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Chemotherapy Induced Febrile Neutropenia and Its Association with Nosocomial Bacteraemia: Risk Factors and Prognosis

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Abstract: For decades, febrile neutropenia (FN) in cancer patients has been treated with utmost urgency, necessitating immediate initiation of empirical broad spectrum intravenous antibiotics. Recently, it has become evident that neutropenic cancer patients are not a homogeneous group and that practice guidelines may vary on their risk status. Thus, this study aimed to evaluate the significance and risk factors predisposing to a positive blood culture in febrile pediatric cancer patients with chemotherapy-induced FN, and to study the impact of nosocomial bacteraemia on clinical course and outcome of these febrile episodes. A prospective cohort study included febrile episodes occurring in a large group of pediatric patients with chemotherapy-induced FN at the National Cancer Institute over a period of one year. Blood cultures were drawn and micro-organisms were identified. Among 729 episodes of fever and neutropenia recorded in 475 patients, bacteraemia was detected in 46.2% of episodes of which 56% showed a lengthy episode (≥ 7days). Coagulase-negative Staphylococci (CoNS) were associated with the least complications while Gram negative bacteraemia (GNB) were associated with the most severe blood stream infections (BSI). The overall mortality rate was 7.5% (n=55) and was significantly higher among BSI (11%) than those episodes that were not bacteraemic (4.6%). In addition, the mortality was significantly higher in GNB and mixed BSI, than in Gram positive BSI with $p< 0.001$. Logistic regression determined BSI, a lengthy episode, younger age of child with a relapsing tumor and presence of a canula as independent factors affecting mortality and thus prognosis of the child with FN. Results of the study suggest significant differences in the clinical characteristics of BSI by the different classes of micro-organisms in pediatric cancer patients with chemotherapy-induced FN. BSI profoundly influences course and outcome of episodes. Continuous multi-disciplinary surveillance of BSI is warranted in this group of patients to develop strategies for antimicrobial resistance control and treatment of infectious complications.

Keywords: Febrile Neutropenia; Nosocomial Bacteraemia; Pediatric Oncology.

INTRODUCTION:

Overall, childhood cancer constitutes a major problem of public health importance. The incidence of childhood cancer worldwide varies between 100 and 180 per 1,000,000 child/year [1]. Childhood cancer differs tremendously from adults and the

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principal groups are leukemias, and lymphomas [2].

Over the past few decades, management of childhood cancer has improved dramatically. However, significant morbidity and mortality from infectious complications still limit the success of newer modes of therapy. Children with cancer have an added risk of infection because of the use of immunosuppressive chemotherapy and radiation. In recent years, the risk has increased by the use of indwelling central venous catheters, more intensive chemotherapy, and the use of stem cell transplantation [3]. Moreover, children with neoplastic diseases have more prolonged and repeated contact with the hospital environment, increasing the risk of nosocomial infections [4].

Febrile neutropenia affects an ever-increasing number of persons worldwide and poses a major burden in health care and economic terms [5]. Febrile neutropenia among pediatric oncology patients is a frequent complication of chemotherapy. It occurs in 10 – 50% of pediatric patients with solid tumors and in over 85% of those with blood malignancies. It usually requires treatment for 7 – 12 days, at an estimated daily cost of over 1500 US $, and is also associated with a mortality rate of nearly 10% [6].

In a potentially life-threatening situation, the major challenge in cancer care presents as nosocomial infection in terms of clinical assessment, diagnosis and treatment. Blood stream infections (BSI) comprise about 20% of all nosocomial infections affecting cancer patients, including children and adults, with reported proportions ranging from 10% to 36% [7].

Hence this study was conducted to gain insight of the risk factors predisposing to blood stream infections, and to identify the most important micro-organisms involved, as well as to assess the prognosis of pediatric cancer patients with febrile neutropenia.

Subjects and Methods:

Study site and design: This prospective, single center cohort study was conducted at the National Cancer Institute, Cairo University.

Study population: All pediatric cancer in-patients treated with chemotherapy for a malignant disease and developing a febrile episode necessitating a blood culture test were included in the study. During the period from January to December 2007, 729 episodes were recorded in 475 patients.

