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The effects of food safety guidelines in comparison to the neutropenic diet on infection rates and nutritional status in patients with acute myeloid leukemia undergoing remission induction chemotherapy: a randomized clinical trial

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Abstract

Background

The clinical benefit of the neutropenic diet (ND) in reducing infection risk among patients undergoing intensive chemotherapy remains controversial. Food safety guidelines (FSGs) endorsed by regulatory authorities emphasize safe food handling rather than dietary restriction. This randomized clinical trial compared ND with FSGs in terms of infection outcomes and nutritional status in adult patients with acute myeloid leukemia (AML) receiving remission induction chemotherapy.

Methods

In this single-center, randomized controlled trial, 63 adult patients with AML undergoing induction chemotherapy were allocated to receive either ND (n = 31) or FDA-endorsed FSGs (n = 32) for one chemotherapy cycle. The primary outcome was neutropenic infection, defined as fever occurring in the presence of neutropenia (absolute neutrophil count < 500×10^9/L). Secondary outcomes included documented infections, antimicrobial use, nutritional intake, anthropometric changes, and nutritional status assessed using the Patient-Generated Subjective Global Assessment (PG-SGA). Dietary adherence and acceptability were also evaluated.

Results

There were no significant differences between the ND and FSG groups in the incidence or duration of neutropenia, rates of bacteremia, pneumonia, fungal infections, antimicrobial use, anthropometric measures, or overall nutritional status (all $P > 0.05$). The mean number of febrile days was marginally lower in the ND group compared with the FSG group ($P = 0.047$). Both groups experienced a significant decline in energy and micronutrient intake during chemotherapy; however, reductions in several micronutrients were more pronounced in the ND group. Patients assigned to ND reported greater difficulty adhering to the diet compared with those following FSGs.

Conclusion

The neutropenic diet did not confer a clinical advantage over food safety guidelines in preventing infections among adult patients with AML undergoing induction chemotherapy and was associated with greater dietary burden. These findings support the replacement of restrictive neutropenic diets with evidence-based food safety guidelines in oncology care settings.

Introduction

Multimodal treatments, such as aggressive chemotherapy, have significantly improved cancer survival rates but also pose risks like severe neutropenia and increased infection susceptibility, particularly among patients with hematological malignancies undergoing intensive chemotherapy (1–3). Chemotherapy-induced neutropenia leads to complications including fever, infections, and compromised clinical outcomes, with infection-related mortality rates ranging from 4%–6% in severe cases (4–8). Concurrently, cytopenia and mucositis, exacerbated by dysbiosis caused by chemotherapy and antibiotics, increase the risk of bloodstream infections (9–14).

To reduce infection risks, strategies like the neutropenic diet (ND) have been employed, restricting high-bacteria foods such as fresh produce, soft cheeses, and undercooked meat (14–20). However, ND guidelines vary widely, and evidence supporting its effectiveness is weak (21–25). While some institutions advocate ND, the FDA and CDC, emphasize safe food-handling practices over dietary restrictions (2, 15, 17). Moreover, dietary restrictions may exacerbate malnutrition and reduce the quality of life in cancer patients, particularly those experiencing gastrointestinal side effects (2, 26, 27).

A Cochrane review and small randomized trials found no significant differences in infection rates between patients following ND and those on standard or food-safety-based diets (8, 13, 17). These studies were inconclusive and limited by small sample sizes and uncontrolled variables like neutropenia duration and nutritional status. Despite these findings, ND remains a common practice in some settings (2, 15, 20, 27). To address these gaps, a randomized clinical trial was conducted to compare infection rates and clinical outcomes between patients with acute myeloid leukemia adhering to either ND or FDA food safety guidelines. The study also assessed nutritional status, diet tolerability, and adherence, hypothesizing no significant differences in clinical outcomes between groups.

Methods

This was a randomized, controlled trial of adult patients admitted to the blood unit at Shariati Hospital in Tehran, Iran from March 2022 to November 2024. Other eligibility criteria included being aged 20–65 years, diagnosis of acute lymphocytic leukemia, receiving induction chemotherapy, no evidence of active infection, Karnofsky performance status score of greater than 80%, ability to read and write in Persian, and informed consent to participate in research. In addition, patients were required to be taking > 50% of their calories by mouth at the time of enrollment. Specifically, if patients were being fed through a G-tube and they were taking > 50% of their average daily calories from formula they were excluded from participation. Exclusion criteria included documented fever or infection at the time of enrollment, comorbid immunosuppressive disease, getting COVID-19 during the study, and patients who could not tolerate oral feeding. Patients undergoing concurrent radiation to the CNS (central nervous system) or GIT (gastrointestinal tract) were also excluded because of the increased need for TPN (total parenteral nutrition) in this population. Patients were randomized into two groups; One group followed FSGs and the other group received the ND.

Randomization and blinding

After consent and collection of baseline data, patients were randomly assigned by a statistician to either the FSGs or the ND. Patients were randomized in blocks of 2, stratified by age and gender which was prepared by random numbering using a computer-based system developed by the statistician. We concealed the patients' diet allocation from study staff and patients. Although the primary examiner was aware of the diet given to each patient, the patients and the rest of the medical team were blinded, that is they did not know if the patient was receiving a FSGs or ND diet.

