely reduce quality of life by compromising nutrition and ventilation, as oropharyngeal secretions, food, or liquids may enter the airway.[9]

In children with dysphagia, limited oral intake often leads to unmet energy and macronutrient needs, elevating the risk of malnutrition.[6,10,11] Therefore, feeding therapy is typically the first-line intervention, often requiring a multidisciplinary approach. Both enteral nutrition and therapeutic strategies aim to enhance nutritional status and improve overall quality of life in these children.

Texture-modified foods and thickened liquids are commonly used in dysphagia management to support safer intake without compromising nutritional adequacy.[3,6,11]Thickeners are widely used for this purpose, as they can slow bolus transit and improve cohesion during swallowing.[12-14] Although a wide range of thickeners—food-based and commercial—are used in paediatric[15], efforts to standardise terminology (e.g., the International Dysphagia Diet Standardisation Initiative, IDDSI) are challenged in practice by variability in preparation instructions and product-specific performance.[16] These issues make product-level evaluation using the IDDSI syringe-flow framework clinically relevant.

Main Points

- Thickening is Inconsistent: Even when following a 7-minute rest protocol, a majority of formulas failed to reach the desired IDDSI Level 1 consistency, with only one of 15 formulas meeting the criteria at this time point.
- Nutritional Content Isn't a Predictor: The study found no statistically significant association between a formula's macronutrient content (e.g., protein, fat, or carbohydrates) and its ability to thicken.
- Standardized Protocols Are Needed: The study concludes that the lack of clear manufacturer instructions on the appropriate waiting time and amount of thickener for specific IDDSI outcomes makes the product's use insufficient for safe paediatric care.

Dysphagia and gastro-oesophageal reflux (GERD) are distinct clinical entities. The product evaluated here is marketed locally for reflux and is not approved for dysphagia; accordingly, this study examines laboratory IDDSI syringe-flow behaviour only and does not assess clinical outcomes or imply clinical efficacy. In Türkiye, a maltodextrin/carob-gum thickener is routinely used in paediatric feeding practice and, to our knowledge, is effectively the sole option in routine use; therefore, we adopted a single-thickener design to reflect real-world availability.

The primary objectives of this study were to:

1. Determine whether commercially available paediatric formulas achieve IDDSI Level 1 (slightly thick) consistency when prepared with a commonly used starch-based thickener in Türkiye.
2. Assess whether formula type and macronutrient composition influence thickening outcomes.
3. Evaluate the time to reach target consistency and the stability of thickness over time.

Methods

This study evaluated the effectiveness of a widely used commercial paediatric thickener in Türkiye for achieving desired consistency in infant and child formulas. We also assessed the thickener's preparation instructions due to the lack of standardized guidance on the amount and thickening time. A total of 15 formulas, including both powder-based (n=5) and ready-to-feed liquid (n=10) varieties commonly used in paediatric clinical settings, were included in the analysis.

Sample preparation

Each formula sample (100 mL) was prepared according to the manufacturer's instructions. Bebelac Gold thickener (Numil Food Products Industry and Trade Inc., Türkiye), composed of maltodextrin and carob gum, was added at a concentration of 1.7 g per 100 mL. Preparation water was 37–38 °C; testing occurred under standard room conditions (21- 22°C ambient). The mixture was stirred horizontally for 5 seconds and vertically for 20 seconds, then allowed to rest for 7 minutes to approximate the viscosity stabilization time of starch-based thickeners.[17-19]

Flow test

The consistency of the thickened formulas was assessed using the International Dysphagia Diet Standardization Initiative (IDDSI) flow test, in accordance with the IDDSI Framework and Testing Methods.[3,20] The test was conducted using a 10 mL slip-tip syringe, which was validated for compatibility with IDDSI standards in terms of barrel length and flow characteristics. Syringes were checked prior to testing to ensure standardization, as variations in dimensions can affect measurement accuracy.[20]

To perform the test, 10 mL of each sample was drawn into the syringe, and the nozzle was unblocked for 10 seconds. The IDDSI level was determined by measuring the volume remaining in the syringe after 10 seconds of flow time:

IDDSI Level 0 (Thin): <1 mL remaining

IDDSI Level 1 (Slightly Thick): 1-4 mL remaining

IDDSI Level 2 (Mildly Thick): 4-8 mL remaining

IDDSI Level 3 (Moderately Thick): 8-10 mL remaining

Flow tests were performed under consistent environmental and serving conditions, including temperature, to ensure clinical relevance.[20] All measurements were conducted in duplicate. If the difference between the two measurements exceeded 1 mL, a third trial was conducted.

Measurements were taken at five post-preparation time points (baseline (without thickener), 7, 15, 30, and 45 minutes) to evaluate the stability of the thickened liquids over time. All tests were carried out independently by two researchers to ensure inter-rater reliability. Only samples initially identified as IDDSI Level 0 were subjected to thickening procedures. The primary outcome was whether the thickened formula achieved IDDSI Level 1 following the standardized thickening and resting protocols.

Statistical analyses

Data were analysed using R version 4.3.1 and SPSS version 26. Descriptive statistics were used to summarize IDDSI success rates and viscosity changes over time. Inter-rater reliability between assessors was evaluated using the intraclass correlation coefficient (ICC) with 95% confidence intervals.

Independent samples t-tests were conducted to compare the mean nutritional content (Energy, Protein, Fat, Saturated fat, Carbohydrates, Sugar, Fibre) between formulas classified as IDDSI Level 0 and those classified as IDDSI Level 1 or higher at 45 minutes.

An exploratory linear regression analysis was conducted to investigate potential associations between macronutrient content and the time required to reach IDDSI Level 1. Given the study sample size (n=15), these analyses are interpreted as preliminary observations rather than predictive modelling. Additionally, repeated measures ANOVA were conducted to assess changes in flow test results across the five time points (0, 7, 15, 30, and 45 minutes). For all statistical tests, a p-value < 0.05 was considered statistically significant.

Results

A total of fifteen infant and child formulas, including both powder-based and ready-to-feed liquid products, were included in the analysis. At baseline, all formulas (100%) were classified as thin (IDDSI level 0). Peptamen junior (liquid) consistently over-thickened to Level 2. Alfamino (powder) demonstrated stability, maintaining Level 1 after 15 minutes (Figure 1).

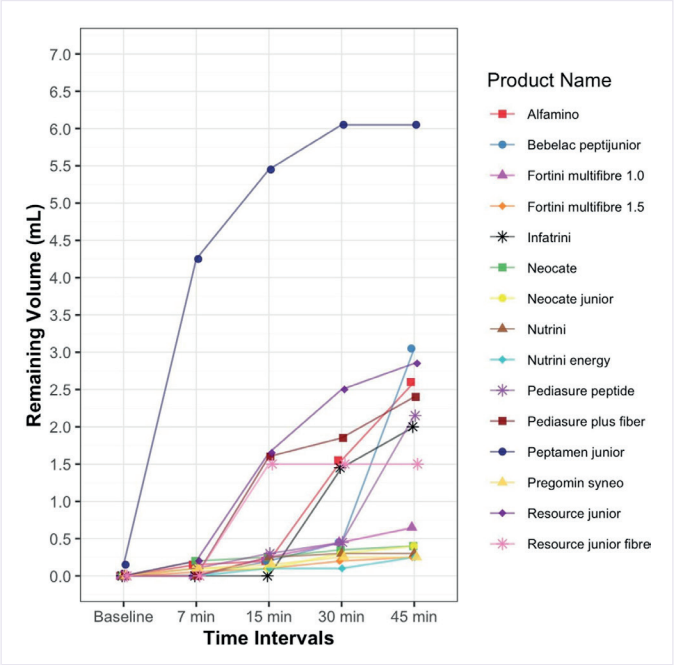

Figure 1. Remaining amount (mL) after the flow test for each product

Table 1 summarizes the thickening performance and macronutrient composition of the 15 commercial formulas categorized as hypoallergenic, oral, and enteral. Among oral formulas, a greater proportion successfully thickened (e.g., Pediasure and Resource Junior variants). Although, Peptamen Junior, a high-protein formula, thickened beyond the target to Level 2. Notably, none of the enteral formulas achieved the desired consistency, highlighting variability across categories despite identical thickening protocol. On average, formulas contained 2.9 g of protein, 13.4 g of carbohydrates, and 5.1 g of fat per 100 mL (Table 1).

