J Compr Ped. 2025 February; 16(1): e148125 https://doi.org/10.5812/jcp-148125

Published Online: 2025 March 9 **Research Article**

Predictive Factors for Duration of Fever in Neutropenic Febrile Episodes in Children with Cancer

Elham Shahgholi [1], Mohsen Jafari [1], Mohammad Kajiyazdi [1,*], Mohammad Ali Ehsani [1], Mahdi Lahni [1]

[1] Bahrami Children Hospital, Tehran University of Medical Sciences, Tehran, Iran

[*] ***Corresponding Author:*** Bahrami Children Hospital, Tehran University of Medical Sciences, Tehran, Iran. Email: mkajiyazdi50@gmail.com

Received: 15 May, 2024; **Revised:** 26 January, 2025; **Accepted:** 25 February, 2025

Abstract

Background: Febrile neutropenia (FN) is one of the most important complications in pediatric oncology. The present study aimed to determine the predictive factors of fever duration in Iranian pediatric patients with FN.

Methods: This cross-sectional study was conducted on episodes of FN in children with cancer undergoing chemotherapy, admitted to the hospital with an oral temperature ≥ 38.3°C or at least two readings of oral temperature ≥ 38°C within one hour, and an absolute neutrophil count (ANC) ≤ 1500/μL at the time of admission. All children were treated according to our routine protocol for the management of FN. Potential predictive factors were recorded at the time of admission. The time of defervescence was considered the outcome variable. Ordinal regression analysis was used to determine the independent factors that could significantly predict the duration of fever in febrile neutropenic episodes.

Results: One hundred and eighty FN episodes in children with cancer (53.3% boys, 46.7% girls, mean age 5.48 ± 3.44 years) were included in our study. Independent predictive factors were the severity of neutropenia (P = 0.01), patients' general condition (P = 0.02), higher temperature ≥ 39°C (P = 0.006), higher serum C-reactive protein (CRP) > 90 (P = 0.04), positive central catheter culture (P = 0.00), and having at least one positive culture (P = 0.005).

Conclusions: We conclude that the severity of neutropenia, patients' poor general condition, higher temperature, higher serum CRP, and having at least one positive blood, urine, or central catheter culture are significant predictors of the duration of fever in FN episodes.

Keywords: Febrile Neutropenia, Fever, Chemotherapy, Predictive Factors, Child

1. Background

Febrile neutropenia (FN) is one of the most important complications in pediatric patients undergoing chemotherapy for their underlying malignancies (1). During FN episodes, patients are potentially at risk of bacterial infections, ranging from mild to severe (2, 3), which can increase mortality and morbidity in individuals with hematologic malignancies (4). In clinical practice, most children who develop chemotherapy-induced neutropenia associated with fever are immediately hospitalized for further diagnostic evaluation and empiric therapy with broad-spectrum parenteral antibiotics until resolution of fever and recovery of absolute neutrophil count (ANC) (5). This approach leads to increased length of hospital stay, drug resistance, nosocomial infections, overtreatment, emotional burden on patients and parents, and increased costs for families and the healthcare system (6, 7). Additionally, FN can potentially occur due to viral infections, blood transfusions, drugs, and the underlying malignancy, and hence, an aggressive approach to such patients may not always be necessary (7).

To reduce the morbidities and costs associated with the management of FN episodes, clinical practice guidelines strongly recommend oncologists incorporate validated risk stratification models into the routine clinical management of FN patients (8). According to various systematic reviews, many prediction rules have been used to stratify FN pediatric patients into high- and low-risk groups for invasive bacterial infections based on predictive factors such as

the type of underlying malignancy, patients' clinical signs and symptoms, laboratory markers, and chemotherapy regimen (9-13). However, no single prediction rule can be universally recommended due to differences in study populations, the definition of outcomes, included risk factors, and statistical methods (14, 15).

According to a recent guideline, risk prediction rules for FN patients should be locally validated before being used in a specific geographical and healthcare setting (14). This is particularly important in developing countries where healthcare resources are limited and social security coverage is low (16). So far, no risk prediction model has been used in the Iranian pediatric population.

2. Objectives

The present study aimed to determine the clinical and para-clinical predictors of fever duration in FN episodes in Iranian pediatric oncology patients.

