Turkish Journal of Pediatric Disease

Original Article

Comparison of febrile neutropenia episodes and outcomes in Turkish versus refugee children with cancer: A single-center experience

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Received : 03.04.2026, Accepted : 31.08.2026 DOI: 10.12956/TJPD.2026.1345

ABSTRACT

Objective: Febrile neutropenia (FN) is a frequent and potentially life-threatening complication of chemotherapy in pediatric oncology. Refugee and immigrant children are often considered to be at higher risk for adverse infectious outcomes due to socioeconomic disadvantage, substandard living conditions, and language barriers. This study aimed to compare FN episodes and short-term clinical outcomes between refugee/immigrant and Turkish pediatric oncology patients managed within a universal healthcare system.

Materials and Methods: This retrospective, single-center study analyzed 50 FN episodes, with one episode included per patient, occurring between May and July 2022 at a tertiary pediatric oncology center. Patients were stratified by residency status as Turkish citizens (n=31) or refugee/immigrant children (n=19), primarily Syrian refugees under temporary protection. Comparative analyses included demographic characteristics, clinical presentation, microbiological findings, treatment characteristics, length of hospital stay (LOS), and socioeconomic parameters. Group comparisons were performed using Chi-square and Mann–Whitney U tests.

Results: Refugee families demonstrated significantly greater socioeconomic disadvantage, with 94.7% having household incomes at or below the minimum wage compared with 38.7% of Turkish families ($p<0.001$). Blood culture positivity was higher among refugee patients (26.3% vs. 3.2%, $p=0.024$). Despite these differences, no significant between-group differences were observed in length of hospital stay (10.42 days for Turkish vs. 12.05 days for refugee patients, $p=0.335$), treatment intensity, or antifungal therapy requirements. Short-term FN-related clinical outcomes during hospitalization were comparable between groups.

Conclusion: Despite marked socioeconomic and housing disadvantages and higher rates of documented bacteremia, refugee and immigrant children experienced short-term FN outcomes comparable to those of Turkish patients when managed in a standardized inpatient setting. These findings suggest that system-level factors—such as universal healthcare access, centralized tertiary care, standardized FN protocols, and language support—may help mitigate the impact of socioeconomic disparities on acute infectious outcomes. However, these results are limited to hospitalized FN episodes and should not be extrapolated to long-term cancer outcomes or outpatient care settings.

Keywords: Febrile neutropenia, global health, health disparities, refugee children

Introduction

Global migration has emerged as a critical humanitarian challenge of the 21st century, placing unprecedented demands on healthcare systems worldwide. Children constitute a particularly vulnerable demographic within displaced populations, especially those diagnosed with life-threatening malignancies. Factors such as the disruption of healthcare continuity, diagnostic delays, malnutrition, substandard living conditions, and limited health literacy may synergistically impair treatment outcomes for pediatric oncology patients displaced by conflict or political instability (1,2).

Currently hosting the world's largest Syrian refugee population, Türkiye serves as a pivotal destination and transit hub for migrants, primarily from the Middle East and Africa. Since the 2011 Syrian conflict, approximately four million Syrians have resided in Türkiye under "temporary

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protection" status (3,4). National legislation and international agreements grant these individuals comprehensive access to healthcare, including tertiary pediatric oncology services. Furthermore, Türkiye's role is expanded by bilateral health agreements that facilitate the admission of pediatric patients from various African nations.

Febrile neutropenia (FN) remains one of the most frequent and life-threatening complications of chemotherapy in pediatric oncology, serving as a primary driver of infection-related morbidity, prolonged hospitalization, and increased resource utilization (5-7). While early recognition and standardized management are key to favorable outcomes, refugee populations often face socioeconomic deprivation, language barriers, and suboptimal hygiene. These factors, coupled with limited caregiver education, may elevate both the incidence and clinical severity of infectious episodes (8,9) .Although existing literature suggests that refugee children often present with advanced-stage disease and higher rates of treatment-related complications, data specifically focused on FN episodes in this population remain scarce—particularly in countries like Türkiye, which offer structured healthcare integration (10-12). Comparative studies evaluating FN outcomes between native and refugee populations are notably limited.