FSG

The food safety guidelines used in this study were based on FDA recommendations for immunocompromised patients. They represent a practical guide to decreasing illness from food through safe food handling, preparation, and consumption. These guidelines include recommendations concerning food shopping, food storage, food preparation, safe cooking, and safe serving of food (Supplementary 1). Patients were only required to follow the dietary recommendations regarding consuming foods. Specific foods restricted by this diet include unpasteurized juice, unpasteurized dairy products, and undercooked eggs, meat, fish, and poultry. In addition, these subjects received a handout outlining listed in the FDA-endorsed FSGs. Food safety guidelines were made accessible to patients in this study through earlier consultation with kitchen services; hence, patients continued to follow the diet to which they were assigned. The regular hospital diet at this site met FSG requirements, so patients assigned to this arm received the standard hospital diet.

ND

The ND, as defined in this study, was established based on a wide literature review and consensus among cooperating institutions. Dietary restrictions included restriction of raw fruits (except for oranges and bananas, which could be peeled by hand), raw vegetables, raw nuts, aged cheese, cold meat cuts, takeout, and fast food.

Study procedures

Baseline data included demographic information (age, sex, employment status, education status, ward); medical history (diagnosis, date of diagnosis, chemotherapy regimen, medications, surgeries), weight, height, BMI, and Charlson comorbidity index collected after informed consent was obtained.

For both intervention arms (FSGs and ND), diet assignment handouts were given to subjects and any caregivers present at the time of the study beginning. These handouts were reviewed orally in detail, by the study investigator, and any questions were answered at that time. Diet orders were placed on admitted subjects consistent with their diet assignment. Adherence to diet and amount of food intake was obtained using three 24-hour, 3-day diet diaries that were conducted daily at the beginning, middle, and the end of intervention with patients. Patients on both arms were instructed to initiate their diet

assignments at the beginning of the cycle of induction chemotherapy and continue until the completion of that cycle (about 3–4 weeks).

All patients were cared in a high-efficiency particulate air-filtered room. All of the patients had tunneled central venous catheters placed previous to initiation of the conditioning regimen and were placed on antibiotic, antifungal, and antiviral prophylaxis. Antibacterial therapy included metronidazole 500 mg by mouth three times per day and ciprofloxacin 750 mg by mouth twice per day. Antiviral coverage included acyclovir 400 mg by mouth twice per day. Antifungal therapy was fluconazole 400 mg by mouth daily. With the first neutropenic fever, all patients were started on broad-spectrum antibiotics therapy of ceftazidime 2 grams every eight hours, and vancomycin 2 mg/kg daily.

Results of all studies obtained during the hospitalization, including complete blood counts (CBCs), cultures, fever, medications, and radiographs, were recorded. Patient's CBCs were followed from the start of the chemotherapy cycle until Absolute Neutrophil Count (ANC) recovery, defined as an ANC greater than 500×10^9/L on 2 consecutive complete blood counts.

Outcome parameters and measures

Neutropenic infection was chosen as the primary outcome and defined as an ANC less than 500×10^9/L, which was measured at baseline and end of study enrollment by laboratory studies. Fever was defined as a single oral temperature of ≥ 38.3°C, or two oral temperatures of ≥ 38.0°C taken 1 hour apart (as measured by hospital staff).

Secondary outcomes included documented infections, such as positive blood, urine, or stool cultures; radiographic evidence of infection (e.g., pneumonia); duration of additional antibiotic and antifungal therapy; nutritional assessments; number of days on chemotherapy; and yeast colonization for the analysis of gram-negative bacilli. All secondary outcomes were recorded throughout the chemotherapy cycle.

A diagnosis of pneumonia required a computed tomography scan or compatible chest x-ray. If no resolution had occurred after 3 to 5 days, bronchoalveolar lavage to isolate a causative organism was conducted. A diagnosis of bacteremia required two positive blood cultures as a result of frequent contaminants such as coagulase-negative Staphylococcus.

Food diaries were collected to measure dietary intake in each group and as a way to validate adherence to the assigned diet. Patients recorded what they ate for three days through these 24-hour diet diaries at baseline, middle, and end of the study. After the gram weights of all foods consumed during each day, dietary intake was analyzed using Nutritionist 4 software to determine energy, macronutrient, and fiber intake. This method was chosen because it is a reliable way to evaluate food intake. All patients remained on the correct diet throughout the study. Diet acceptability was evaluated using the FAQ, a ten-item self-report instrument assessing palatability, ease of preparation, perceived advantages, and diet-

related adverse effects. Nine of ten questions are answered using 4-point response scales, and 1 question has a yes/no format.

To determine nutritional status, the validated Patient-Generated Subjective Global Assessment (PG-SGA) tool was administered at baseline and at the end of the study to the patients. It includes questions regarding the presence of short-term weight loss and nutritional symptoms. The scored PG-SGA provides a numeric score and incorporates a global rating of well nourished, moderately or suspected of being malnourished, or severely malnourished. This questionnaire includes questions on body weight and recent weight changes (score 0–5), food intake (score 0–4), symptoms affecting food intake (score 0–24), and physical activity level (score 0–3), comorbidities associated with malnutrition (score 0–7), metabolic needs (score 0–6), and physical examination (score 0–3). A total score is then summed, which provides a guide to the level of nutritional intervention needed. A score of nine or higher indicates a critical need for nutrition intervention.

Statistical analysis

Statistical analysis was completed using SPSS Statistics software package version 26. Data were tested for normality using Q-Q and Kolmogorov–Smirnov test. To describe the variables, mean, standard deviation, frequency, and percentage were used. The mean of the variables between the two study groups was compared using an independent-sample t-test, chi-square, Fisher's Exact, or repeated measures ANOVA statistical tests. To compare the mean of the variables at the beginning and end of the study within each group, a Paired Samples T-Test was used. Finally, we eliminate the effect of possible confounders such as baseline values and the effect of the interaction of variables by using the ANCOVA test. A two-sided $p < 0.05$ was regarded as statistically significant.