3. Methods

3.1. Study Characteristics

This cross-sectional study was conducted from January 2016 to January 2018 at Bahrami Children's Hospital, Tehran, managed by the Blood Department. The study population consisted of admitted children with FN undergoing chemotherapy for hematological or non-hematological malignancies. Sampling was done using a simple method, and the sample size was determined using the variable of pulmonary infection (33%) from the Bakhshi et al.'s study and the Cochran's formula ($\alpha = 0.05$, $d = 0.2P$) (2). All available patients who met the inclusion criteria were included in the study. The study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.CHMC.REC.1400.163). The principles of the Declaration of Helsinki were observed throughout the study.

3.2. Inclusion and Exclusion Criteria

The study population consisted of admitted children with FN undergoing chemotherapy for hematological or non-hematological malignancies. Only patients with a single oral temperature of 38.3°C or at least two oral temperatures ≥ 38°C within one hour and an ANC ≤ 1500/μL at the time of admission were included in the study (1). Confounding variables that may cause bias were included in the study's exclusion criteria. Children who developed an FN episode during hospitalization, had a history of recent allogeneic stem cell transplantation, or had an apparent source of infection at the time of admission (e.g., acute gastroenteritis and acute otitis media) were excluded.

3.3. Patient Management

After obtaining a detailed history and a complete physical examination, the children were admitted to hematology-oncology wards and managed according to our FN management guidelines (17). Laboratory tests included hemoglobin level, total leukocyte count (TLC), ANC, platelet count, erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP) levels. Blood, urine, and central catheter cultures were also obtained, and a chest radiograph was performed. After obtaining the cultures, the patients were treated empirically with intravenous amikacin 5 mg/kg and ceftazidime 50 mg/kg every 8 hours. In FN patients with an indwelling portal catheter, hemodynamic instability, chemotherapy-induced mucositis, those admitted during the first 48 hours following prior discharge, or those who received fluoroquinolones as prophylaxis, amikacin was replaced with vancomycin 15 mg/kg every 6 hours. In the case of persistent fever despite 120 hours of broad-spectrum antibiotic therapy, empiric antifungal therapy was started.

3.4. Study of Variables

The outcome variable was defined as the duration of fever, categorized as < 72 hours, 72 - 120 hours, and > 120 hours. The independent predictive variables included age, gender, underlying malignancy (hematologic/non-hematologic), the time interval between the last session of chemotherapy and initiation of FN, oral temperature, patients' general condition (classified as poor; poor general condition defined as altered consciousness, unstable vital signs, hypoxia, and inability to maintain oral intake), indwelling portal catheter, hemoglobin level, TLC, ANC (further categorized as mild, 1000 - 1500/μL; moderate, 500 - 1000/μL; severe, < 500/uL), platelet count, ESR, CRP, positive cultures (blood, urine, central catheter), and changes in the chest radiograph.

3.5. Statistical Analysis

Statistical analysis was performed using the SPSS statistical package, version 21 (SPSS, Inc, Chicago, IL). Descriptive data were presented as mean ± SD for continuous variables and percentages for categorical variables. Univariate analysis was used to determine the independent variables associated with the study outcome. The potential predictors statistically

associated with the duration of fever were selected for ordinal regression analysis. A collinearity test was used to determine any strong correlation among the predictor variables. The model's goodness-of-fit was also determined. A P-value of ≤ 0.05 was regarded as statistically significant.

4. Results

4.1. Patients' Characteristics

From January 2016 to January 2018, a total of 180 episodes of FN in children with underlying malignancy who met the inclusion criteria were recruited into the study. Ninety-six (53.3%) of the participants were boys, with a mean age of 5.48 ± 3.44 years (ranging from 1 to 16 years). The most common malignancies were of the hematological type, with acute lymphoblastic leukemia contributing to 60%. All patients had an oral temperature ≥ 38°C and ANC ≤ 1500/μL at presentation. A total of 26 (14.4%) patients had a documented infection, revealed by having at least one positive blood, urine, or catheter culture. The majority of patients (59.4%) achieved defervescence during the first 72 hours after admission. In 23.9% of patients, fever resolved during the 72-120 hour period after admission. Thirty patients (16.7%) were still febrile after 120 hours of hospitalization. Clinical and paraclinical characteristics of participants are summarized in Table 1.

4.2. Predictors of Fever Duration

According to the univariate analyses, there was a statistically significant association between the duration of fever and body temperature, general condition, indwelling portal catheter, ANC, degree of neutropenia, hemoglobin, platelet count, serum CRP > 90, positive blood culture, positive catheter culture, having at least one positive culture, and chest radiograph changes (Table 2). The collinearity test revealed a strong correlation between ANC and the grade of neutropenia, as well as between blood culture, urine culture, portal catheter culture, and having at least one positive culture. To avoid estimation problems, the grade of neutropenia and having at least one positive culture were used in the final ordinal regression model as they explained more of the variability in the outcome variable.