This study aimed to compare the clinical characteristics, socioeconomic determinants, and febrile neutropenia outcomes between Turkish citizens and refugee/immigrant children treated at a tertiary pediatric oncology center. We specifically sought to evaluate whether disparities in living conditions and socioeconomic status translate into measurable differences in FN-related clinical outcomes.

Materials and Methods

Study design and population

This retrospective, single-center observational study was conducted at the pediatric oncology department of a tertiary referral hospital -Ankara Bilkent City Hospital- in Türkiye. Febrile neutropenia (FN) episodes occurring in children receiving chemotherapy between May 2022 and July 2022 were retrospectively reviewed.

To ensure statistical independence, only one FN episode per patient was included in the analysis, even if a patient experienced multiple FN episodes during the study period. When a patient had more than one episode, the first qualifying episode within the study period was selected. Accordingly, each FN episode represents a unique patient encounter. This approach was chosen to preserve the statistical independence of observations and to allow a focused evaluation of acute FN management, while avoiding the clustering effects and intra-patient correlation that would arise from including repeated episodes in the same individual.

Patients were categorized into two groups based on legal residency status: Turkish citizens and refugee/immigrant patients. Refugee/immigrant patients were defined as individuals under temporary protection status granted by the Turkish government (primarily Syrian refugees) or those admitted through bilateral international healthcare agreements. All patients, regardless of residency status, received care under Türkiye's universal healthcare system with equal access to diagnostic and therapeutic services.

Inclusion criteria were as follows:

- Age <18 years
- Confirmed diagnosis of malignancy (solid tumor or lymphoma)
- Active receipt of chemotherapy during the study period
- Occurrence of at least one FN episode during the specified timeframe

Exclusion criteria included FN episodes with incomplete medical records and episodes in which fever was clearly attributable to non-infectious causes in the absence of neutropenia.

Data collection and variables

Data were extracted from electronic medical records and archived physical files by trained research personnel. The following variables were systematically collected:

- Demographic characteristics: age, sex, and residency status (Turkish citizen vs. refugee/immigrant)
- Disease-related variables: type of malignancy (solid tumor or lymphoma) and disease status (remission vs. active disease) at the time of the FN episode
- Clinical presentation: presenting symptoms, physical examination findings, and the interval between the last chemotherapy administration and onset of fever

Baseline laboratory values at admission were compared between the two groups. The median white blood cell count was lower in refugee/immigrant patients (500 vs. 700 cells/mm^3, p=0.026), whereas the median C-reactive protein level was significantly higher (83 vs. 50 mg/L, p=0.029). No significant between-group differences were observed in absolute neutrophil count (50 vs. 120 cells/mm^3, p=0.133), hemoglobin (9.0 vs. 9.3 g/dL, p=0.303), platelet count (50 vs. 88 $\times 10^3/mm^3$, p=0.219), erythrocyte sedimentation rate (36 vs. 27 mm/h, p=0.294), interleukin-6 (35 vs. 20 pg/mL, p=0.107), or procalcitonin (2.0 vs. 0.7 ng/mL, p=0.667).

Microbiological evaluation consisted of blood cultures obtained prior to initiation of empirical antibiotic therapy, with identification of causative organisms and antimicrobial susceptibility testing when cultures were positive. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction testing and a comprehensive respiratory viral panel (including influenza A/B, respiratory syncytial virus, parainfluenza virus, adenovirus, and other respiratory pathogens) were performed when clinically indicated.

Clinical management and outcome variables included empirical antibiotic regimens, treatment modifications based on microbiological results or clinical response, use of antifungal agents, duration of antimicrobial therapy, fluid resuscitation or vasopressor support was required in only one Turkish patient (1/31, 3.2%) and in no refugee/immigrant patients (0/19), with no significant difference between groups (p=1.000).

Socioeconomic data—including monthly household income, parental education level, and housing conditions—were obtained from standardized social work assessments routinely performed during hospitalization. Household income was categorized relative to the Turkish minimum wage at the time of data collection (5.004 TL/month in 2022, approximately $300 USD). Housing conditions were assessed based on the number of rooms, the number of individuals living in the household, adequacy of heating systems, and overall housing quality, as documented in the medical record. Household crowding was estimated as the number of persons per room.