Ethical approval

The study protocol was approved by the Medical Ethics Committee of the Tehran University of Medical Science, Iran (ethical code:IR.TUMS.MEDICINE.REC.1400.1391, register date 05/02/2021) . This study was registered with irct.ir and approval was obtained from all Institutional Review Boards prior to recruitment and consent of patients at the site. The study protocol was registered online at http://www.IRCT.ir (code: IRCTID: IRCT20220208053971N1, register date 04/16/2022).

Results

Population demographics

Of 361 patient chart reviews, 127 patients were diagnosed with AML. 105 participants met eligibility criteria and were approached to take part in the study; 37 declined to participate due to concerns about additional risks of the diets during neutropenia, or due to a lack of interest in participating in research. Patients also preferred to conform to the hospital’s policy of eating a diet containing no raw fruits and vegetables. The remaining sixty-eight patients were enrolled in the trial and consented to be randomly assigned to either the FSGs or the ND group; however, two patients on the FSGs arm and three on ND

arm were lost to follow-up. 32 patients on the FSGs and 31 on the ND arms were evaluated for all study outcomes (Fig 1). Thirty-five patients (55.6%) were male and twenty-eight (44.4%) were female. The mean age was 40.56 years. Patients were involved in the study for 35.17 days. In the whole sample, most patients (73.0%) received 7+3 chemotherapy regimen, while the remaining patients received FLAG (12.7%), CLANG (9.5%), and 5+2 (4.8%) chemotherapy regimens. However, the two groups were equally likely to receive high-dose therapy. There were no significant differences between the two groups at baseline concerning patient demographics; gender, inpatient ward, age, weight, height, BMI, disease characteristics, Charlson comorbidity index, and Chemotherapy regimen. The population characteristics are shown in Table 1.

Food intake

The 24-hour, 3-day diet diaries were used to measure food consumption. There were no statistically significant differences in the mean amount of energy, carbohydrate, protein, fat, fiber, and micronutrient intake from baseline to follow-up between the two groups ($P>0.05$ for all comparisons). Both groups' average intake of macronutrients and micronutrients, decreased during the study which was statistically significant in Energy, Carbohydrate, Protein, Thiamin, Riboflavin, Niacin, Pyridoxine, Calcium, and Phosphorus in both arms. In addition, average intake of some micronutrients such as Vitamin C, Vitamin A, Biotin, Magnesium, and Potassium, reduced significantly during the intervention only within the ND group. The macronutrients and micronutrients consumption are shown in Tables 2 and 3 respectively.

Anthropometric indices

Patients in both the FSGs and ND groups had lost weight when they came off the study although these weight and BMI changes were not statistically significant within and between the two groups during the study. The anthropometric changes are shown in Table 4.

Nutritional status

With regard to the PG-SGA scores measured by the QLQ-C30 questionnaire, patient scores and categories in both FSGs and ND groups showed a significant increase in the degree of nutritional intervention needed and number of symptoms from baseline to follow-up. Many patients develop gastrointestinal complications within 1-2 weeks following therapy, limiting their nutritional intake. However, there were no statistically significant differences in the PG-SGA score and PG-SGA categories between the two groups. Nutritional status is shown in Table 5.

Infection

A total of 63 patients were evaluated for fever, neutropenia, bacterial and fungal infections during the study. With respect to presenting fever, two patients on FSGs (3.17%) and two patients on ND (3.17%) had not documented a fever. However, the remaining patients developed fevers during their time in the study. The mean number of febrile days in the ND group was almost significantly lower than that in the FSGs group ($P=0.047$). However, the mean days from the chemotherapy cycle onset until the first febrile

day did not vary between the two groups (P>0.05). All patients except one in the FSGs group in both arms developed neutropenia (ANC<500×10^9/L). There was no statistically significant difference between the FSGs arm and the ND arm in the mean number of days with neutropenia, the first day of neutropenia, pneumonia, and fungal infections (Table 6).

No significant differences were found between the groups in the percentage of positive blood cultures. 26 (41.26%) of 32 participants in the FSGs group and 24 (38.09%) of 31 participants in the ND group had positive blood cultures. Isolated organisms from positive blood cultures were likewise similar in the two groups including Pseudomonadaceae, Xanthomonadaceae, Enterobacteriaceae, Staphylococcaceae, Moraxellaceae, Entrococcaceae, and non-albicans candida. Therefore, no significant differences were observed in any clinical outcomes and blood infections between the two groups (Table 7).

Medications intake

The average number of days receiving antibiotic, antifungal (fluconazole), and antiviral (acyclovir) medications were not statistically significant between the FSGs and the ND group during the study. It should be noted that this lack of difference was expected given that all patients in both groups received antifungal and antiviral medications as prophylaxis. Medications intake is shown in Table 8.

Discussion

This study aimed to compare the clinical outcomes between patients who received a Neutropenic Diet (ND) and those who followed Food Safety Guidelines (FSGs) to evaluate their association with infectious outcomes in adult patients with acute myeloid leukemia (AML) undergoing induction chemotherapy. The results revealed no significant differences in clinical outcomes, including febrile days and blood infections, between the two diet groups. Although the ND group experienced more days with fever, this finding approached statistical significance, suggesting that the observed difference may be influenced by chemotherapy regimen variations between the groups rather than the diet itself. Notably, ND was not independently associated with infectious outcomes in the sample studied.