The final model, referred to as the general model with influencing variables denoted as X, was statistically significant (P < 0.05) when compared to the intercept-only model. The intercept-only model is a regression model that does not take into account the main and secondary variables of the study. This indicates that the variables listed in Table 3 have an impact on the duration of fever. Furthermore, the proposed model, along with the results from the ordinal regression analysis, demonstrates a goodness-of-fit ($X^2 = 310$, with P = 0.885), indicating the suitability of the model. Table 3 demonstrates that several variables, including CRP, body temperature, general condition, positive culture, and neutropenia levels, significantly impact the duration of fever (P < 0.05). For example, a one-degree increase in fever temperature leads to a 1.369-step increase in the duration of fever (transitioning from 72 > hours to 119 - 72 hours or from 119 - 72 hours to ≥ 120 hours). Additionally, a poor general condition is associated with a 1.392-step increase in the duration of fever compared to a good general condition.

5. Discussion

Children with FN are a heterogeneous group at risk of severe infections and their complications. Recently, there has been much emphasis on risk stratification of FN patients based on the early prediction of adverse outcomes so that children categorized as low-risk (according to validated prediction rules) can be treated less aggressively with a better quality of life, even on an outpatient basis (5-9). In this regard, several studies have been conducted to develop models for predicting adverse outcomes, mainly severe infection and/or mortality in pediatric FN patients; however, validated predictive scores and algorithms are still lacking and urgently needed (1-16, 18). Persistence of fever is one of the criteria for changing antibiotics or adding antifungal drugs. To our knowledge, very few studies have investigated the predictive factors of fever duration as the main adverse outcome in children with FN.

In the present study, the risk factors related to prolonged fever in children with FN were investigated in two centers. In general, although most episodes of FN are assumed to result from an infection, blood cultures were positive in less than a third of febrile neutropenic episodes (18). Similar to the literature, the present study had a bacteremia rate of 21%. It should be noted that other factors such as viral infection, blood products, and chemotherapy agents can also cause fever in neutropenic children (2). Phillips et al. reported that a history of more than two previous episodes of FN, abnormal chest radiograph, and being on oral antibiotic therapy at presentation could predict invasive bacterial or fungal infection and/or mortality in children with FN (10).

Table 1. Characteristics of Children with Febrile Neutropenic Episodes

Parameters	N	Mean ± SD	Min - Max
Age (y)	180	5.4 ± 3.44	1 - 16
Oral temperature (°C)	180	38.5 ± 0.43	38 - 40
Time since last chemotherapy session (d)	172	12.6 ± 21.78	0 - 240
WBC (mL)	180	1117 ± 818.25	100 - 5800
Hb (g/dL)	180	8.9 ± 2.04	3 - 14.5
PLT (10^3/mm^3)	180	118.5 ± 105.16	3 - 468
ANC (mL)	44	647.18 ± 454.94	16 - 1500
CRP (mg/L)	180	54.3 ± 35.38	2 - 136
Gender (n = 180) [a]			
Male	96 (53.3)	-	-
Female	84 (46.7)	-	-
Underlying malignancy (n = 180) [a]			
Hematological	138 (76.7)	-	-
Non-hematological	42 (23.3)	-	-
Indwelling portal catheter (n = 180) [a]			
Yes	29 (16.1)	-	-
No	151 (83.9)	-	-
Patients' general condition (n = 180) [a]			
Fair	121 (67.2)	-	-
Poor	59 (32.8)	-	-
Chest radiograph changes (n = 180) [a]			
Yes	35 (19.4)	-	-
No	145 (80.6)	-	-
Grade of neutropenia (n = 180) [a]			
Mild	13 (7.2)	-	-
Moderate	38 (21.1)	-	-
Severe	129 (71.7)	-	-
Blood culture (n = 180) [a]			
Positive	24 (13.3)	-	-
Negative	156 (86.7)	-	-
Catheter lumen culture (n = 180) [a]			
Positive	8 (4.4)	-	-
Negative	172 (95.6)	-	-
Urine culture (n = 180) [a]			
Positive	3 (1.7)	-	-
Negative	177 (98.3)	-	-

Abbreviations: N, number of patients; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; ANC, absolute neutrophil count; CRP, C-reactive protein.
[a] Values are expressed as No. (%).