Study Definitions:

- Fever was taken by axillary temperatures and was defined as a single reading of 38.5^{o} C or more or between 37.5 – 38.0^{o} C on two occasions during a 24 hour period.
- Patients were considered neutropenic if their Absolute Neutrophilic Count (ANC) was < 0.5 x 10^{9}/L or between 0.5 – < 1.0 x 10^{9}/L and was expected to decline dramatically below this level in the two successive days. During this period, children presenting with febrile neutropenia during their hospitalization for chemotherapy were treated with empirical, double agent, broad spectrum parentral antimicrobial therapy. Antibiotic therapy was continued until the patient became afebrile and ANC exceeded 1.0 x 10^{9}/L. The episode was considered to be successfully controlled when patients remained afebrile for 72 hours and clinical signs resolved. Persistence of fever for 7 days or more was defined a lengthy episode.
- Bloodstream infections (BSI) were considered in case of any organism isolated from blood and included both bacteraemia and fungemia.
- Clinically documented infections (CDI) were considered when there was a focus of infection on physical examination.

Microbiology: Two blood culture sets

were usually drawn from each patient within the first two days of fever from two separate veins. If the cannula site, portacath, or CVC was suspected as the source of infection, a blood sample was obtained from it as well. Collected blood was directly injected into Bactec® (Becton Dickinsion, USA) culture vials. Vials were incubated in the Bactec 9050 incubator after collection. Identification of isolates was carried out utilizing Sensititre AP80 and AP90 auto-identification plates (Accumed International Ltd.Intehone Lane East Grinsted, West Sussex, UK) for Gram-negative and Gram-positive organisms; respectively. Antimicrobial susceptibility testing was determined by using the criteria established by the ***National Committee for Clinical Laboratory Standards, 2000*** [8]**.** Blood cultures were performed in parallel with other cultures from existing clinical sites of infection whenever possible.

Ethical considerations: Verbal consent to participate in the study was obtained from the legal guardian of all patients before any data were included in the study. Data confidentiality was preserved throughout the study.

Statistical methods: Multiple episodes of infection in the same patient were considered as independent events. Outcome variables were defined as continuous fever at day 7 as a morbid condition and death as an end status of disease. Data was analyzed using the statistical packages SPSS version 15 and EpiInfo version 3.5.1 (to compute the relative risk and 95% confidence intervals). Quantitative data were expressed as mean $\pm$ SD. Qualitative data were expressed as frequency and percentage. Inferential comparisons between study groups employed Chi-square test (for qualitative data), as well as Student's ***t- test*** and one way ***ANOVA*** (to test for equality of means between other quantitative study variables). Stepwise Logistic regression

forward modeling was used to predict the estimate of the relative risk for factors affecting unfavorable prognosis (i.e. death of patients). A P – value < 0.05 was considered significant for all statistical tests.

Results:

During a one year period, 729 febrile episodes were admitted to the pediatric inpatient department of the National Cancer Institute. These episodes were identified in 408 (56%) males and 321 (44%) females. Of all febrile episodes, 337 (46.2%) were BSI of which 45.8% (n=187) and 46.7% (n=150) were recognized in males and females respectively with no statistically significant difference detected (P = 0.81). Patients' age ranged from 5 months to 18 years, with an overall mean age of 7.47 ± 4.63 years. The mean age for males and females was 7.75 ± 4.57 and 7.12 ± 4.68 years respectively which was statistically insignificant (P = 0.068). The original diagnoses at admission were acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), Lymphoma, and solid tumors in 38% (n=277), 25.7% (n=187), 13.7% (n=100), and 22.6% (n=165) of episodes respectively. Collectively 77.4% of episodes occurred in patients with hematological malignancies (n=564) with relapsing disease occurring in nearly 16% of episodes (n=116) [Table 1].

A clinically documented focus of infection (CDI) was detected in 58% (n=422) of episodes whereas 42% of episodes (n=307) lacked a focus. Gastroenteritis manifested by diarrhea with or without vomiting and abdominal pain was present at the time of fever in 18.5% (n=135) of patient episodes. Lower respiratory tract infections (LRTI) were recorded in 13.3% of occurrences (n=97). Pharyngitis and sore throat was reported in 7% (n=52), skin infections (perianal cellulitis or ulcers, skin abcesses or infected bed sores) were found in 8% of episodes (n=59) while catheter related infections were found in 6% (n=43) of

episodes. Evident eye and ear infections accounted for nearly 2% each while urinary tract infections were detected in only 0.8% (n=6) of patients [Table 2].