These findings align with prior studies in various patient populations, including adults with acute leukemia, pediatric cancer patients, and stem cell transplant (SCT) recipients (2, 11, 13, 16, 17), which found no significant differences in febrile days or infection rates between groups on ND and those on FSGs. However, one retrospective study of SCT recipients (28) found a higher infection rate in patients following a ND, which may be attributed to the higher severity of gastrointestinal toxicity in SCT patients. Despite this discrepancy, our study identified a borderline-significant trend toward more days of fever in the ND group, consistent with the overall direction reported in the literature.

Previous studies have suggested that food-derived organisms, particularly Gram-negative bacteria, are often implicated in infections. While ND was hypothesized to reduce the risk of infections by preventing the translocation of gut bacteria, our results did not show significant differences in infection rates between groups, even though the ND group had a slightly higher incidence of Gram-negative bacterial

infections. This supports the argument that food-derived bacteria might not play a direct role in infection development in this patient group. In chemotherapy patients, multiple factors, including impaired gut motility, mucositis, bacterial overgrowth, and compromised immunity, contribute to the risk of gut-derived infections, complicating the understanding of the ND's clinical relevance in preventing infections.

Another key finding of this audit was the inconsistent initiation of ND protocols across institutions. There is no standardized practice regarding when to start an ND relative to neutropenia onset. This lack of uniformity is a common challenge faced by medical institutions globally, as protocols vary between and within institutions. Some use different criteria, such as absolute neutrophil count (17) or chemotherapy start dates, to determine when to initiate ND, further complicating the interpretation of its clinical effectiveness. Additionally, studies have shown that adherence to ND protocols can be low, and patient satisfaction is often poor due to the restrictive nature of the diet (21, 24, 29). Given these challenges and the apparent lack of benefits in improving patient outcomes, the practicality and effectiveness of imposing ND on patients undergoing chemotherapy should be reconsidered.

The ND also poses potential risks to patients' nutritional status, as it restricts many food groups, potentially leading to deficiencies in vitamins, minerals, and fiber. These nutritional deficits can exacerbate chemotherapy-induced malnutrition, which may, in turn, delay neutrophil recovery and increase susceptibility to bacterial infections. Although our study did not find statistically significant differences in infection rates between the groups, the higher infection rates observed in the ND group could be clinically relevant. This warrants further investigation in larger studies with greater statistical power to confirm these findings. Previous studies have shown that the ND is lower in fiber, vitamins, and minerals due to the elimination of fresh fruits and vegetables and cooking-induced nutrient losses (31, 34, 35), potentially contributing to delayed immune response, bacterial translocation, and increased infection risk.

Research Implications

This randomized clinical trial meaningfully contributes to the growing body of evidence challenging the necessity of the neutropenic diet in the management of hematological malignancies. By demonstrating the equivalence of FSGs and ND with respect to infection rates, bacteremia profiles, neutropenic episodes, and nutritional outcomes, this study supports a paradigm shift toward evidence-based, patient-centered dietary practices in oncology.

From a research perspective, this trial highlights the urgent need for larger, multicenter randomized controlled trials with adequate statistical power to definitively confirm the non-inferiority of FSGs over ND. Future studies should incorporate pre-specified subgroup analyses based on chemotherapy intensity, degree and duration of neutropenia, gut microbiome composition, and baseline nutritional status, as these variables may modulate the relationship between dietary practice and infectious risk. Longitudinal designs that follow patients across multiple chemotherapy cycles would also address the limitation of single-episode observation and capture infections with longer incubation periods.

Additionally, the within-group micronutrient deficiencies observed exclusively in the ND group, particularly reductions in vitamin C, vitamin A, biotin, magnesium, and potassium, warrant further mechanistic investigation. Whether these deficits translate into clinically meaningful immune suppression, delayed wound healing, or impaired neutrophil recovery, is a question that warrants dedicated nutritional immunology research. Standardization of the ND definition across institutions, which currently varies considerably, is also needed before meaningful cross-study comparisons can be made.

Clinical Implications

Clinically, these findings carry direct and actionable implications for oncology practice. The absence of a significant benefit of the ND over FSGs, together with evidence that the ND is associated with greater micronutrient deficiencies and imposes a higher burden on patients—as reflected by greater difficulty adhering to the diet supports a shift away from the routine, blanket implementation of ND protocols.

Oncology dietitians and clinical teams should consider replacing the restrictive ND with FDA-endorsed food safety guidelines, which emphasize safe food handling, preparation, and storage rather than broad food group elimination. This approach can better preserve dietary variety, support adequate micronutrient intake, and improve patients' quality of life during an already burdensome period of treatment. Notably, since the standard hospital diet at the study site was already aligned with FSGs, implementing this recommendation may require minimal institutional restructuring in settings with similar practices.

From a nursing and dietary counseling standpoint, patient education on proper food safety behaviors such as appropriate cooking temperatures, avoidance of unpasteurized products, and safe food storage should be incorporated into routine pre-chemotherapy patient preparation. This approach empowers patients with practical and sustainable tools while reducing the psychological and nutritional burden of overly restrictive dietary regimens.

Strengths of the Study

This study possesses several methodological strengths that enhance the validity and relevance of its findings. First, its prospective randomized controlled design minimizes selection bias and allows for causal inference, representing a higher level of evidence compared to retrospective or observational designs that characterize much of the existing literature on this topic.