Clinical definitions

Febrile neutropenia was defined according to international guidelines as a single oral temperature ≥38.3°C or a sustained temperature ≥38.0°C for at least one hour in the presence of an absolute neutrophil count (ANC) <500 cells/mm³, or an ANC expected to decrease to <500 cells/mm³ within 48 hours.

Remission status was determined based on disease-specific response criteria (e.g., RECIST criteria for solid tumors and Lugano criteria for lymphomas) as documented at the time of the FN episode. Length of hospital stay was defined as the number of days from admission for FN to hospital discharge. Treatment intensity was defined as the number of different antimicrobial agents administered during the FN episode and the overall duration of antimicrobial therapy.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are reported as medians with ranges for continuous variables and frequencies with percentages for categorical data. Between-group comparisons (Turkish citizens vs. refugees/immigrants) were performed using the Chi-square test or Fisher's exact test (when expected cell counts were <5) for categorical variables. The Mann-Whitney U test was employed for continuous variables due to non-normal distribution. A two-tailed p-value <0.050 was considered statistically significant.

Results

Patient demographics and baseline characteristics

A total of 50 febrile neutropenia (FN) episodes were analyzed: 31 (62%) occurring in Turkish patients and 19 (38%) in refugee/immigrant patients. The median age was similar between groups (p=0.060). Male patients comprised 72% (n=36) of the cohort, with no significant sex distribution differences between Turkish and refugee groups (p=1.000). Detailed demographic characteristics are presented in Table I.

Regarding underlying malignancies, solid tumors predominated in both groups: 22/31 (71.0%) in Turkish patients versus 18/19 (94.7%) in refugee patients, while lymphomas accounted for 9/31 (29.0%) versus 1/19 (5.3%), respectively (p=0.067). At the time of FN episodes, 25/31 (80.6%) Turkish patients were in remission compared to 19/19 (100%) of refugee patients; this difference was not statistically significant (p=0.071).

Table I: Patient characteristics

Variable	Turkish Patients	Refugee/ Immigrant Patients	p
Total number of patients	31	19	
Demographics			
Male sex*	22 (71.0)	14 (73.7)	1.000
Disease characteristics*			
Type of malignancy			
Lymphoma	9 (29.0)	1 (5.3)	0.067
Solid tumor	22 (71.0)	18 (94.7)	
Remission status at FN			
In remission	25 (80.6)	19 (100)	0.071
Non-remission	6 (19.4)	0 (0)	
Socioeconomic characteristics*			
Monthly household income ≤1× minimum wage	12 (38.7)	18 (94.7)	<0.001
Parental education			
Pre-primary/primary	10 (32.3)	14 (73.7)	0.008
Secondary or higher	21 (67.7)	5 (26.3)	
Living conditions			
Number of rooms			
2 rooms*	6 (19.4)	0 (0)	0.041
3 rooms*	25 (80.6)	19 (100)	
Mean (range)	2.8 (2-3)	3.0 (3-3)	
Heating system*			
Central heating	18 (58.1)	14 (73.7)	0.366
Other heating systems	13 (41.9)	5 (26.3)	
Household members†	4 (2-7)	4 (2-6)	0.638
Persons per room†	1.33 (0.5-3.0)	1.33 (0.75-3.0)	0.507

**: n(%) (Fisher's exact test), †: median(range) (Mann–Whitney U), At the time of data collection (2022), the Turkish minimum wage was 5004 TL/month (approximately $300 USD). Income at or below this threshold represents extreme poverty in the Turkish socioeconomic context.*

Clinical presentation and physical findings

The most common presenting symptoms were fever (96%, n=48), fatigue (22%, n=11), and sore throat (10%, n=5). Physical examination revealed mucositis in 62% (n=31) of patients and oropharyngeal hyperemia in 30% (n=15) of patients. The distribution of presenting symptoms and physical findings was comparable between Turkish and refugee groups (p>1.000 for all comparisons). Detailed clinical presentation and physical findings are presented in Table II.

The median time interval between the last chemotherapy administration and the onset of fever was 5.0 days for both Turkish (IQR: 3.5-6.0, range: 1-10 days) and refugee children (IQR: 4.5-6.5, range: 2-12 days), with no significant difference between groups (p=0.473).