At the beginning of febrile episodes, ANC was below 0.1 x 10^9/L in about 51% (n=371), from 0.1 – < 0.5 x 10^9/L in 27% (n=197), and more than 0.5 – < 1.0 x 10^9/L in 22% (n=161) of episodes with no statistically significant difference detected between males and females. Platelet count below 25,000 x 10^9/L was recorded in nearly 31% (n=225) of episodes and the average length of all episodes was 7.72 ± 4.65 with insignificant statistical differences between males and females [Table 1].

BSI was detected in 46.2% of the febrile neutropenic episodes, by growth of blood cultures (n=337). As a single isolate, Gram-positive organisms were the observed cause of BSI in 44.8% of episodes (n=151). Gram-negative organisms accounted for 43.3% (n=146) of BSIs. Mixed infections were detected in nearly 11% (n=37) of the episodes. Fungi were found in 18 of isolates, being mixed with bacterial isolates in 15 cases and pure fungal growth in only 3 cases (0.9%). Results of etiologic agents of BSI are summarized in [Table 3].

Among the Gram-positive bacteraemia (GPB), 43.9% of the coagulase negative Staphylococci (CoNS) had no evident focus of infection (n=25/57). Twelve CoNS bacteraemia (21%) showed episodes ≥ 7 days and all these had an additional CDI; which was diarrhea or skin infections. Of the Streptococcal bacteraemia, 50% (n=20/40) showed no CDI and 37.5% (n=15/40) had episodes extending from 7 to 17 days; with LRTI and pharyngitis the commonest accompanying CDI in these prolonged episodes. Methicillin-resistant *S. aureus* (MRSA) accounted for 51.5% (n=17/33) of *S. aureus* isolates and were significantly associated with longer episodes, with mean episode duration of 11.90 ± 4.18 days, compared to Methicillin-

sensitive *S. aureus* (MSSA) which showed mean episode duration of 7.59 ± 4.61 with a P - value < 0.001. Moreover, all MRSA episodes, whether single isolates or mixed infections, had one or more concomitant infections, while 6 MSSA episodes showed no evident CDI.

A CDI was evident in 73% of Gram-negative bacteraemia (GNB) (n=107/146). Length of episode was found to be longer when Gram-negative organisms were isolated from blood cultures (8.96 ± 5.04 days). *Klebsiella positive cultures* were associated with a longer episode, but were not significantly different than other causes of GNB, with an episode duration of 8.67 ± 3.78 days compared to 7.68 ± 4.68 days (P = 0.31). Only 2 cases of *Klebsiella* episodes lasted less than 7 days. As regards other Gram-negative BSIs, 60% (n=15/25), 48% (n=10/21), and 47% (n=8/17) of Enterobacter spp., Pseudomonas spp., and Acinetobacter spp., respectively caused episodes ≥ 7 days. Of the mixed bacteraemia, 83% (31/37) showed an evident CDI.

A lengthy episode, extending for 7 days or more, was recorded in 41.4% of all episodes (n=302). The mean length of episodes for Gram-positive, Gram-negative and mixed infections were 7.61 ± 4.53, 8.96 ± 5.04 and 11.78 ± 5.41 days respectively while episodes that showed no growth on blood culture showed an average length of episode of 6.89 ± 4.16 days. Comparison of length of episodes by types of organisms detected, showed a highly significant difference between groups. Mixed infections showed a significantly longer length of episode as compared to other groups, while episodes with no growth showed a significantly shorter length that differed statistically from episodes of Gram-negative and mixed infections [Table 4].

The risk factors identified in the episodes with BSI and an isolated microorganism in comparison to those with

no growth show that age ≤ 7 years, length of episode, thrombocytopenia, profound neutropenia (< 0.1 x 10^9/L) and presence of a canula were highly significant with relative risks (RR) and 95% confidence intervals (95%CI) of; 1.68 (1.41 – 2.01), 1.8 (1.54 – 2.10), 1.65 (1.42 – 1.91), 1.74 (1.47 – 2.07) and 2.07 (1.82 – 2.36) respectively. The association between presence of a CDI and BSI was statistically significant with an increased risk of 1.54 (95% CI = 1.29 – 1.84) with P < 0.001. A solid tumor only increased the risk of BSI by 1.15 times and a relapsing tumor similarly increased the risk by 1.14 times. However these latter findings were statistically insignificant [Table 5].