Second, the rigorous blinding strategy whereby patients and the broader clinical team were unaware of dietary group assignment reduces performance and detection bias. The primary investigator's awareness of group allocation was an unavoidable limitation, though efforts were made to standardize data collection procedures across both arms.

Third, the use of validated, standardized instruments for nutritional assessment (PG-SGA) and dietary intake (three-day, 24-hour diet diaries analyzed via Nutritionist 4 software) strengthens the internal

validity of nutritional outcome measurements. These tools have established reliability and clinical relevance in the oncology setting.

Fourth, the homogeneity of the study population, adult patients with AML undergoing a clearly defined induction chemotherapy protocol at a single center, reduced confounding from disease heterogeneity and treatment variability. Baseline demographic and clinical equivalence between groups further supports the comparability of study arms.

Fifth, the comprehensive outcome assessment encompassing infection rates, microbiological culture profiles, medication use, anthropometry, nutritional status, and dietary intake provides a multidimensional evaluation of the effects of both dietary interventions, enabling nuanced interpretation of results beyond simple infectious endpoints.

Limitations of the Study

Our study was limited by its single-center design, which may reduce the generalizability of the findings. The patient population consisted of those undergoing induction chemotherapy, limiting the applicability of the results to other types of cancer or treatment regimens. The sample size was also a limiting factor; a larger cohort would have helped to definitively answer the question of whether relaxing ND restrictions in favor of FSGs can reduce adverse outcomes. Additionally, the study only followed patients during a single episode of neutropenia, which may have been too short a period to detect infections with longer incubation periods, such as those caused by Salmonella typhi.

Despite these limitations, the results of our study suggest that both the ND and FSGs were generally well tolerated, with the FSGs being easier for patients to adhere to. This is particularly relevant given that patients undergoing chemotherapy often report that food restrictions negatively impact their quality of life (17, 39, 40). Our findings support earlier research showing that cancer patients prefer a general diet over a ND due to its less restrictive nature and greater flexibility in meeting caloric and nutritional needs. Furthermore, most patients indicated they could continue their respective diets for the duration of their chemotherapy, although those on the ND group experienced more complaints about food limitations. The major limitation of this study is its sample size, which restricted the power needed to draw definitive conclusions. A larger sample size, along with studies that account for various patient variables, would help better understand the impact of different dietary approaches on infection rates in neutropenic patients. Additionally, prior knowledge of ND restrictions among patients might have influenced their diet adherence and could have led to biases in the study.

Conclusion

In conclusion, we found no significant differences between groups in any clinical outcome using the matched subsample. Our results demonstrate that an ND offers no benefit over the FDA-endorsed FSGs in the prevention of infection in adult patients with AML undergoing induction chemotherapy and adherence requires additional effort on the part of patients. Moreover, the use of ND is constrained by its

lack of standardized practice across institutions and its impacts on nutritional status remain unclear. Thus, its use in other institutions may need to be reconsidered. Institutions caring for patients with cancer should consider replacing neutropenic guidelines with FSGs, and safe food handling practices should be emphasized in all institutions. Nonetheless, the conclusions drawn from this trial should be regarded as hypothesis-generating rather than definitive, given the limitations of sample size and single-center design. Future large-scale, multicenter randomized controlled trials that incorporate gut microbiome analysis, patient-reported outcome measures, and long-term follow-up across multiple chemotherapy cycles are essential to provide definitive guidance and inform evidence-based dietary recommendations for neutropenic patients.

Declarations

Contributors: YH, ST-S, SA-M and SM: data extraction, drafting of the manuscript, revision of the manuscript and final approval. HM: conception and design, analysis and interpretation of data, drafting of the manuscript, revision of the manuscript and final approval. HI, FJ, and SH: Writing - Review & editing.

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Data availability statement: Data and analytical codes used for the present study will be available upon reasonable request.

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Tables

Table 1
Comparison of demographic and clinical characteristics between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

Characteristics	All patients	FSGs	ND	p-value*
	(n = 63)	(n = 32)	(n = 31)	
Age (years, mean ± SD)	40.56 ± 12.29	39.63 ± 12.81	41.52 ± 11.87	0.545[a]
Weight (kg, mean ± SD)	71.81 ± 15.72	70.60 ± 13.18	72.70 ± 14.86	0.664[a]
Height (cm, mean ± SD)	169.70 ± 9.97	171.81 ± 8.83	167.52 ± 10.74	0.087[a]
BMI (kg/m^2, mean ± SD)	24.96 ± 5.09	23.92 ± 4.41	25.87 ± 4.60	0.181[a]
CCI (mean ± SD)	2.33 ± 0.74	2.44 ± 0.88	2.23 ± 0.56	0.260[a]
Gender				
Male, n (%)	35 (55.6%)	21 (33.3%)	14 (22.2%)	0.102[b]
Female, n (%)	28 (44.4%)	11 (17.5%)	17 (27.0%)	
Inpatient ward				
Blood A, n (%)	36 (57.1%)	19 (30.2%)	17 (27.0%)	0.716[b]
Blood B, n (%)	27 (42.9%)	13 (20.6%)	14 (22.2%)	
Chemotherapy regimen, n (%)				
7 + 3, n (%)	46 (73.0%)	23 (36.5%)	23 (36.5%)	0.686[b]
5 + 2, n (%)	3 (4.8%)	2 (3.2%)	1 (1.6%)	
CLANG, n (%)	6 (9.5%)	4 (6.3%)	2 (3.2%)	
FLAG, n (%)	8 (12.7%)	3 (4.8%)	5 (7.9%)	
* Obtained from independent-sample t-test[a] □ chi-square[b]				
BMI; Body mass index, CCI; Charlson comorbidity index				