Thickening efficacy was assessed at 45 minutes, with 53% of all formulas achieving at least IDDSI Level 1 (Slightly Thick) (Figure 2).

A significant main effect of time was observed in the repeated measures ANOVA, $F(1.81, 23.53) = 12.89$, $p < 0.001$, indicating that thickness (measured by flow remaining) changed significantly over the 45-minute period. However, when comparing powder and liquid formulas at each time point, no statistically significant differences were found ($p > 0.05$). Descriptive trends in flow remaining by formula type are presented in Table 2.

Table 1. Thickening outcomes, and macronutrient composition of infant and child formulas by product type

Product Type	n (%)	Baseline (no thickener)	Ability to thicken (45 min after thickener added)
Hypoallergenic	5 (33.3%)		
Alfamino		Thin	Level 1
Bebelac peptijunior		Thin	Level 1
Neocate		Thin	Level 0
Neocate junior		Thin	Level 0
Pregomin syneo		Thin	Level 0
Oral	8 (53.4%)		
Fortini multifibre 1.0		Thin	Level 0
Fortini multifibre 1.5		Thin	Level 0
Infatrini		Thin	Level 1
Pediasure peptide		Thin	Level 1
Pediasure plus fiber		Thin	Level 1
Peptamen junior		Thin	Level 2
Resource junior		Thin	Level 1
Resource junior fibre		Thin	Level 1
Enteral	2 (13.3%)		
Nutrini		Thin	Level 0
Nutrini energy		Thin	Level 0
Macronutrients		**Mean**	**SD**
Energy (kcal/100mL)	15	126.1	55.6
Protein total (g/100 mL)	15	2.9	0.9
Carbohydrate total (g/100 mL)	15	13.4	5.0
Sugar (g/100 mL)	14	2.3	2.7
Fibre (g/100 mL)	10	0.8	0.6

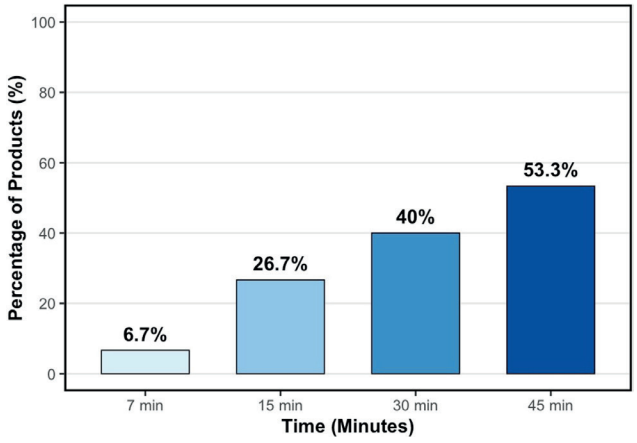

Figure 2. Achieving rates at least Level 1 based on the IDDSI flow test

Across all time points, the difference between the two researchers' measurements did not exceed 1 mL for any sample, thus a third trial was not required. Inter-rater reliability was consistently excellent, with intraclass correlation coefficients (ICC) ranging from 0.89 at baseline to 0.99 at all post-thickening time points. The 95% confidence intervals ranged from 0.67 to 1.00, confirming a high degree of measurement agreement between researchers using the IDDSI syringe method.

Regarding the nutritional content of formulas grouped by IDDSI level at 45 minutes, no statistically significant differences were found for Energy, Protein, Fat, Carbohydrates, Sugar, and Fibre between formulas achieving Level 0 and those achieving Level 1 or higher ($p > 0.05$ for all, Table 3).

A linear regression model was conducted to evaluate whether formula type and macronutrient content could predict the time required to reach IDDSI Level 1 consistency. None of the predictors showed a statistically significant association with time-to-thickening ($p > 0.05$). The model explained 34% of the variance ($R^2 = 0.343$) (Table 4).

Discussion

This study evaluated the effectiveness of a starch-based thickener in achieving IDDSI Level 1 consistency in infant and child formulas commonly used in Türkiye. Despite following the manufacturer's preparation and rest protocols, only 53% of formulas achieved the desired consistency after 45 minutes. Liquid formulas demonstrated a higher success rate than powder-based formulas (60% vs. 40%), but this difference was not statistically significant.

Compared to other literature, our results show lower thickening success rates. For example, Frakking et al.[19] found that approximately 75% of Australian formulas reached IDDSI Level 1 using similar protocols. Differences in thickener type, formula composition, and testing time likely explain this variability. Our results are more in line with Ng et al.[21], who reported inconsistent thickening performance under variable storage conditions.

The type of thickener is a known factor affecting the thickening process.[22] One study using starch-based thickeners observed that the viscosity increased by 1.5 times in the first 10 minutes.[23] Similarly, another study using a xanthan gum-based thickener reported that it took 45 minutes to reach the desired level of consistency in an infant formula.[24] In our study, which used a thickener containing carob gum, the percentage of formulas reaching IDDSI Level 1 (Slightly Thick) increased over time: 27% at 15 minutes, 40% at 30 minutes, and 53% at 45 minutes. These findings indicate that the response of formulations to thickeners may vary

Table 2. Mean remaining volume (mL) over time by formula type

Time Point	All Formulas (Mean ± SD)	Powder (Mean ± SD)	Liquid (Mean ± SD)
7 minutes	0.34 ± 1.1	0.11 ± 0.07	0.46 ± 1.33
15 minutes	0.81 ± 1.4	0.18 ± 0.05	1.12 ± 1.66
30 minutes	1.2 ± 1.5	0.58 ± 0.54	1.48 ± 1.79
45 minutes	1.7 ± 1.6	1.34 ± 1.36	1.84 ± 1.76

Time: $F(1.81, 23.53) = 12.89$, $p < 0.001$
Formula Type: $F(1, 13) = 0.834$, $p = 0.378$
Time x Formula Type Interaction: $F(1.81, 23.53) = 0.895$, $p = 0.413$
SD: Standard Deviation, Greenhouse-Geisser correction applied for within-subject's effects due to violation of sphericity.

Table 3. Assessment of nutritional content of formulas by IDDSI level (45-minute flow test results)

	IDDSI Level	n	Mean	SD	p
Energy	Level 0	7	136.6	72.6	0.517
	Level 1 +	8	117.0	38.4	
Protein	Level 0	7	2.70	0.79	0.557
	Level 1 +	8	2.98	0.98	
Fat	Level 0	7	4.83	140	0.563
	Level 1 +	8	5.28	1.57	
Saturated fat	Level 0	7	0.80	0.84	0.083
	Level 1 +	8	1.82	1.20	
Carbohydrates	Level 0	7	12.54	4.70	0.576
	Level 1 +	8	14.07	5.50	
Sugar	Level 0	7	1.31	2.72	0.196
	Level 1 +	7	3.22	2.43	
Fibre	Level 0	5	0.72	0.75	0.916
	Level 1 +	5	0.77	0.56	

t-test, SD: Standard Deviation

Table 4. Linear regression predicting time to IDDSI level 1

Predictor	B (95% CI)	p
Intercept	68.67 (0.18 to 118.74)	0.02
Formula Type[1]	-4.28 (-31.14 to 22.57)	0.73
Protein	-0.33 (-21.24 to 20.59)	0.97
Fat	-4.55 (-20.99 to 11.90)	0.55
Carbohydrates	-0.66 (-4.49 to 3.18)	0.71

[1] Formula Type coded as 0 = Liquid, 1 = Powder. All macronutrient coefficients reflect change per gram per 100 mL of formula. The dependent variable is the minimum time (in minutes) at which each formula first reached IDDSI Level 1 or higher (i.e., Level 1, 2, or 3). Model R^2 = 0.343, Adjusted R^2 = 0.080, p= 0.332.

significantly across different countries, and that resting time is a crucial factor in achieving the targeted IDDSI consistency level. Relying on standard practices without considering variables like formula type, temperature, storage conditions, and waiting time may be insufficient to provide safe and effective nutrition. Therefore, on-site viscosity assessments for each formulation are of great importance for the clinical decision-making process.