An unfavorable outcome of febrile episodes, identified by death of patients, was reported in 55 of all 729 episodes with a mortality rate of 7.5%. BSI was clinically evaluated to have either contributed to or caused the terminal event through septicemia in 67% of all deaths (n=37/729). A significantly higher mortality rate of 11% was found among patients with BSI (n=37/337) as compared to those without BSI or no growth who showed a mortality rate of 4.6% (n=18/392) – P = 0.001. Additionally, a significantly higher mortality rate of 18.0% was observed for GNB and mixed infections (n=33/183), while GPB contributed to 2.7% of deaths (n=4/151) with P < 0.001. The risk of death was analyzed by stepwise forward logistic regression to identify the independent prognostic factors. BSI significantly increased the risk of death by more than 2 folds with RR = 2.36 and 95% CI = 1.26 – 4.39. Similarly the length of episode more than 7 days also increased the risk by 2.78 times (95%CI = 1.26 – 4.39), while a relapsing tumor and age ≤ 7 years increased the risk more than 3 folds each. On the other hand, presence of a canula increased the risk of death to nearly four folds, and all findings were statistically significant [Table 6].

Discussion:

The most common toxicity in pediatric cancer is chemotherapy – induced neutropenia. It is associated with considerable morbidity and mortality directly linked to duration and severity of episodes [9]**.** Findings from our study identified 46% of febrile episodes with BSI. Similar high figures were recorded by other researchers who carried out a surveillance study of nosocomial infections in pediatric hematology oncology patients, in Germany[10]**.**

The first line of defense in controlling bacterial invasion of the bloodstream is predominantly the neutrophils. Risk of developing infection significantly increases as the ANC falls below < 0.5 x 10^9/L and is highest when it falls below 0.1 x 10^9/L [11]**.** This is consistent with findings of our study where an ANC level below 0.1 x 10^9/L significantly increased the risk of BSI by more than 70%. Additionally, episodes extending for more than 7 days were encountered more frequently in BSI episodes than in non-BSI episodes (56% versus 29% respectively) with an increased risk 1.8 times which was statistically significant. These findings are in line with those from another study that reported profound neutropenia and duration of episodes as strongly associated with bacteraemia [12]**.** ANC < 0.1 x 10^9/L has consistently been reported as an important risk factor for bacteraemia [13] with some studies reporting more than a two-fold risk [14]**.**

Indicators of a positive blood culture in febrile children with cancer could be of help to stratify patients into low and high risk groups. In the present study, younger age group less than 7 years and the presence of CDI were significantly associated with more frequent BSIs. These are in line with other studies that reported young age as a risk factor for BSI [15]**.** It general, it is expected that younger children are more susceptible to infection and thus to bacteraemia especially with presence of

cancer. Additionally, another study reported 64% of their patients displaying overt CDIs of which 14% were positive for blood cultures [16]**.** Other factors that were found, in our study, to increase the risk of BSI were presence of a central venous catheter (RR = 2.07), and thrombocytopenia (RR=1.65). However, although a relapsing tumor was associated with a 14% increased risk for BSI, yet this finding was statistically insignificant. Similar studies reported presence of a catheter as a risk factor for bacteraemia [17]**,** and others found relapsing leukemia and low platelet count to increase the risk of BSI by 80% and 70% respectively [18]**.** The type of underlying disease although associated with a minor increased risk of bacteraemia in our patient population yet proved statistically insignificant. Likewise, other authors found no significant effect of underlying disease in relation to BSI [19].

In recent years, Coagulase-negative Staphylococci (CoNS) have been the most prevalent organisms [4]**.** In agreement, our results showed that CoNS were the commonest organisms isolated; they accounted for nearly 17% of all BSIs. Yet, not all CoNS bacteraemia constituted significant infections, as the majority of episodes were short with no CDI detected. Only 21% of CoNS bacteraemia in the present study had episodes of 7 days or longer and all these cases showed a concomitant infection of diarrhea or skin infections. None of the cases with CoNS bacteraemia had an unfavorable outcome, either as a single isolate or mixed. Similarly, other studies reported up to 13% of blood cultures positive for CoNS as true bacteraemia [20]. Thus, CoNS could be considered of low virulence. Streptococcal bacteraemia were not as subtle as CoNS bacteraemia, with nearly 38% of episodes extending for up to 17 days. Of these latter cases, LRTI and pharyngitis were the commonest CDIs. The severest infections of the entire GPB were manifesting by

MRSA. These were associated with significantly longer episodes. Moreover, all MRSA cases, whether single isolates or mixed infections, had one or two concomitant infections. Comparable results were previously reported on the morbidity and mortality caused by MRSA in patients with hematological malignancies [21].