Table 2

Comparison of macronutrients intake between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

		Baseline	Middle	End	p*	p**	P***
Energy (kcal/d)	FSGs	1533.37 ± 630.62	1150.36 ± 765.66	1201.93 ± 783.57	0.003	0.959	0.717
	ND	1450.60 ± 643.15	1168.30 ± 794.79	1241.29 ± 849.62	0.037		
Carbohydrate (g/d)	FSGs	224.65 ± 95.41	172.14 ± 120.81	183.98 ± 121.76	0.011	0.665	0.840
	ND	215.72 ± 96.12	173.18 ± 116.47	188.77 ± 123.41	0.036		
Protein (g/d)	FSGs	62.38 ± 30.52	45.55 ± 33.01	50.14 ± 36.92	0.014	0.661	0.984
	ND	58.63 ± 27.58	42.88 ± 29.73	47.71 ± 32.81	0.011		
Fat (g/d)	FSGs	45.24 ± 17.92	33.37 ± 22.55	31.43 ± 19.85	< 0.001	0.851	0.314
	ND	41.59 ± 19.64	56.08 ± 26.62	35.17 ± 29.19	0.211		
Fiber (g/d)	FSGs	12.17 ± 6.14	9.56 ± 6.70	11.83 ± 9.69	0.199	0.932	0.941
	ND	12.33 ± 7.44	9.54 ± 6.86	11.31 ± 8.24	0.082		

Variables are expressed as mean ± SD

* Obtained from General linear model, Tests of Within-Subjects Effects

** Obtained from General linear model, Tests of Between-Subjects Effects

*** Obtained from repeated measures ANOVA

Table 3

Comparison of micronutrients intake between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

		Baseline	Middle	End	p*	p**	P***
Vitamin C (mg/d)	FSGs	69.94 ± 42.76	52.97 ± 42.88	61.29 ± 46.70	0.219	0.757	0.829
	ND	76.88 ± 50.93	55.38 ± 43.41	59.96 ± 49.42	0.004		
Vitamin A (RE/d)	FSGs	487.52 ± 612.19	444.27 ± 488.29	305.18 ± 238.11	0.160	0.175	0.244
	ND	406.22 ± 316.78	234.26 ± 256.57	290.20 ± 336.65	0.026		
Thiamin (mg/d)	FSGs	1.36 ± 0.69	0.98 ± 0.70	1.13 ± 0.81	0.009	0.852	0.843
	ND	1.30 ± 0.69	1.00 ± 0.73	1.07 ± 0.72	0.042		
Riboflavin (mg/d)	FSGs	0.938 ± 0.433	0.706 ± 0.473	0.788 ± 0.536	0.023	0.731	0.930
	ND	0.884 ± 0.396	0.667 ± 0.504	0.778 ± 0.521	0.038		
Niacin (mg/d)	FSGs	16.25 ± 7.42	11.79 ± 8.05	11.88 ± 8.64	0.001	0.699	0.944
	ND	15.40 ± 7.57	10.97 ± 7.52	11.59 ± 8.28	0.003		
Pyridoxine (mg/d)	FSGs	1.26 ± 0.57	0.94 ± 0.62	0.96 ± 0.59	0.005	0.856	0.572
	ND	1.24 ± 0.55	0.92 ± 0.58	1.07 ± 0.68	0.005		
Biotin (Ug/d)	FSGs	12.10 ± 7.25	9.85 ± 7.08	11.40 ± 7.82	0.218	0.743	0.244
	ND	13.55 ± 8.56	8.59 ± 6.74	9.71 ± 7.93	0.005		
Magnesium (mg/d)	FSGs	203.19 ± 106.52	155.48 ± 107.41	178.73 ± 141.25	0.093	0.730	1.000
	ND	194.64 ± 105.98	146.95 ± 108.13	170.38 ± 119.34	0.025		
Potassium (mg/d)	FSGs	2186.67 ± 1022.73	1662.87 ± 1102.80	1938.47 ± 1346.99	0.056	0.625	0.989

Variables are expressed as mean ± SD

* Obtained from General linear model, Tests of Within-Subjects Effects

** Obtained from General linear model, Tests of Between-Subjects Effects

*** Obtained from repeated measures ANOVA

	ND	2057.47 ± 990.89	1570.21 ± 1049.42	1813.99 ± 1180.51	0.019		
Calcium (mg/d)	FSGs	389.26 ± 176.91	282.21 ± 193.73	330.21 ± 229.23	0.012	0.987	0.967
	ND	395.92 ± 186.48	278.67 ± 209.88	324.98 ± 220.13	0.006		
Phosphorus (mg/d)	FSGs	793.16 ± 376.11	593.83 ± 409.55	689.72 ± 490.43	0.030	0.676	0.978
	ND	756.95 ± 352.80	567.13 ± 404.80	642.56 ± 425.30	0.016		
Variables are expressed as mean ± SD							
* Obtained from General linear model, Tests of Within-Subjects Effects							
** Obtained from General linear model, Tests of Between-Subjects Effects							
*** Obtained from repeated measures ANOVA							

Table 4
Comparison of anthropometric indices between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