Frakking et al.[19] reported that formulas with higher protein content were more likely to thicken, whereas formulas with higher sugar content were less likely to thicken. In our study, although we observed a trend of decreased thickening time as the amount of fat increased, this relationship was not statistically significant. In contrast to Frakking et al.'s findings, the macronutrient content in our study did not show a statistically significant relationship with the probability of thickening success. These findings suggest that under the tested preparation conditions, macronutrient composition alone may not be a reliable predictor of thickening outcomes for the evaluated starch-based thickener.

A study in Australia found that powdered formulas generally reached low to medium consistencies after 45 minutes, while liquid formulas showed greater variability.[25] This aligns with the findings by Gosa and Choquett[26], who also reported broad outcome variability. Our findings partially contradict Frakking et al.'s[19]conclusion that powdered formulas consistently perform better than

liquids. These discrepancies may reflect differences in timing, thickener type (starch vs. gum), or environmental variables. These factors highlight the importance of product-specific evaluation and the need for broader standardization studies.

From a clinical standpoint, the inconsistency of thickening outcomes highlights the importance of on-site IDDSI flow testing before administration, particularly in settings where thickeners are used empirically. Additionally, the absence of manufacturer-specific guidance on rest time and the amount of thickener limits their effective clinical use. Even while following the commercial thickener's instructions, only 53% of the formulas reached at least Level 1 at 45 minutes.

Limitations

This was a laboratory (in-vitro) study; IDDSI flow test results reflect rheological properties and should not be used as a direct proxy for clinical swallowing safety or aspiration risk. Generalisability is limited by the modest product sample (n=15) and the exploratory nature of the statistical models Evaluation of a single commercially available thickener, and testing under a single controlled condition. The tested thickener was selected because it is the only product in Türkiye approved for infants and children under three years of age; this strengthens contextual relevance but may limit applicability to other thickener types and brands. Larger, multi-centre studies comparing multiple thickener formulations and testing across varied environmental conditions are warranted.

Conclusion

This study demonstrates that the thickening outcomes of infant and child formulas varied between products but were not reliably predicted by formula type or macronutrient content. While the manufacturer's instructions (1.7 g/100 mL with a 7-minute rest) were followed, approximately half of the products did not achieve IDDSI Level 1 consistency in more than half of the products tested. Importantly, the commercially available starch-based thickener evaluated in this study lacks clear manufacturer instructions regarding the appropriate resting time, amount of thickener, or expected IDDSI outcomes for different formula types. This absence of guidance limits the safe and effective use of thickeners in clinical practice. Our findings emphasize the urgent need for standardized, evidence-based thickening protocols tailored to individual formula characteristics to support safer feeding practices in paediatric dysphagia management.

Practical applications

This study provides the first data from Türkiye evaluating the thickening behaviour of paediatric formulas using a standardized IDDSI framework. The findings can assist clinicians, dietitians, and hospital nutrition services in selecting appropriate formulas for children with dysphagia, ensuring safer and more effective feeding strategies. Additionally, manufacturers of paediatric nutrition products may use this information to improve labelling, formulation, and instructions for use of thickeners to meet clinical texture standards.

Ethical approval

This study does not involve any human or animal testing.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: TK, SU, ÇB; data collection: TK, SU; analysis and interpretation of results: TK, ÇB; draft manuscript preparation: TK, ÇB. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Malnutrition screening tools as predictors of depression in community-dwelling older adults: A comparative analysis of MNA-SF, SCREEN II and GLIM

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ABSTRACT

Background: Malnutrition and depression are common and interrelated conditions among community-dwelling older adults, leading to adverse health outcomes. This study aimed to compare the predictive value of Mini Nutritional Assessment–Short Form (MNA-SF), the Seniors in the Community: Risk Evaluation for Eating and Nutrition, version II (SCREEN II), and the Global Leadership Initiative on Malnutrition (GLIM) in assessing depression risk among community-dwelling older adults.

Methods: This cross sectional study was performed in community dwelling older adults. Nutritional status was assessed using the MNA-SF, SCREEN II, and GLIM criteria, and depression risk was evaluated by the Geriatric Depression Scale (GDS).

Results: This study included 251 participants. The median age of participants was 62 years (IQR: 61–70), and 53.4% were female. After adjusting for age, gender, marital status, and employment status, all three nutritional tools were significantly associated with depression risk (MNA-SF: OR = 0.621 [95% CI: 0.523–0.736], p < 0.001; SCREEN II: OR = 0.920 [95% CI: 0.885–0.957], p < 0.001; GLIM: OR = 0.298 [95% CI: 0.141–0.629], p = 0.001). ROC analysis indicated that MNA-SF had the highest predictive accuracy (AUC: 0.765, p < 0.001), followed by SCREEN II (AUC: 0.700, p<0.001) and GLIM (AUC: 0.590, p = 0.014). Delong test showed no significant difference between MNA-SF and SCREEN II (p = 0.18), whereas GLIM had lower accuracy (MNA-SF vs. GLIM: p < 0.001; SCREEN II vs. GLIM: p=0.013).

Conclusion: MNA-SF, SCREEN II, and GLIM were all associated with depression risk, with MNA-SF showing the strongest predictive ability. Comprehensive nutritional screening may support early identification and intervention for depression among community-dwelling older adults.

Keywords: depression, malnutrition, malnutrition screening tools, older adult

Introduction

Malnutrition and depression are prevalent and interrelated health concerns among older adults, and both are associated with adverse outcomes such as reduced functional capacity, increased morbidity, lower quality of life, and higher healthcare utilization.[1-3] Depression is linked to decreased appetite, diminished motivation to prepare or consume meals, and weight loss[4-6], while malnutrition can exacerbate depressive symptoms through metabolic, inflammatory, and neurocognitive pathways.[1,7] Understanding this bidirectional relationship

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is essential for early identification and intervention in aging populations.

Accurate nutritional assessment is central to identifying older adults at risk for adverse health outcomes. Several validated tools are commonly used in clinical and community settings. The Mini Nutritional Assessment–Short Form (MNA-SF) is brief and has strong predictive validity, focusing on undernutrition and weight loss-related risk.[8,9] The Seniors in the Community: Risk Evaluation for Eating and Nutrition, version II (SCREEN II) provides a broader evaluation, including unintentional weight loss and gain, dietary behaviors, psychosocial factors such as mood and motivation, and social participation, making it particularly suitable for community-dwelling older adults.[10,11] In contrast, the Global Leadership Initiative on Malnutrition (GLIM) criteria offer a concise, diagnosis-oriented approach that emphasizes objective phenotypic and etiologic indicators, such as weight loss and reduced muscle mass, providing a definitive diagnostic framework rather than a risk screening.[12]

Despite the widespread use of these tools, few studies have compared their efficacy in identifying older adults at risk of depression. Understanding the differences in assessment focus—MNA-SF targeting undernutrition, SCREEN II evaluating dietary and psychosocial factors, and GLIM emphasizing diagnostic phenotypic indicators—may inform optimal tool selection. This study aimed to compare the predictive performance of MNA-SF, SCREEN II, and GLIM for identifying depression risk in community-dwelling older adults.