Microbiological evaluation

Blood cultures were obtained from all patients prior to antibiotic initiation. Culture positivity was observed in 6 of 50 (12.0%) patients, with a significantly higher rate among refugee patients (5/19 [26.3%] vs. 1/31 [3.2%], p=0.024) (13,14). The identified organisms were *Escherichia coli* (n=2), *Klebsiella pneumoniae* (n=1), *Staphylococcus epidermidis* (n=2), and *Staphylococcus aureus* (n=1). All three Gram-negative *Enterobacterales* isolates (two *E. coli* and one *K. pneumoniae*) were identified in the refugee/immigrant group, and both *E. coli* isolates were extended-spectrum β-lactamase (ESBL)-producing; these two

Table II: Clinical features and outcomes of febrile neutropenia episodes

Variable	Turkish patients	Refugee/ Immigrant patients	p
Total number of patients	31	19	-
Presenting symptoms*			
Fever at presentation	30 (96.8)	18 (94.7)	1.000
Fatigue	7 (22.6)	4 (21.1)	1.000
Sore throat	3 (9.7)	2 (10.5)	1.000
Physical examination findings*			
Mucositis on examination	19 (61.3)	12 (63.2)	1.000
Oropharyngeal hyperemia	9 (29.0)	6 (31.6)	1.000
Treatment and outcomes† Length of hospital stay, days	10.42 (5-30)	12.05 (6-30)	0.335

**: n(%) (Fisher's exact test), †: median (range) (Mann–Whitney U)*

Table III: Treatment characteristics and clinical outcomes

Variable	Turkish citizens	Refugees	p
Total number of patients	31	19	-
Empirical antibiotic regimen*			
Single-agent	16 (51.6)	8 (42.1)	0.718
Combination therapy	15 (48.4)	11 (57.9)	
Antifungal therapy*	8 (25.8)	5 (26.3)	1.000
Length of hospital stay, days †	10.4±5.6	12.1±5.9	0.335
Median (IQR)	8.0 (7.0-14.0)	11.0 (8.0-14.0)	
Treatment intensity†	1.74±0.82	1.84±0.76	0.668

**: n(%) (Fisher's exact test), †: mean±SD (Independent Samples T Test)*

patients were escalated to meropenem in accordance with antimicrobial susceptibility results. As all patients had indwelling port catheters, the *S. epidermidis* isolates (one in each group) were regarded as clinically significant catheter-associated organisms rather than contaminants. All patients tested negative for SARS-CoV-2, and respiratory viral panel testing identified one positive case of influenza (2.0%).

Socioeconomic characteristics

Significant socioeconomic disparities were identified between groups (Table I). Household income at or below the minimum wage (≤1× minimum wage; 5004 TL/month in 2022, approximately $300 USD) was documented for 18/19 (94.7%) of refugee families compared to 12/31 (38.7%) of Turkish families (p<0.001). This marked income disparity reflects profound differences in economic status between the two populations.

Parental education levels also differed significantly. Among refugee families, 14/19 (73.7%) of parents had primary education only, compared to 10/31 (32.3%) of Turkish families (p<0.008). Secondary or higher education was attained by 21/31 (67.7%) of Turkish parents versus 5 /19 (26.3%) of refugee parents.

Housing conditions and household composition revealed additional differences (Table I). The number of individuals living in the same household was comparable between the two groups (median 4 persons in both groups; p=0.638), as was the degree of household crowding expressed as the number of persons per room (median 1.33 in both groups; p=0.507). Assessment of other housing parameters, including the number of rooms and heating systems, showed some differences, with detailed comparisons presented in Table I.

Treatment and clinical outcomes

The mean length of hospital stay was 10.42 days (range, 5-30) for Turkish patients and 12.05 days (range, 6-30) for refugee/immigrant patients (Table III). Despite the slightly longer hospital stay observed in the refugee group, this difference did not reach statistical significance (p=1.000). This comparable length of stay occurred despite the marked socioeconomic disparities described above, suggesting that standardized inpatient care protocols effectively normalized acute FN management outcomes between the two groups.