According to Haeusler et al., the advanced stage of underlying malignancy, concomitant comorbidities, and bacteremia could predict mortality in children with FN (11). Gurlinka et al. found that laboratory markers, namely thrombocytopenia (platelet count < 50,000) and serum CRP (> 90 mg/L), were predictors of mortality in the FN population (13). On the other hand, Lehrnbecher et al. published findings showing that white blood cell (WBC) counts, ESRs, and ANCs do not differ significantly between fever of unknown origin and documented infection in FN (14).

In our study, despite the initial associations found between the duration of fever, patient's general condition, indwelling portal catheter, ANC, degree of neutropenia, hemoglobin, platelet count, serum CRP, positive blood culture, positive catheter culture, having

Table 2. Univariate Analysis of Predictor Variables by Duration of Fever [a]

Parameters	Duration of Fever			P-Value
	< 72 h (n = 107)	72 - 119 h (n = 43)	≥ 120 h (n = 30)	
Sex				0.642
Male	57 (53.3)	21 (48.8)	18 (60)	
Female	50 (46.7)	22 (51.2)	12 (40)	
Age (y)	5.69 ± 3.28	5.48 ± 4.03	4.54 ± 2.65	0.339
Underlying malignancy				0.96
Hematological	84 (60)	33 (23.6)	23 (16.4)	
Non-hematological	23 (57.5)	10 (25)	7 (17.5)	
Indwelling portal catheter				0.003
Yes	14 (13.1)	4 (9.3)	11 (36.7)	
No	93 (86.9)	39 (90.7)	19 (63.3)	
General condition				0.000
Fair	91 (85)	26 (60.5)	4 (13.3)	
Poor	16 (15)	17 (39.5)	26 (86.7)	
Last chemotherapy sessionmedian IQR (d)	8 (6-13)	7 (6-13)	7 (2.5-9.5)	0.189
Oral temperature (°C)	38.37 ± 0.38	38.71 ± 0.45	38.74 ± 0.43	0.000
Chest radiograph changes				0.000
Yes	13 (12.14)	6 (13.9)	14 (46.7)	
No	91 (85.0)	37 (86.0)	16 (53.3)	
WBC (/mL)	1145.79 ± 714.972	1206.28 ± 1109.946	886.67 ± 640.438	0.222
ANC (/mL)	638.27 ± 348.99	591.16 ± 326.124	414.7 ± 221.79	0.005
Grade of neutropenia				0.000
Mild	13 (12.1)	4 (9.3)	1 (3.33)	
Moderate	52 (48.6	14 (32.6)	3 (10)	
Sever	42 (39.3)	25 (58.1)	26 (86.66)	
Hb (mg/dL)	9.14 ± 1.95	8.9 ± 2.01	7.92 ± 2.18	0.014
PLT (10^3/mm^3)	132.58 ± 103.04	130.88 ± 117.94	50.86 ± 60.16	0.000
CRP (g/L)	46.5 ± 34.8	61.4 ± 32.6	75.3 ± 31.3	0.000
Blood culture				0.001
Positive	7 (6.5	7 (16.3)	10 (33.3)	
Negative	100 (93.5)	36 (86.7)	20 (66.7)	
Catheter lumen culture				0.000
Positive	1 (0.9)	1 (2.2)	6 (20)	
Negative	106 (99.1)	42 (97.7)	24 (80)	
Urine culture				0.615
Positive	1 (0.9)	1 (2.2)	1 (3.3)	
Negative	106 (99.1)	42 (97.7)	29 (80)	
At least one positive culture				0.001
Yes	8 (7.5)	7 (16.3)	11 (36.7)	
No	99 (92.5)	38 (83.7)	19 (63.3)	

Abbreviations: WBC, white blood cell; Hb, hemoglobin; PLT, platelet; ANC, absolute neutrophil count; CRP, C-reactive protein.

[a] Values are expressed as mean ± SD or No. (%).

at least one positive culture, and chest radiograph changes, the ordinal regression analysis revealed that only higher serum CRP (> 90 mg/L), patients' poor general condition, higher oral temperature at presentation, having at least one positive culture, and severe neutropenia (ANC < 500/uL) could significantly predict the duration of fever in neutropenic children with underlying malignancy.