Methods

Study design, population

This study employed a cross-sectional design and was conducted among community-dwelling older adults.

Main Points

- Poor nutritional status is associated with a higher risk of depression in older adults.
- MNA-SF, SCREEN II, and GLIM remained significantly associated with depression risk even after adjusting for sociodemographic factors.
- MNA-SF showed the strongest predictive value for depression risk, followed by SCREEN II, while GLIM demonstrated the lowest performance.

Participants were recruited using a convenience sampling approach by a clinical dietitian experienced in geriatric care between July and September 2025. Eligible participants were individuals aged 60 years and older living in the community. Exclusion criteria included a diagnosis of advanced malignancy, Alzheimer's disease, depression, or receipt of enteral or parenteral nutritional support. A minimum sample size of 104 was calculated using G*Power software, based on an alpha of 0.05, power of 0.80, and a medium effect size (Cohen's d = 0.5). All participants provided written informed consent. This study protocol was approved by ***** University Ethics Committee (Number: 298, Date: 26.06.2025).

Data collection

Data on age, gender, marital status, income, smoking and alcohol use, and chronic diseases were recorded via self-report. Body weight was measured using a calibrated digital scale (accuracy: 0.1 kg) with participants fasting and wearing light clothing. Height was measured using a wall-mounted stadiometer (accuracy: 0.1 cm), with participants standing barefoot in the Frankfurt horizontal plane. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Nutritional assessment

Nutritional status of the study participants was assessed using the MNA-SF, SCREEN II, and the GLIM criteria. When participants were unable to provide accurate information, caregivers were consulted for clarification.

The MNA-SF evaluates six domains: recent decline in food intake, unintentional weight loss, mobility, the presence of psychological stress or acute illness, neuropsychological problems, and body mass index or calf circumference. MNA-SF scores were interpreted as follows: 0–7 indicated malnutrition, 8–11 indicated risk of malnutrition, and 12–14 indicated normal nutritional status.[8]

SCREEN II was used to assess dietary habits, recent weight changes, meal preparation and grocery shopping abilities, social eating patterns, physical limitations such as chewing or swallowing difficulties, and changes in daily routines. SCREEN II scores were classified as 0–49 for high malnutrition risk, 50–54 for malnutrition risk, and ≥55 for normal nutritional status.[10]

The GLIM framework was applied through a standardized two-step diagnostic approach. In the first step,

malnutrition risk was screened using the MNA-SF. Participants identified as at risk were then evaluated using the GLIM diagnostic criteria. A diagnosis required the presence of at least one phenotypic and one etiologic criterion. Phenotypic criteria included unintentional weight loss, low body mass index, and reduced muscle mass. Etiologic criteria included reduced food intake or assimilation and the presence of acute or chronic inflammation.[12]

Depression assessment

Depressive symptoms were assessed using the Geriatric Depression Scale (GDS), a widely used self-report screening tool designed to identify depressive symptoms in older adults. The scale consists of 30 yes/no items that evaluate mood, cognitive, and somatic symptoms related to depression. Total scores range from 0 to 30, with higher scores indicating greater depressive symptomatology. Scores between 0 and 9 are considered normal, 10 to 19 indicate mild depression, and 20 to 30 indicate severe depression [13]. In this study, a GDS score of ≥10 was used to indicate the presence of depression.

Statistical analysis

All statistical analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are presented as medians with interquartile ranges (IQRs), and categorical variables as frequencies and percentages. Group comparisons were conducted using the Mann–Whitney U test for continuous variables and the Chi-square test for categorical variables. Multiple logistic regression models were applied to examine the associations between malnutrition screening tools (MNA-SF, SCREEN II, and GLIM) and depression, adjusting for potential confounders including age, gender, marital status, and employment status. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test and Nagelkerke R^2. Multicollinearity was checked using variance inflation factors (VIF < 5 was considered acceptable). Receiver operating characteristic (ROC) curve analyses were performed to evaluate the discriminative ability of each tool for identifying depression (GDS ≥ 10). The area under the ROC curve (AUC) and optimal cut-off points (Youden index) were reported, along with 95% confidence intervals (CI) for sensitivity and specificity. Pairwise comparisons of AUCs were performed using DeLong's test to assess differences in predictive accuracy. A two-tailed p-value < 0.05 was considered statistically significant.

Results

A total of 251 participants were included in the study. The median age of the study population was 62 years (IQR: 61–70), and 53.4% were female. Of the total, 107 participants were identified as being at risk of depression. Participants with depression risk were significantly older than those without depression (median age: 65 [IQR: 60–71] vs. 62 [IQR: 60–66], p = 0.003). The proportion of females was higher in the depression group compared with the non-depression group (65.5% vs. 44.4%, p = 0.001).

Regarding marital status, individuals with depression were less likely to be married (72.0% vs. 88.2%) and more likely to be divorced or widowed (27.1% vs. 9.7%), differences which were statistically significant (p = 0.001). Unemployment was more prevalent among participants with depression compared with those without (63.6% vs. 47.2%, p = 0.012) In terms of comorbidities, hypertension was significantly more common in the depression group than in the non-depression group (43.0% vs. 26.4%, p = 0.006) (Table 1).

According to MNA-SF, 34.7% of participants were at risk of malnutrition, and 4.8% were classified as malnourished. Using SCREEN II, 18.3% of participants were at nutritional risk, and 13.1% were at high nutritional risk. Based on GLIM criteria, 16.7% of the study sample were malnourished.

As shown in Figure 1, the prevalence of depression increased progressively with worsening nutritional status across all tools. According to MNA-SF, 23.7% of well-nourished participants had depression, compared with 69.0% of those at risk of malnutrition and 91.7% of malnourished participants. Similarly, using SCREEN II, depression was present in 33.1% of well-nourished participants, 54.3% of those at nutritional risk, and 75.8% of participants classified as high nutritional risk. According to GLIM, 37.3% of well-nourished participants had depression, whereas 73.0% of malnourished participants exhibited depression. Individuals classified as malnourished by all three assessment tools had significantly higher rates of depression (p < 0.001 for all tests).

Logistic regression analysis exhibited that MNA-SF, SCREEN II, and GLIM classifications were all significantly associated with depression risk (MNA-SF: OR = 0.585, 95% CI: 0.497–0.689, p < 0.001; SCREEN II: OR = 0.904, 95% CI: 0.870–0.939, p < 0.001; GLIM: OR = 0.267, 95% CI: 0.131–0.544, p < 0.001). After adjustment for age,

gender, marital status, and employment status, poorer nutritional status remained significantly associated with higher odds of depression (MNA-SF: OR = 0.621, 95% CI: 0.523–0.736, p < 0.001; SCREEN II: OR = 0.920, 95% CI: 0.885–0.957, p < 0.001; GLIM: OR = 0.298, 95% CI: 0.141–0.629, p = 0.001) (Table 2).