Treatment characteristics and clinical outcomes are summarized in Table III. Empirical antibiotic regimens were comparable between Turkish and refugee patients, with single-agent therapy used in 51.6% versus 42.1% and combination therapy in 48.4% versus 57.9%, respectively (p=0.718). Antifungal therapy was required in similar proportions between groups (25.8% vs. 26.3%, p=1.000). Hospital length of stay was significantly longer in patients receiving antifungal therapy compared to those who did not (16.7±7.3 vs. 9.1±3.4 days, p<0.001), regardless of residency status. However, the mean length of hospital stay showed no significant difference between Turkish and refugee patients (10.4±5.6 vs. 12.1±5.9 days, p=0.335). Treatment intensity, defined as the mean number of antimicrobial agents used, was similar between groups (1.74±0.82 vs. 1.84±0.76, p=0.668). In summary, despite significant socioeconomic disadvantages affecting the refugee population—including markedly lower household income (94.7% vs. 38.7% at or below minimum wage, p<0.001) and lower parental education (73.7% vs. 32.3% primary or less, p=0.008)—clinical outcomes during FN episodes, including length of hospital stay and treatment intensity, were comparable between Turkish and refugee children.

Discussion

In this retrospective study, we compared febrile neutropenia (FN) episodes in Turkish and refugee/migrant children with cancer and evaluated the potential impact of socioeconomic and living conditions on FN-related outcomes. Our findings demonstrate marked socioeconomic and housing disparities between the two groups. The vast majority of refugee families (94.7%) had a household income at or below the minimum wage level, compared with 38.7% of Turkish families, and parental education levels were significantly lower among refugees, with 73.7% having only primary education or less. Despite these profound disadvantages, no statistically significant differences were observed in length of hospital stay or intensity of antimicrobial treatment during FN episodes.

Children from refugee populations are generally considered to be at increased risk for infectious complications due to poor hygiene, overcrowded living environments, nutritional deficiencies, limited access to preventive health services, and language barriers that may delay medical care. Based on these factors, worse FN-related outcomes might be anticipated in refugee children. However, our results do not support this assumption for short-term inpatient FN outcomes.

One explanation for these findings is that all FN episodes were managed in the same standardized inpatient setting. Regardless of home living conditions or socioeconomic status, both refugee and Turkish patients were hospitalized and treated under identical infection control measures, including strict hospital hygiene protocols, standardized FN management algorithms, and neutropenic diets prepared according to food safety regulations. These institutional practices likely minimized exposure to environmental risk factors present in the home setting and contributed to comparable short-term outcomes during hospitalization.

Importantly, although overall clinical outcomes were similar, blood culture positivity was significantly higher among refugee patients. This finding may reflect delayed presentation to healthcare facilities, higher baseline microbial colonization, and suboptimal living and sanitation conditions (13,14). Nevertheless, this increased rate of documented bacteremia did not translate into longer hospitalization or greater treatment intensity. Early initiation of empirical broad-spectrum antibiotics, adherence to standardized FN treatment protocols, and close inpatient monitoring likely mitigated the clinical impact of microbiologically documented infections, resulting in similar short-term outcomes between groups.

All three Gram-negative Enterobacterales isolates—one Klebsiella pneumoniae and two *Escherichia coli*—were identified in the refugee/immigrant group, and both *E. coli* isolates were ESBL-producing. The remaining isolates comprised one *Staphylococcus aureus* in the refugee/immigrant group and one *S. epidermidis* in each group; given that all patients had indwelling port catheters, these latter isolates were regarded as clinically significant catheter-associated organisms rather than contaminants. This predominance of Gram-negative and multidrug-resistant organisms among refugee children is consistent with prior reports documenting high rates of ESBL-producing Enterobacterales and other multidrug-resistant infections, including carbapenem-resistant bloodstream infections, in vulnerable pediatric oncology populations (15). Several mechanisms may contribute, including prior antibiotic exposure, disrupted healthcare continuity, crowded living conditions during displacement, and differences in baseline gastrointestinal colonization. Importantly, both patients with ESBL-producing *E. coli* were promptly escalated to meropenem in accordance with culture results, and their clinical course was comparable to that of the overall cohort. This observation reinforces the central finding of our study: when a standardized inpatient protocol with timely, culture-guided antimicrobial escalation is applied, the higher burden of resistant pathogens among refugee children does not necessarily translate into worse short-term outcomes. Nonetheless, this pattern underscores the importance of incorporating local and population-specific resistance epidemiology into empiric antimicrobial decision-making and supports the potential value of targeted admission screening for multidrug-resistant organisms to guide both empiric therapy and infection-control practices in this population.