Regarding the association of high CRP (> 90 mg/L) with the duration of fever and response to initial treatment, the results were consistent with the Gurlinka et al. study (13). It is noted that none of the other risk

Table 3. Predictors of Fever Duration in Children with Febrile Neutropenia from Ordinal Regression Analysis

Variables	Estimate	Std. Error	95% Confidence Interval		P-Value
			Lower Bound	Upper Bound	
Platelet	-2.796E-6	2.304E-6	0.00	1.72E-6	0.225
Hemoglobin	0.056	0.114	-0.19	0.25	0.621
C-reactive protein	0.012	0.006	0.001	0.02	0.040
Temperature	1.369	0.498	-	-	0.006
Poor general condition vs. good general condition	1.392	0.612	0.68	2.48	0.020
Portal catheter + vs. portal catheter-	0.139	0.502	-1.13	0.98	0.782
CXR changes + vs. CXR changes-	0.806	0.468	-0.37	1.42	0.085
At least 1 positive culture vs. no positive culture	1.692	0.607	-1.92	3.09	0.005
Severe neutropenia	-1.193	0.464	-2.05	1.10	0.010
Moderate neutropenia vs. mild neutropenia	-0.747	0.701	-1.27	0.85	0.287

factors in our study were found to be significant predictors of fever duration in the study of Gurlinka et al. (13).

5.1. Conclusions

Febrile neutropenia is a common and serious complication in pediatric oncological patients undergoing chemotherapy, leading to increased morbidity and mortality. The present study aimed to identify prognostic risk factors for FN, specifically in terms of fever duration. According to our findings, several factors, including serum CRP levels, the overall condition of the patients, initial oral temperature, positive culture result, and neutropenia grade, were found to be significant predictors of fever duration. These factors can be utilized in the risk stratification of children with FN. However, it is important to note that our study had a limited sample size, which is a notable limitation. To further investigate risk factors and develop accurate treatment guidelines based on risk prediction, it is recommended to conduct larger and more comprehensive studies.

Acknowledgements

The authors wish to thank the Research Development Center of Bahrami Children's Hospital.

Footnotes

Authors' Contribution: E. Sh.: Study concept and design; M. L.: Acquisition of data; M. K.: Analysis and interpretation of data; M. L.: Drafting of the manuscript; M. K., M. J., and M. A. E.: Critical revision of the manuscript for important intellectual content; E. Sh.: Statistical analysis; M. k.: Administrative, technical, and material support; E. Sh., M. K., and M. J.: Study supervision.

Conflict of Interests Statement: The authors declared no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after its publication.

Ethical Approval: The study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.CHMC.REC.1400.163).

Funding/Support: The present study was partially supported by Bahrami Hospital, Faculty of Medicine, and an educational and research scholarship from Tehran University of Medical Sciences.

Informed Consent: Informed consent was obtained from all participants.

References

1. Castagnola E, Fontana V, Caviglia I, Caruso S, Faraci M, Fioredda F, et al. A prospective study on the epidemiology of febrile episodes during chemotherapy-induced neutropenia in children with cancer or after hemopoietic stem cell transplantation. *Clin Infect Dis*. 2007;**45**(10):1296-304. [PubMed ID: 17968824]. https://doi.org/10.1086/522533.
2. Bakhshi S, Padmanjali KS, Arya LS. Infections in childhood acute lymphoblastic leukemia: an analysis of 222 febrile neutropenic episodes. *Pediatr Hematol Oncol*. 2008;**25**(5):385-92. [PubMed ID: 18569840]. https://doi.org/10.1080/08880010802106564.
3. Kanathezhath B, Radhakrishnan A, Kumar S, Warrier N. Infections and Febrile Neutropenia in Pediatric Acute Lymphoblastic Leukemia Patients from South India: Microbial Profile and Outcome Analysis. *Blood*. 2015;**126**(23):4513. https://doi.org/10.1182/blood.V126.23.4513.4513.