Table 1. Sociodemographic and clinical characteristics of the study participants

Variable	Overall (n=251)	Depression (+) (n=107)	Depression (-) (n=144)	p
Age, years	62 (61-70)	65 (60-71)	62 (60-66)	**0.003**
Gender, n (%)				
Male	117 (46.6)	37 (34.5)	80 (55.6)	**0.001**
Female	134 (53.4)	70 (65.5)	64 (44.4)	
BMI, kg/m²	27.8 (24.8-32.0)	27.0 (24.7-32.7)	28.2 (25.0-31.6)	0.591
Marriage status, n (%)				
Married	204 (81.3)	77 (72.0)	127 (88.2)	**0.001**
Single	4 (1.6)	1 (0.9)	3 (2.1)	
Divorced/Widowed	43 (17.1)	29 (27.1)	14 (9.7)	
Employment Status, n(%)				
Employed	56 (22.3)	15 (14.0)	41 (28.5)	**0.012**
Unemployed	136 (54.2)	68 (63.6)	68 (47.2)	
Retired	59 (23.5)	24 (22.4)	35 (24.3)	
Living arrangement				
Living alone	32 (12.7)	18 (16.8)	14 (9.7)	0.161
Living with partner	59 (23.5)	27 (25.2)	32 (22.2)	
Living with partner and children	160 (63.7)	62 (57.9)	98 (68.1)	
Income status, n (%)				
Income > Expenses	44 (17.5)	19 (17.8)	25 (17.4)	0.060
Income = Expenses	143 (57.0)	53 (49.5)	90 (62.5)	
Income < Expenses	64 (25.5)	35 (32.7)	29 (20.1)	
Current smokers, n (%)	60 (23.9)	25 (23.4)	35 (24.3)	0.863
Alcohol users, n (%)	13 (5.2)	6 (5.6)	7 (4.9)	0.778
Comorbidities, n (%)				
Hypertension	84 (33.5)	46 (43.0)	38 (26.4)	**0.006**
Diabetes mellitus	45 (17.9)	23 (21.5)	22 (15.3)	0.204
Cardiovascular disease	41 (16.3)	25 (23.4)	16 (11.1)	0.864
Pulmonary disease	20 (8.0)	11 (10.3)	9 (6.3)	0.668
Malignancy	8 (3.2)	2 (1.9)	6 (4.2)	0.305
Chronic kidney disease	7 (2.8)	4 (3.7)	3 (2.1)	0.431
Dyslipidemia	6 (2.4)	2 (1.9)	4 (2.8)	0.641
Hypothyroidism	4 (1.6)	4 (3.7)	-	0.082

BMI: Body mass index.

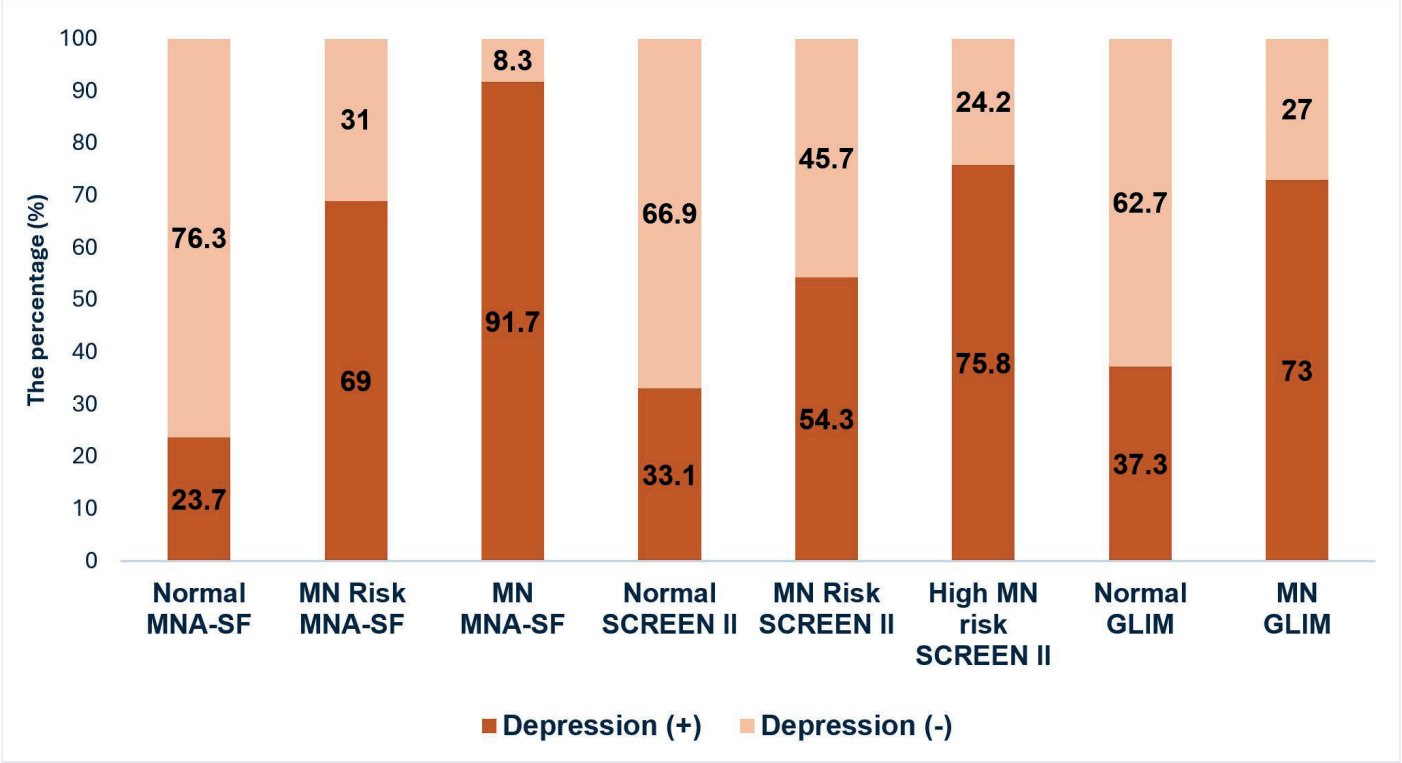

Figure 1. Proportion of depression risk according to MNA-SF, SCREEN II, and GLIM classifications

ROC analyses were performed to evaluate the predictive performance of the three tools. MNA-SF had the highest predictive accuracy (AUC = 0.765, 95% CI: 0.704–0.826, p < 0.001) at a cut-off point of 11.5, yielding a sensitivity of 80.6% and specificity of 66.4%. SCREEN II showed moderate predictive performance (AUC = 0.700, 95% CI: 0.635–0.766, p < 0.001) at a cut-off of 42.5, with sensitivity of 63.9% and specificity of 66.4%. GLIM had the lowest predictive ability (AUC = 0.590, 95% CI: 0.518–0.663, p = 0.014) (Figure 2).

Pairwise DeLong comparisons indicated that MNA-SF and SCREEN II had significantly higher AUCs than GLIM (MNA-SF vs. GLIM: p < 0.001; SCREEN II vs. GLIM: p = 0.013), whereas the difference between MNA-SF and SCREEN II was not statistically significant (p = 0.18), suggesting comparable predictive performance for these two screening tools.

Discussion

To our knowledge, this study is the first to compare the predictive value of MNA-SF, SCREEN II, and GLIM for depression risk among community-dwelling older adults. All three tools were significantly associated with poorer nutritional status and higher depression risk, even after adjusting for sociodemographic factors. Furthermore, MNA-SF and SCREEN II showed similar predictive

Table 2. Logistic regression analysis of MNA-SF, SCREEN II, and GLIM for Depression Risk

	CRUDE		ADJUSTED	
	OR (95%CI)	p-value	OR (95%CI)	p-value
MNA-SF	0.585 (0.497-0.689)	<0.001	0.621 (0.523-0.736)	<0.001
SCREEN II	0.904 (0.870-0.939)	<0.001	0.920 (0.885-0.957)	<0.001
GLIM	0.267 (0.131-0.544)	<0.001	0.298 (0.141-0.629)	0.001

Adjusted for age, gender, marriage status, and employment status.

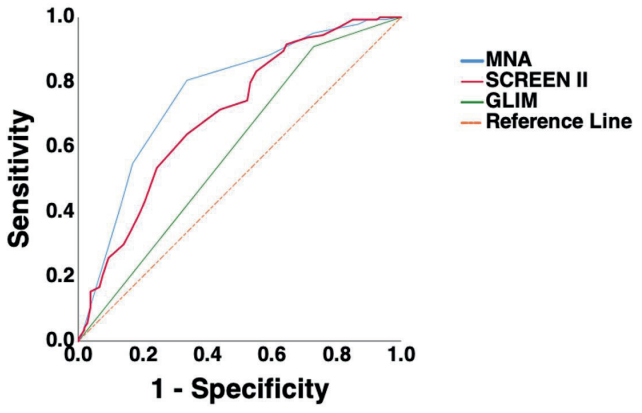

Figure 2. ROC analysis of MNA-SF, SCREEN II, and GLIM for predicting depression risk

performance, whereas GLIM demonstrated significantly lower discriminative ability.