On the other hand, many centers are reporting an increase in the incidence of GNB [22]. This could be explained by the use of more intensified regimens of chemotherapy. In our study, 43.3% of all BSIs were attributed to Gram-negative organisms. A possible explanation could be that BSI in neutropenic patients is more likely derived from endogenous sources, such as the gastrointestinal tract [23], and hence the high frequency of diarrhea in our patients might explain the high prevalence of GNB. Additionally, a significantly longer episode was recorded for GNB and mixed infections when compared to GPB. Moreover, an unfavorable outcome, recognized by death of patients, was encountered more frequently with GNB and mixed infections, (18.0%), than in GPB (2.7%) and this finding was highly significant. These results follow other reports that showed BSI with Gram negative bacilli to be significantly associated with an increased risk of mortality [24].

The overall mortality rate reported in our study was 7.5%. It was also recorded that mortality in episodes with BSI was significantly higher than those of episodes with no growth (11% versus 4.6% respectively). Our results are slightly higher than those found in other studies that reported a mortality rate of 3%, with mortality, for BSI, to be 9% versus 2% among patients without BSI [25].

BSI and increased length of episodes were shown in our study to be independent factors for mortality, as they increased the risk by more than a double. A relapsing tumor and younger age of the child triples the risk for death while presence of a

canula significantly increased the risk to about four folds. These findings are consistent with other studies that showed infants' age, presence of BSIs, in the form of Gram-negative and Gram-positive organisms, as well as presence of I.V. site infection, to be independent significant risk factors for death [18]**.** Additionally, others confirmed that prolonged profound neutropenia (> 14 days) and disease status were indicators of likelihood for complications [12]**.**

Conclusions:

Prospective surveillance for nosocomial infections in pediatric oncology units is an indispensable tool for its' internal quality control [10]**.** Findings of the present study, mainly high prevalence of BSI and an increased rate of GNB, point to the importance of continuous monitoring of the pattern of infecting organisms in each center. In agreement with our conclusion, it was stated that although many infections in this high-risk population may not be preventable through infection control measures, the careful evaluation of specific infection rates permits the identification of risk factors that may be targeted by infection control proGrams. Nowadays, there is a growing interest in risk stratification of febrile neutropenia in pediatric cancer patients, based on predictive models in order to apply risk directed therapy and suitable preventive and management strategies**.**

Findings of this study have also demonstrated that BSI affects clinical course and outcome of FN in pediatric cancer patients and that the type of organism isolated plays a major role. The length of episode and outcome were significantly worse in patients with BSI compared to those with non-BSI, confirming the impact of BSI on costs and morbidity of patients. The different types of microorganisms isolated as a cause of BSI displayed profound effects on course of episode. Moreover, GNB and mixed BSIs

constituted a group significantly associated with morbid episodes and with higher mortality rate.

Recommendations:

Our data emphasize the importance of the influence of BSI on clinical course and outcome in pediatric patients with chemotherapy induced FN. Furthermore, based on local epidemiology and microbiology results of BSI and susceptibility data, internal recommendations for empirical treatment of FN should be elaborated on and periodically revised. Finally, continuous evaluation of infection control programs is mandatory to prevent hospital acquired infections with pathogens known to cause severe BSIs.

Table (1): Initial and clinical characteristics of episodes found in enrolled patients.

Patient Characteristics	Males No. (%)	Females No. (%)	Total No. (%)	*P* – value
Sex	408 (56.0)	321 (44.0)	729 (100)	----
Age (Mean ± SD)	7.75 ± 4.57	7.12 ± 4.68	7.47 ± 4.63	0.068†
Tumors				
Hematological	308 (75.5)	256 (79.8)	564 (77.4)	0.172*
Solid	100 (24.5)	65 (20.2)	165 (22.6)	
Relapse				
Yes	72 (17.6)	44 (13.7)	116 (15.9)	0.149*
No	336 (82.4)	277 (86.3)	613 (84.1)	
ANC				
< 100	206 (50.5)	165 (51.4)	371 (50.9)	0.692*
100 - < 500	115 (28.2)	82 (28.5)	197 (27.0)	
500 - < 1000	87 (21.3)	74 (23.1)	161 (22.1)	
Thrombocytopenia				
≤ 25,000	120 (29.4)	105 (32.7)	225 (30.9)	0.34*
> 25,000	288 (70.6)	216 (67.3)	504 (69.1)	
Blood Stream Infection (BSI)				
Yes	187 (45.8)	150 (46.7)	337 (46.2)	0.810*
No	221 (54.2)	171 (53.3)	392 (53.8)	
Length of Episode (Mean ± SD)	7.53 ± 4.64	7.95 ± 4.65	7.72 ± 4.65	0.223†

* **Chi square test [All insignificant]** † **Student's *t* –test [All insignificant]**

Table (2): Infectious foci detected among episodes of study patients.