4. Ghosh S, Chakraborty M, Samanta S, Sinha N, Saha S, Chattopadhyay A, et al. Analysis of blood stream infections, antibiograms and clinical outcomes in haematological patients with febrile neutropenia: data from a tertiary care haematology institute in India. *Ann Hematol*. 2021;**100**(2):395-403. [PubMed ID: 33140134]. https://doi.org/10.1007/s00277-020-04324-8.
5. Seth R, Bhat AS. Management of common oncologic emergencies. *Indian J Pediatr*. 2011;**78**(6):709-17. [PubMed ID: 21399956]. https://doi.org/10.1007/s12098-011-0381-5.
6. Rosa RG, Goldani LZ. Factors associated with hospital length of stay among cancer patients with febrile neutropenia. *PLoS One*. 2014;**9**(10). e108969. [PubMed ID: 25285790]. [PubMed Central ID: PMC4186788]. https://doi.org/10.1371/journal.pone.0108969.
7. Miedema KG, Tissing WJ, Abbink FC, Ball LM, Michiels EM, van Vliet MJ, et al. Risk-adapted approach for fever and neutropenia in paediatric cancer patients--a national multicentre study. *Eur J Cancer*. 2016;**53**:16-24. [PubMed ID: 26700076]. https://doi.org/10.1016/j.ejca.2015.10.065.
8. Downes KJ, Zaoutis TE, Shah SS. Guidelines for Management of Children With Fever and Neutropenia. *J Pediatric Infect Dis Soc*. 2013;**2**(3):281-5. [PubMed ID: 26619484]. https://doi.org/10.1093/jpids/pit035.
9. Haeusler GM, Carlesse F, Phillips RS. An updated systematic review and meta-analysis of the predictive value of serum biomarkers in the assessment of fever during neutropenia in children with cancer. *Pediatr Infect Dis J*. 2013;**32**(10):e390-6. [PubMed ID: 23673421]. https://doi.org/10.1097/INF.0b013e31829ae38d.
10. Phillips RS, Sutton AJ, Riley RD, Chisholm JC, Picton SV, Stewart LA, et al. Predicting infectious complications in neutropenic children and young people with cancer (IPD protocol). *Syst Rev*. 2012;**1**:8. [PubMed ID: 22588015]. [PubMed Central ID: PMC3351734]. https://doi.org/10.1186/2046-4053-1-8.
11. Haeusler GM, Phillips RS, Lehrnbecher T, Sung L, Ammann RA. The reporting of outcomes in studies of fever and neutropenia in children with cancer: time for consensus. *Pediatr Blood Cancer*. 2013;**60**(10):1563-4. [PubMed ID: 23813563]. https://doi.org/10.1002/pbc.24662.
12. Ammann RA, Bodmer N, Hirt A, Niggli FK, Nadal D, Simon A, et al. Predicting adverse events in children with fever and chemotherapy-induced neutropenia: the prospective multicenter SPOG 2003 FN study. *J Clin Oncol*. 2010;**28**(12):2008-14. [PubMed ID: 20231680]. https://doi.org/10.1200/JCO.2009.25.8988.
13. Gurlinka S, B N, Kini P, Aroor S, Mundkur S. Factors Associated with Adverse Outcome in Pediatric Febrile Neutropenia: Results from a Tertiary Care Hospital. *J Pediatric Perspectives*. 2017;**5**(12):6447-55. https://doi.org/10.22038/ijp.2017.26484.2273.
14. Lehrnbecher T, Robinson P, Fisher B, Alexander S, Ammann RA, Beauchemin M, et al. Guideline for the Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients: 2017 Update. *J Clin Oncol*. 2017;**35**(18):2082-94. [PubMed ID: 28459614]. https://doi.org/10.1200/JCO.2016.71.7017.
15. Phillips RS, Sung L, Ammann RA, Riley RD, Castagnola E, Haeusler GM, et al. Predicting microbiologically defined infection in febrile neutropenic episodes in children: global individual participant data multivariable meta-analysis. *Br J Cancer*. 2016;**114**(6):623-30. [PubMed ID: 26954719]. [PubMed Central ID: PMC4800297]. https://doi.org/10.1038/bjc.2016.28.
16. Prasad M, Chinnaswamy G, Arora B, Vora T, Hawaldar R, Banavali S. Risk predictors for adverse outcome in pediatric febrile neutropenia: Single center experience from a low and middle-income country. *Indian J Cancer*. 2014;**51**(4):432-7. [PubMed ID: 26842150]. https://doi.org/10.4103/0019-509X.175321.
17. Ritchey EDF KA, Meade JC; David. The Leukemias. In: Kliegman R, Joseph W, editors. *Nelson Textbook of Pediatrics*. Amsterdam, Netherlands: Elsevier Health Sciences; 2024.
18. Feld R. Bloodstream infections in cancer patients with febrile neutropenia. *Int J Antimicrob Agents*. 2008;**32 Suppl 1**:S30-3. [PubMed ID: 18778919]. https://doi.org/10.1016/j.ijantimicag.2008.06.017.