Our findings are consistent with previous studies demonstrating a strong association between malnutrition and depression in older adults. A study of 262 older adults reported that individuals with depressive symptoms, as assessed by GDS, were approximately five times more likely to be at risk of malnutrition or malnourished according to MNA-SF (OR=5.82, 95%CI=2.27–14.89) than those without depression.[14] Similarly, Pehlivan et al., in a study of 695 older adults, found that a 1-unit increase in MNA score was associated with a 1.201-unit decrease in GDS score.[15] Another study also reported that the presence of malnutrition, as reflected by MNA, was linked to an increased risk of depression among older adults.[16] In addition, research in 189 geriatric rehabilitation patients demonstrated that the severity of malnutrition assessed by GLIM criteria was associated with higher odds of depressive mood at discharge (moderate malnutrition: OR=3.84, p=0.005; severe malnutrition: OR=5.11, p=0.003).[17] While prior studies have examined the association between MNA-SF or GLIM-defined malnutrition and depression, to our knowledge, no previous studies have specifically investigated the relationship between SCREEN II scores and depressive symptoms in older adults.

ROC analyses in our study revealed differences in the predictive performance of the three malnutrition assessment tools. MNA-SF demonstrated the highest accuracy (AUC = 0.765), with a cut-off of 11.5 yielding a sensitivity of 80.6% and specificity of 66.4%, indicating its strong ability to identify individuals at risk of depression. SCREEN II showed moderate predictive performance (AUC = 0.700) at a cut-off of 42.5, with balanced sensitivity and specificity (63.9% and 66.4%, respectively). The lower predictive ability of SCREEN II compared to MNA-SF may be explained by the fact that SCREEN II evaluates both unintentional weight loss and weight gain, whereas depression is more strongly associated with weight loss and appetite reduction. In contrast, GLIM displayed the lowest discriminative ability (AUC = 0.590), suggesting that while GLIM-defined malnutrition is associated with depression at the group level, it is less effective at predicting depression in individuals.

Although GLIM was strongly associated with depression in logistic regression, its ROC-based predictive performance was limited. This discrepancy may be attributed to the binary nature of GLIM classification, which captures only the presence or absence of malnutrition, whereas MNA-SF and SCREEN II provide continuous gradations of nutritional risk. The non-significant difference between MNA-SF and SCREEN II suggests that both tools perform comparably in predicting depression risk, although MNA-SF had a slightly higher AUC. These results emphasize the complementary value of combining screening and diagnostic nutritional assessments when evaluating the relationship between nutrition and mental health in older adults.

This study has several limitations that should be acknowledged. First, its cross-sectional design precludes any inference of causality between malnutrition and depression; the observed associations do not establish temporal relationships. Second, although the Geriatric Depression Scale (GDS) is a validated screening tool, it relies on self-report, which may be influenced by recall bias or social desirability. Thirdly, the study did not assess longitudinal changes in nutritional status or depressive symptoms, limiting the ability to evaluate the dynamic interplay between malnutrition and depression over time. Fourth, due to the convenience sampling method, findings cannot be generalized to all community-dwelling older adults.

In conclusion, MNA-SF, SCREEN II, and GLIM were all significantly associated with an increased risk of depression among community-dwelling older adults. MNA-SF demonstrated the highest predictive accuracy, supporting its utility for early identification of individuals at risk. Routine nutritional assessment may help facilitate timely and targeted interventions to mitigate depression risk in older populations.

Ethical approval

This study protocol was approved by Agrı Ibrahim Cecen University Ethics Committee (Number: 298, Date: 26.06.2025).

Author contribution

The author declare contribution to the paper as follows: Study conception and design: NTÖ; data collection: NTÖ; analysis and interpretation of results: NTÖ; draft manuscript preparation: NTÖ. The author reviewed the results and approved the final version of the article.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Neuro-nutraceuticals in medicine: Rationale and narrative insights

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ABSTRACT

Neuronutrient supplements are widely marketed as adjunctive treatments for neurological disorders, but their scientific validity is limited. This review highlights the disconnect between consumer-driven use and the lack of compelling clinical evidence. While a mechanistic possibility exists, the proliferation of these products risks undermining evidence-based neurology without standardized assessment frameworks.

Keywords: neuro-nutraceutical, neuronutrient, oxidative stress, dementia, marketing strategy, evidence-based medicine

Introduction

Neuro-nutraceuticals are increasingly marketed for neurological health, yet their scientific validity remains limited. Despite plausible biological mechanisms, clinical evidence is fragmented, and consumer demand often outpaces regulatory and methodological rigor.[1] This review addresses the gap between popularity and evidence, advocating for structured assessment to protect the integrity of evidence-based neurology.

Terminology

The term "Functional Food" refers to nutritional products specifically formulated to achieve targeted health outcomes, such as disease treatment, prevention, or overall health improvement, by introducing new ingredients or modifying the structure and quantity of existing ones. These products, also known as "Health Functional Foods (HFF)", are available in forms such as tablets, capsules, powders, granules, and syrups. They are known by different names worldwide: "Dietary Supplements" in the U.S., "FOSHU" (Food for Specific Health Use) in Japan, and "Food Supplements" in Europe. More than 50,000 HFF products claim neurological benefits. In 1989, Dr. Stephen L. DeFelice coined the term "Nutraceutical", merging "nutrition" and "pharmaceutical," to describe a subset of HFFs.[2] Today, this category includes around 60 subgroups, with approximately 1,000 compounds recognized for their medical importance. In this article, we refer to nutraceuticals developed specifically for the treatment of neurological diseases as neuro-nutraceuticals.

Knowledge Generation in Clinical Nutrition Science

Evidence that a nutritional substance can positively impact a disease generally stems from five hierarchical sources: "Concept formation", "Research into the relationship between the nutraceutical and the disease prevalence in the normal populations", "Studies of the

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nutraceutical's effects in the diseased population", "Uncontrolled efficacy studies", and "randomized controlled trials (RCT)" (Figure 1).[3,4]

Emergence of hypotheses/opinions regarding the effects of a nutraceutical: The notion that a nutraceutical may have an effect on a disease typically stems from animal or in vitro experimental studies, case studies, case series, or descriptive epidemiological surveys. This means that a causal mechanism by which the nutraceutical may have an effect on the disease must be hypothesized. This opinion/hypothesis can be expressed in scientific articles, such as expert opinions, editorials, or opinion articles on the subject.

Epidemiological studies investigating the change in disease frequency with nutraceutical consumption in the normal population: These analytical studies are observational in nature and may be cross-sectional, case-control, or cohort studies. They may be retrospective or prospective in design. Some are not hypothesis-driven and are based on new findings identified in the study. Various methods have been used to investigate the relationship between dietary intake and disease prevalence. The first involves determining the amount of a particular food present in the diet and analyzing its correlation with the frequency or prevalence of a disease. This can help identify whether higher or lower consumption of a food is associated with greater or lesser risk. The second method includes measuring specific biomarkers or molecules found in the food, sometimes after its dietary amount is determined, and evaluating their levels in biological samples such as serum, cerebrospinal fluid (CSF), or tissues. The relationship between these measured levels and disease frequency is then examined to understand potential physiological mechanisms. The third approach is to evaluate the effect of supplementation. Researchers investigate whether individuals who consume the food intentionally as a supplement show differences in disease prevalence compared to those who do not. Finally, the fourth method involves manipulating the dietary intake of the food and observing its effects on disease epidemiology. This may include increasing, decreasing, or eliminating the food from the diet and studying the subsequent changes in disease incidence.