Beyond hospitalization-related factors, the structure of the Turkish healthcare system may have contributed substantially to these findings. Refugees under temporary protection status are granted free and unrestricted access to pediatric oncology services, eliminating financial barriers that might otherwise delay care. This is particularly relevant given that nearly all refugee families in our cohort lived in extreme poverty. In addition, referral of pediatric oncology patients to tertiary centers ensures access to experienced multidisciplinary teams and standardized care pathways, which may further reduce outcome disparities.

Effective communication also plays a critical role in FN management. Prompt recognition of fever, early hospital referral, and accurate reporting of symptoms are essential for optimal outcomes. These processes can be challenging for families with low educational attainment and language barriers. At our center, the availability of professional interpreters and telephone-based translation services supported by the national health system likely facilitated timely communication, improved caregiver understanding of warning signs, and enhanced adherence to medical recommendations.

It is important to emphasize that our findings should not be extrapolated to long-term cancer outcomes. Febrile neutropenia represents an acute complication managed intensively in a controlled hospital environment. In contrast, overall survival and treatment success depend on multiple factors beyond inpatient FN management, including adherence to outpatient therapy, nutritional status, continuity of care, and living conditions between chemotherapy cycles. Previous studies have shown poorer long-term outcomes among refugee children with cancer despite access to healthcare, suggesting that socioeconomic disadvantages continue to influence survival outside the hospital setting (16-20).

From a health policy perspective, our results highlight the potential of structured healthcare integration to reduce short-term outcome disparities in vulnerable populations. While studies from Europe have reported persistent inequalities in cancer outcomes among migrant populations, often related to delayed diagnosis and inadequate supportive care, our findings suggest that universal health coverage, centralized tertiary care, standardized treatment protocols, and comprehensive language support may help equalize outcomes for acute complications such as FN (21,22).

Nevertheless, significant challenges remain. Extreme poverty, inadequate housing and sanitation, food insecurity, and limited social support continue to affect refugee families and may increase the risk of infection during outpatient treatment periods. The lack of adequate sanitation infrastructure, in particular, represents an ongoing risk factor for recurrent FN episodes, even if individual episodes are effectively managed during hospitalization (23). Addressing these broader social determinants of health will require sustained policy efforts, intersectoral collaboration, and international support aimed at improving living conditions and environmental health (24,25).

Limitations

This study has several limitations. Its retrospective, single-center design and modest sample size limit generalizability. The analysis focused on short-term inpatient outcomes, and no multivariable analyses were performed; therefore, the

findings reflect associations rather than causal relationships. To ensure statistical independence, only a single FN episode per patient was included in the analysis; while this approach avoided clustering effects arising from repeated episodes within the same individual, it does not capture the full burden of recurrent FN, which may disproportionately affect socioeconomically disadvantaged children, and this should be taken into account when interpreting our findings. In addition, the small number of positive blood cultures limits the conclusions that can be drawn regarding pathogen distribution and antimicrobial resistance patterns. Finally, psychosocial factors, nutritional status, and vaccination history were not systematically assessed. Future prospective, multicenter studies incorporating both short- and long-term outcomes are needed to better understand FN risk and cancer care trajectories in refugee populations.

Conclusion

In conclusion, despite profound socioeconomic disadvantages, refugee children with cancer experienced short-term FN outcomes comparable to those of Turkish patients when managed in a standardized inpatient setting. These findings suggest that system-level interventions—such as universal access to healthcare, centralized specialized care, evidence-based protocols, and language support—may help mitigate the impact of socioeconomic inequalities on acute treatment-related complications.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Bilkent City Hospital (04.02.2026, reference number: TABED 2-26-1944).

Contribution of the authors

Study conception and design: FBK,SÇ,İİE; data collection: FBK, AYE; analysis and interpretation of results: FBK,DÖ,AY,SÇ ; draft manuscript preparation: FBK,AÖP,NS. All authors reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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