Infectious focus by site	Patients' episodes	
	No.	(%)
Gastroenteritis	135	18.5
Lower Respiratory Tract	97	13.3
Skin infections	59	8.1
Pharyngitis + sore throat	52	7.1
Catheter-related infection	43	6.0
Eye infection	16	2.2
Ear infection	14	1.9
Urinary Tract Infection	6	0.8
No Focus	307	42.1
Total	**729**	**100.0**

Table 3: Distribution of organisms isolated from blood cultures taken from study patients.

Type of organisms		Blood Stream Infection (BSI)	
		No.	%
Gram Positive	*Coagulase neg. Staphylococci*	57	16.9
	Staphylococcus aureus	33	9.8
	Streptococci	40	11.9
	Others	21	6.2
	Total Gram Positive	**151**	**44.8**
Gram Negative	*Klebsiella spp.*	28	8.3
	Enterobacter spp.	25	7.4
	Pseudomonas spp.	21	6.2
	Acinetobacter spp	17	5.1
	Others	55	16.3
	Total Gram Negative	**146**	**43.3**
Mixed Infections	*With Bacterial*	22	6.5
	With Fungal	15	4.5
	Total Mixed	**37**	**11.0**
Fungal Infections		3	0.9
Grand Total – All BSI Growths		**337**	**100.0**

Table 4: Comparison of average length of episodes by type of organisms

Length of Episodes	Mean ± SD	Post – Hoc Analysis†
Gram Positive (A)	7.61 ± 4.53	A – C
Gram Negative (B)	8.96 ± 5.04	B – C, B – D
Mixed Infections(C)	11.78 ± 5.41	C – A, C – B, C – D
No Growth detected (D)	6.89 ± 4.16	D – B, D – C

†ANOVA P ≤ 0.004

Table 5: Risk factors related to positive blood stream infections in febrile neutropenic episodes of study patients.

Risk Factor	Blood Stream Infections (BSI)		RR	95% CI	P – value
	Positive Growth (n=337) No. (%)	No Growth detected (n=392) No. (%)			
Age					
≤ 7 Yrs	232 (68.8)	182 (46.4)	1.68	1.41 – 2.01	< 0.001
> 7 Yrs	105 (31.2)	210 (53.6)			
Tumor					
Solid	85 (25.2)	80 (20.4)	1.15	0.97 – 1.37	0.121
Hematologic	252 (74.8)	312 (77.4)			
Disease Status					
Relapse	60 (17.8)	56 (14.3)	1.14	0.94 – 1.39	0.195
No relapse	277 (82.2)	336 (85.7)			
Neutropenia (<100)					
Yes	217 (64.4)	154 (39.3)	1.74	1.47 – 2.07	< 0.001
No	120 (35.6)	238 (60.7)			
Thrombocytopenia					
≤ 25,000	143 (42.4)	82 (20.9)	1.65	1.42 – 1.91	< 0.001
> 25,000	194 (57.6)	310 (79.1)			
CDI					
Yes	229 (67.9)	193 (49.2)	1.54	1.29 – 1.84	< 0.001
No	108 (32.1)	199 (50.8)			
Presence of Canula					
Yes	97 (28.8)	22 (5.6)			
No	240 (71.2)	370 (94.4)	2.07	1.82 – 2.36	< 0.001
Length of episode					
≥ 7 days	189 (56.0)	113 (28.8)	1.80	1.54 – 2.10	< 0.001
< 7 days	149 (44.0)	279 (71.2)			

Table 6: Logistic regression analysis of the factors affecting prognosis of febrile neutropenic episodes among study patients

Prognostic factors	RR	95% CI	P – Value
Age (≤ 7 years)	3.11	1.67 – 5.81	< 0.001
Relapsing tumor	3.44	1.85 – 6.39	< 0.001
Blood Stream Infection (BSI)	2.36	1.26 – 4.39	0.007
Presence of a Canula	3.98	1.63 – 9.67	0.002
Length of Episode (≥ 7 days)	2.76	1.49 – 5.11	0.001

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