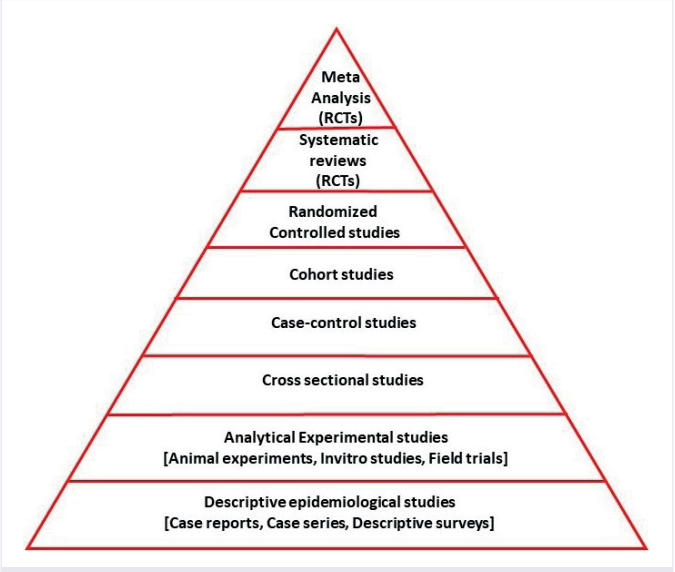

Figure 1. Medical evidence hierarchy

For example, a researcher exploring chocolate's effect on dementia may first categorize individuals by their chocolate intake (e.g., none, low, high consumption). Then, using cohort, cross-sectional, case-control with prospective or retrospective designs, they could examine the correlation between chocolate consumption and dementia incidence.[5] They might also measure levels of a compound like "Flavan-3-ol" (found in cocoa) in the blood and analyze its association with dementia rates.[6] Furthermore, investigating dementia frequency among individuals who consume chocolate as a targeted supplement could offer additional insights.[7] Finally, observing changes in dementia incidence following alterations in chocolate consumption, such as beginning, stopping, or adjusting the amount, can help reveal causal relationships.[8]

Main Points

- A wide variety of neuro-nutraceuticals are available on the global market.
- Nutraceuticals and pharmaceuticals are subject to the same ethical and scientific principles without exception.
- The claimed effects of neuro-nutraceuticals on neurological diseases are often based on low-quality evidence.
- Clinicians need to be familiar with these substances so that they can recognize the potential harms that may occur if their patients consume them on their own.
- It is scientifically rational to recommend avoiding any supplement unless a symptomatic deficiency is proven.

Epidemiological studies investigating the relationship between disease course and characteristics and nutraceutical consumption:

These are prospective or retrospective studies, either cross-sectional, case-control, or cohort, involving individuals with the disease. In other words, they examine the effects of increasing or decreasing dietary intake, adjusting the amount, or adding supplements of a given nutrient on the severity and course of the disease. In this context, studies are conducted on individuals with the disease. For example, studies investigating the effects of increasing or decreasing daily chocolate consumption or consuming chocolate-containing supplements on the course of Alzheimer's disease fall into this category.

Uncontrolled efficacy studies: Beyond the previous two categories, such as cohort, case-control, or cross-sectional studies, observational studies are non-randomized studies that test the effectiveness of a nutraceutical without a suitable control group. These studies examine the clinical efficacy of a nutraceutical consumed in a proof-of-concept manner and its effects on various surrogate markers, such as biomarker levels and neuroimaging. They differ from the previous group in their prospective design and the inclusion of participants based on established criteria rather than field recruitment. For example, this group includes a prospective study in which a pre-defined number (sample size) of Alzheimer's disease patients are selected according to specific pre-defined study-specific criteria and are required to consume a specified amount of chocolate to assess its effects and side effects.

Randomized controlled trials: If above-mentioned studies determine the appropriate dosage and tolerability of side effects, the next step is RCTs. If RCTs meet quality standards and yield positive clinical results, the nutraceutical substance may be recommended for therapeutic use.

Differences Between Drug and Nutraceutical Supplement Studies and Approvals

Drugs and dietary supplements including any nutraceuticals differ significantly in their development, regulatory oversight, and scientific validation (Table 1).

Legal Definition and Regulatory Bodies: Drugs are designed to diagnose, treat, or prevent diseases. They undergo rigorous approval processes by agencies like the FDA (U.S.), EMA (Europe) and Ministry of Health (Türkiye). Nutraceuticals as supplements are intended not only to support general health but also to treat diseases. In the U.S., they are regulated as foods under "the Dietary Supplement Health and Education Act (DSHEA)", with limited pre-market oversight. The system is similar in Türkiye, where a similar approval is given by the Ministry of Agriculture for nutraceuticals to be marketed, that is, sold.

Approval and Marketing: Pharmaceutical agents are subject to rigorous regulatory assessments that necessitates comprehensive data regarding their safety, efficacy, and manufacturing consistency. This approval process, typically overseen by agencies, such as the FDA, EMA and Turkish Ministry of Health, requires longitudinal, phase-based clinical trials and strict adherence to quality control standards. Consequently, drug development timelines can span decades and incur substantial financial costs. In contrast, nutraceutical products are generally exempt from regulatory approval before launch. They are classified under food legislation, and while manufacturers are responsible for ensuring product safety, they are not mandated to provide evidence of therapeutic efficacy prior to market introduction. This discrepancy reflects the differing regulatory paradigms and evidence expectations assigned to compounds intended for consumer health, which differ from those designated for clinical intervention.[9]

Table 1. Research and Development Process

Phase	Drugs	Supplements
Preclinical Studies	Animal and cell-based safety and efficacy tests	Often minimal or absent
Clinical Trials	Phases I–IV with thousands of participants	Usually small-scale, Phase I–II only
Efficacy Evidence	Proven via RCTs	Often based on observational or anecdotal data
Safety Monitoring	Long-term pharmacovigilance systems	Limited tracking, often reliant on manufacturers

Scientific and Clinical Reliability: Drugs are backed by high-level evidence and undergo peer-reviewed trials. Supplements often rely on lower-tier evidence, and their claims may not be scientifically validated.

The Antioxidant Paradox: An example of the never-ending disparity and struggle between the generation of scientific knowledge and the promotional mechanisms of the food industry

The term " Antioxidant paradox" was coined by Professor Barry Halliwell.[10,11] This concept offers a compelling lens through which to examine the tension between scientific understanding of neuronutraceutical supplementation and the marketing practices of the food industry. One example Halliwell gave in his original article was that people with diets rich in fruits and vegetables have a decreased chance of developing cancer and an increase in the concentration of β-carotene in the blood. Supplements of β-carotene, however, do not have an anti-cancer effect, but rather the opposite in smokers.[10,12] The antioxidant paradox is the notion that numerous studies have shown that an antioxidant-rich diet positively impacts health, primarily by protecting against atherosclerosis-related vascular diseases such as cancer and stroke/coronary artery disease.[13,14] However, the findings of numerous randomized controlled trials consistently demonstrated that antioxidant supplementation does not confer measurable neurological or general health benefits. In fact, high-frequency supplementation has been associated with increased mortality in certain populations, particularly older adults. In brief, the antioxidant paradox refers to the fact that dietary antioxidants work, while supplemental antioxidants do not. Thus, the antioxidant paradox reinforces the idea that whole-food-based dietary interventions are preferable to isolated supplement strategies for both vascular and cognitive protection.