	Time	Group		P-value
		FSGs	ND	
Weight (kg)	Baseline	70.60 ± 13.18	72.70 ± 14.86	0.664**
	End	69.68 ± 13.94	71.91 ± 14.82	0.889***
	P-value*	0.159	0.109	-
BMI (kg/m^2)	Baseline	23.92 ± 4.41	25.87 ± 4.60	0.181**
	End	23.64 ± 4.89	25.54 ± 4.40	0.820***
	P-value*	0.206	0.067	-
BMI; Body mass index				
Variables are expressed as mean ± SD				
* Obtained from paired-sample t-test				
** Obtained from Independent-sample t-test				
*** Obtained from ANCOVA model, adjusted for baseline value				

Table 5

Comparison of nutritional status between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

	Time		Group		P-value
			FSGs	ND	
PG-SGA score	Baseline		7.47 ± 4.81	6.13 ± 4.62	0.264**
	End		12.50 ± 8.95	10.52 ± 7.63	0.735***
	P-value*		0.001	< 0.001	-
PG-SGA categories	Baseline	Stage A[a]	21 (33.3%)	26 (41.3%)	0.204**
		Stage B[b]	10 (15.9%)	5 (7.9%)	
		Stage C[b]	1 (1.6%)	0 (0.0%)	
	End	Stage A[a]	18 (28.6%)	18 (28.6%)	0.853**
		Stage B[b]	4 (6.3%)	5 (7.9%)	
		Stage C[c]	10 (15.9%)	8 (12.7%)	

PG-SGA; Patient-Generated Subjective Global Assessment

[a] Stage A, Well-nourished

[b] Stage B, Moderate/suspected malnutrition

[c] Stage C, severely malnourished

Variables are expressed as mean ± SD or n (%)

* Obtained from paired-sample t-test

** Obtained from Independent-sample t-test

*** Obtained from ANCOVA model, adjusted for baseline value

Table 6

Comparison of clinical outcomes between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

	All patients	**FSGs**	**ND**	**p-value***
	(n = 63)	**(n = 32)**	**(n = 31)**	
No. of febrile days (mean ± SD)	9.15 ± 7.19	10.94 ± 7.69	7.30 ± 6.22	0.047[a]
First febrile day (mean ± SD)	7.93 ± 4.72	8.39 ± 4.24	7.60 ± 5.19	0.518[a]
No. of days with neutropenia (mean ± SD)	18.12 ± 7.04	18.29 ± 7.85	17.61 ± 6.19	0.707[a]
First day with neutropenia (mean ± SD)	6.83 ± 3.05	7.06 ± 3.09	6.87 ± 3.18	0.809[a]
LOS (day, mean ± SD)	35.17 ± 6.90	35.97 ± 7.01	34.35 ± 6.80	0.358[a]
Pneumonia				
Patients with positive pneumonia n (%)	17 (27.0%)	9 (14.3%)	8 (12.7%)	0.836[b]
Patients with negative pneumonia n (%)	46 (73.0%)	23 (36.5%)	23 (36.5%)	
Fungemia				
Patients with positive fungemia n (%)	7 (11.1)	3 (4.8)	4 (6.3)	0.708[c]
Patients with negative fungemia n (%)	56 (88.9)	29 (46.0)	27 (42.9)	
Serum GM test				
Positive, n (%)	10 (15.9)	6 (9.5)	4 (6.3)	0.732[c]
Negative, n (%)	53 (84.1)	26 (41.3)	27 (42.9)	
Variables are expressed as mean ± SD or n (%)				
[a] Obtained from independent-sample t-test				
[b] Obtained from chi-square				
[c] Obtained from Fisher's Exact Test				
LOS; Leng of stay, GM; galactomannan				

	All patients	FSGs	ND	p-value*
	(n = 63)	(n = 32)	(n = 31)	
Urine Culture				
Positive, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	-
Negative, n (%)	63 (100.0)	32 (50.8)	31 (49.2)	
Stool Culture				
Positive, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	-
Negative, n (%)	63 (100.0)	32 (50.8)	31 (49.2)	
Variables are expressed as mean ± SD or n (%)				
[a] Obtained from independent-sample t-test				
[b] Obtained from chi-square				
[c] Obtained from Fisher's Exact Test				
LOS; Leng of stay, GM; galactomannan				

Table 7
Comparison of isolated organisms in blood culture between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

	All patients	**FSGs**	**ND**	**p-value***
	(n = 63)	**(n = 32)**	**(n = 31)**	
Pseudomonadaceae				
Positive, n (%)	27 (42.9)	14 (22.2)	13 (20.6)	0.884[a]
Negative, n (%)	36 (57.1)	18 (28.6)	18 (28.6)	
Xanthomonadaceae				
Positive, n (%)	14 (22.2)	4 (6.3)	10 (15.9)	0.059[a]
Negative, n (%)	49 (77.8)	28 (44.4)	21 (33.3)	
Enterobacteriaceae				
Positive, n (%)	5 (7.9)	2 (3.2)	3 (4.8)	0.672[b]
Negative, n (%)	58 (92.1)	30 (47.6)	28 (44.4)	
Staphylococcaceae				
Positive, n (%)	13 (20.6)	8 (12.7)	5 (7.9)	0.384[a]
Negative, n (%)	50 (79.4)	24 (38.1)	26 (41.3)	
Moraxellaceae				
Positive, n (%)	2 (3.2%)	2 (3.2)	0 (0.0)	0.492[b]
Negative, n (%)	61 (96.8)	30 (47.6)	31 (49.2)	
Entrococcaceae				
Positive, n (%)	3 (4.8)	1 (1.6)	2 (3.2)	0.613[b]
Negative, n (%)	60 (95.2)	31 (49.2)	29 (46.0)	
Candida non albicans				
Positive, n (%)	2 (3.2)	2 (3.2)	0 (0.0)	0.492[b]
Variables are expressed as n (%)				
[a] Obtained from chi-square				
[b] Obtained from Fisher's Exact Test				