The discrepancy between the benefits of antioxidant-rich diets and the limited efficacy of antioxidant supplements reflects the intricate balance of human redox biology. A certain level of oxidative stress is thought to be necessary for life, and at low levels, it is thought to be paradoxically beneficial as an adaptive defense system. Improvement in general health through calorie restriction and increased regular physical activity has been linked to this mechanism. In these two strategies, ROS production increases in mitochondria. The effects of pro-oxidant molecules such as hydrogen peroxide, peroxynitrite, nitric oxide, superoxide, hydroxyl radical, singlet oxygen, hydroperoxyl radical, and lipid peroxide radical are balanced in the body by endogenous defense mechanisms such as superoxide dismutase, catalase, glutathione, uric acid, and thioreductase, as well as dietary intake of vitamins A, C, E, polyphenols and their related compounds, and minerals such as selenium.[15] The balance between oxidant and antioxidant activity is finely tuned in the body. If this capacity is not measured accurately and supplemented accordingly, a critical imbalance can develop. However, measuring the antioxidant/prooxidant balance is complex because serum levels are not always useful. Tissue levels are more important, but there are differences between tissues. This complexity does not apply to antioxidant-rich whole foods. While these foods provide a good replacement because they contain a variety of bioactive compounds, including antioxidants that act synergistically to support cellular health, isolated supplements often fail to mimic this complexity. Furthermore, antioxidants found in natural sources often exhibit superior bioavailability and enhance resilience by triggering endogenous defense mechanisms through adaptive hormetic signaling. Adaptive hormetic signaling refers to the biological process by which low-level exposure to a stressor, such as reactive oxygen species (ROS), calorie restriction, or phytochemicals, triggers beneficial cellular responses that enhance resilience, repair, and longevity. Conversely, high-dose supplementation can override these subtle regulatory processes, potentially causing reductive stress or interfering with critical ROS-mediated signaling pathways, leading to negative consequences. This highlights that nutrition is not simply about quantity but also a nuanced orchestration of biochemical interactions. It is an orchestra that supplementation alone can rarely manage with skill. The Antioxidant Paradox stems from the contribution of dosage and preparation, or collateral pathways, not the effect itself, but the diet's high fruit and vegetable content.[16] However, the number of products on the market claiming antioxidant effects without scientific support is quite high.

Neuro-nutraceutical use and Disease: Misconceptions that keep circulating

Under this heading, I list the facts and myths that I have identified based on the literature and my own experiences and observations, which have become long-standing and seem to be quite difficult to overcome.

Myth: Neuro-nutraceuticals have no effects or side effects. They are placebos.

The definition of neuro-nutraceutical is vague, but they are not placebos and certainly not harmless compounds. Excluding them from medical education and practice is a flawed policy. Public and commercial media are highly interested in the topic. Marketing touts miraculous effects while concealing side effects.[17] Claiming there is no scientific evidence is useless. This does not protect people or patients. Doctors need to be knowledgeable about nutrition and able to answer patients' questions. "I'm not interested!" is not an option.

Myth: Because neuro-nutraceuticals are food supplements, they are not subject to the same ethical and scientific rules as drugs.

The assumption that nutraceuticals, as dietary supplements, are exempt from the ethical and scientific standards applied to pharmaceuticals is unfounded. In practice, their approval and application must conform to the established hierarchy of evidence that informs drug therapies. This hierarchy encompasses four tiers: Class I evidence, the most robust, requires at least one RCT conducted in a representative population and assessed using masked, objective outcome measures. Class II evidence also involves RCTs, but has certain methodological limitations. Class III evidence is based on non-randomized controlled trials and supports only tentative recommendations. Class IV evidence, comprising expert opinions, consensus statements, and clinical guidelines, is deemed insufficient for contemporary therapeutic guidance.[3] Treating nutraceuticals outside this rigorous evaluation framework compromises both scientific integrity and clinical confidence.

Fact: The effects of neuro-nutraceuticals in neurological diseases are generally based on third- or fourth-tier evidence.

While the same hierarchy of evidence applies to clinical neuronutrition as to pharmaceuticals, large-scale randomized trials are still rare, particularly outside of intensive care settings. Guidance is typically derived from meta-analyses or systematic reviews of small-scale trials. However, such comprehensive syntheses are uncommon in the nutraceutical field, where recommendations primarily based on observational studies and expert consensus.[4] To justify neuro-nutraceutical use with the necessary rigor and confidence, we must adhere to the core principles of drug development and evaluation. At a minimum, evidence must demonstrate a plausible mechanism of action, supported by experimental data. Theoretical justification alone is insufficient. Furthermore, case-control and cohort studies suggesting that nutrient deficiency increases disease risk or that excess may reduce it should not, by themselves, be considered adequate to make treatment recommendations.

Fact: The impact of neuronutrient supplements on neurological diseases or global health is uncertain. Despite this scientific reality, market and product diversity are increasing exponentially.

The effectiveness of neuronutrient supplements in neurological diseases and global health remains scientifically ambiguous, despite an exponential growth in market and product diversity. Observational data alone are insufficient; at least prospective cohort studies must demonstrate that targeted supplementation or replacement of deficiencies leads to measurable biological increases in the absence of RCTs. For instance, although vitamin D deficiency is frequently observed in dementia patients, this association may reflect underlying lifestyle factors such as limited sun exposure, reduced mobility, and poor nutrition, rather than direct causation.[18,19] This observation therefore contradicts the systemic nature of the condition. Moreover, randomized controlled trials have not demonstrated significant plasma level improvements with vitamin D administration, raising questions about tissue-level uptake and actual therapeutic benefit. In light of these not convincing enough RCT results[20], current evidence does not support routine clinical recommendations for vitamin D supplementation (not equivalent to replacement) in patients with dementia.[21]

Fact: Nutraceuticals and pharmaceuticals are subject to the same ethical and scientific rules without exception.

The therapeutic impact of neuronutrient supplements in neurological diseases remains marginal. Much of the literature supporting these products originates from non-peer-reviewed sources, rendering it largely inaccessible to clinical practitioners. Because these compounds are classified as dietary supplements or medical foods, they escape the scrutiny of regulatory bodies. When clinical evidence fails to meet second-tier standards, manufacturers often shift toward marketing strategies that circumvent rigorous drug approval pathways. Tramiprosate serves as a cautionary precedent: after Phase 3 RCTs failed to satisfy FDA benchmarks, the

manufacturer abandoned its pursuit of prescription status.[22,23] The compound resurfaced in commercial channels, where it now circulates without regulatory oversight.

Fact: Supplements shouldn't be taken unless a deficiency is demonstrated.

A notable asymmetry exists between dietary modification and supplementation studies in neuronutrition. Enhancing antioxidant intake through whole-food diets has demonstrated consistent clinical benefits, while isolated antioxidant supplements have shown limited efficacy and, in some cases, negative results in RCTs. This reflects "the Antioxidant Paradox" noted above. Despite these findings, anti-oxidation-targeted neuro-nutraceuticals, particularly multivitamin blends, remain widely available in the commercial market. Clinical practice discourages such supplements in the absence of documented deficiencies, as supra-physiological dosing may pose risks. Conversely, when deficiencies manifest symptomatically, physiological-dose replacement to restore homeostasis is indicated. In summary, current evidence does not support recommending neuro-nutraceuticals for general use. However, clinicians must understand their pharmacological profiles to recognize potential harms in self-directed consumption.

Conclusion

Consequently, while neuronutraceuticals are widely marketed and increasingly consumed, their claimed neurological benefits are largely unsupported by robust evidence. Clinicians must remain vigilant and ethically consistent in their evaluation of these substances, recognizing that pharmacological and nutraceutical interventions adhere to the same principles of evidence-based practice. Given the documented risks associated with unregulated supplements and the prevalence of low-quality efficacy claims, it is clinically prudent to recommend against routine use in the absence of a demonstrable deficiency. This stance not only protects patients from potential harm but also strengthens the integrity of rational treatment decision-making.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: MAT; data collection: MAT; analysis and interpretation of results: MAT; draft manuscript preparation: MAT. All authors reviewed the results and approved the final version of the article.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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