	All patients	FSGs	ND	p-value*
	(n = 63)	(n = 32)	(n = 31)	
Negative, n (%)	61 (96.8)	30 (47.6)	31 (49.2)	
Variables are expressed as n (%)				
[a] Obtained from chi-square				
[b] Obtained from Fisher's Exact Test				

Table 8
Comparison of antibacterial medications intake between patients who received either the food safety guidelines (FSG) or the neutropenic diet (ND).

	All patients	FSGs	ND	p-value*
	(n = 63)	(n = 32)	(n = 31)	
Antiviral (day, mean ± SD)	34.22 ± 7.45	34.44 ± 8.05	34.00 ± 6.90	0.818
Antibiotic (day, mean ± SD)	14.63 ± 6.24	16.06 ± 6.63	13.16 ± 5.32	0.065
Antifungal (day, mean ± SD)	33.35 ± 8.28	32.78 ± 9.37	33.94 ± 7.09	0.584
Variables are expressed as mean ± SD				
* Obtained from independent-sample t-test				

Figures

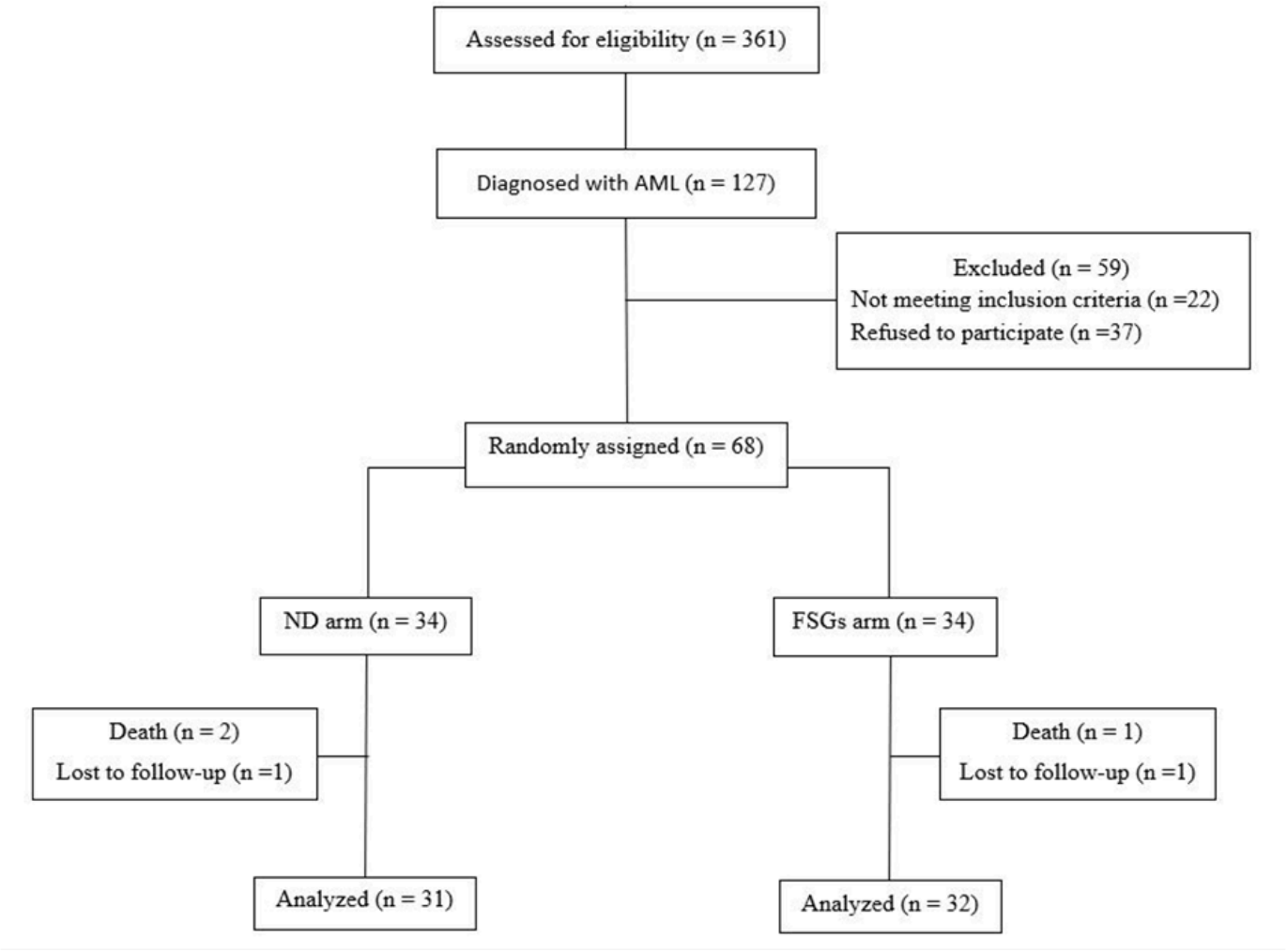


Figure 1

Participant flow diagram

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