

Epidemiological profile of febrile neutropenia in children at three referral hospitals in Rwanda: A 5-year retrospective study

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ABSTRACT

INTRODUCTION: Febrile neutropenia (FN) is an oncological emergency and requires prompt intervention. Recommended management of febrile neutropenia is based on local epidemiology of microorganisms. Rwanda lacks data on local epidemiology for febrile neutropenia. This study aims to highlight the epidemiology of bacteremia causing febrile neutropenia in pediatric populations in Rwanda.

METHODS: A retrospective cross-sectional study was conducted over a period of 5 years at three referral hospitals in Rwanda. This study included patients with febrile neutropenia aged less than 15 years. A structured questionnaire was used for data collection, and Stata version 13 was used for analysis.

RESULTS: This is the 1st study describing the epidemiology of microorganisms in neutropenic cancer patients in Rwanda. A total of 138 children were included in this study; 92 patients (67%) had hemato-oncology diseases, with acute lymphoblastic leukemia (ALL) represented at 50%, while 46 patients (33%) were non-cancer patients. Prevalence of FN in hemato-oncology was 36%. The rate of bacteremia was 37.6% (52/138). Gram-negative pathogens predominated at 65.4% of all isolates, with *Escherichia coli* being more common. Concerning antibiotic susceptibility, Gram negatives were largely resistant to 3rd generation cephalosporins, but most of them showed sensitivity to carbapenems. Unfortunately, 67% of *S. aureus* was mainly MRSA. The 30-day all-cause mortality rate in cancer patients with FN was 19%.

CONCLUSION: This study showed that *E. coli* was the most common organism causing bacteremia in febrile neutropenic pediatric patients, with high resistance to 3rd generation cephalosporins and gentamicin. The use of carbapenems as empiric treatment of febrile neutropenia is highly recommended.

Keywords: Epidemiological Febrile neutropenia, children, hematology, Referral hospitals, Rwanda

INTRODUCTION

Febrile neutropenia (FN) is a life-threatening

condition occurring in oncology [1], but it also happens in other healthy immunocompetent children. FN presented with a temperature of 38°C

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Received: 19th October 2024; **Initial decision given:** 17th May 2025; **Revised manuscript received:** 11th September 2025; **Accepted:** 16th September 2025.

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Citation for this article: A. Tuyisingize; T. Rogo; A. Kanyamuhunga. Epidemiological profile of febrile neutropenia in children at three referral hospitals in Rwanda: A 5-year retrospective study. Rwanda Medical Journal, Vol. 82, no. 3, p. 25-35, 2025. <https://dx.doi.org/10.4314/rmj.v82i3.7>

with an absolute neutrophil count (ANC) of less than $0.5 \times 10^9/L$ [2]. Severity of neutropenia is classified by the American Society of Clinical Oncology as severe, moderate or mild. Severe neutropenia is considered when ANC is less than $0.5 \times 10^9/L$ [3]. Febrile neutropenia can result from the cancer itself or after administration of chemotherapy, radiotherapy, and immunosuppressants [4]. FN is most common in hematological malignancies; it can occur at the time of diagnosis or at the end-stage disease. Patients on chemotherapy have a higher risk for FN episodes [5].

FN has a mortality rate of 24% in high-income countries (HIC) and 33% in lower-income countries (LIC) [6,7]. Despite progress in management, FN is associated with prolonged hospital stays and increased health care costs [8]. Timely and adequate empirical antibiotic treatment has improved the prognosis [9,10]. There is a marked shift of micro-organisms causing infection in neutropenic patients as reported by a European study, where around 70% of bacteraemia was related to Gram-positive organisms by the late 1980s and in the early 1990s [11–13]. Data from low-income countries mostly showed predominance of Gram negatives in studies from Mexico, Ghana, Uganda, and Tunisia [6,10,21,22]. There is a marked shift of micro-organisms from gram-negative to gram-positive, causing infection in neutropenic patients as reported by a European study, where around 70% of bacteraemia was related to Gram-positive organisms by the late 1980s and in the early 1990s [11–13]. Death associated with FN episodes in high-income countries (HICs) ranges from 0.7–3.9% compared to the death rate observed in low-income countries (LICs), which is considerably higher at 4–13.2% [14]. Contrarily, data from low-income countries mostly showed predominance of gram negatives in studies from Mexico, Ghana, Uganda, and Tunisia [6,10,21,22].

FN is most common in patients with oncological conditions. However, many studies have demonstrated the codominance of the virus in causing FN in immunocompetent children, where respiratory syncytial virus (RSV) was found to be the most isolated in the immunocompetent children, as shown by a retrospective study done in Japan (2012–2019), which observed RSV infection in 31(11%) [15]. Another study done from 2013 to 2015 in Israel in non-immunocompromised infants and young children < 2years, found that viruses like Adenovirus, RSV, Parainfluenza virus 1,2,3, and

Influenza A, EBV, and CMV were the primary cause of FN [16].

FN in the oncology department is one of the life-threatening conditions; the microbiology isolates differ between HICs (High Income countries) and LICs (Low Income countries). In HICs, Gram positives predominate, and the treatment is based on bacterial isolates rather than empirical treatment alone. This was shown in studies conducted in Spain, Italy, and the United States of America [17–20]. Although data from low-income countries mostly showed predominance of gram negatives in studies from Mexico, Ghana, Uganda, and Tunisia [6,10,21,22].

HICs treat FN based on their local epidemiology, while LICs have minimal data concerning local epidemiology in FN. Guidelines by the Infectious Diseases Society of America (IDSA) recommend that high-risk patients need hospitalization for intravenous empirical antibiotic monotherapy of an anti-pseudomonal β -lactam agent, with addition of aminoglycosides, fluoroquinolones, or vancomycin to the initial therapy when multidrug resistance is suspected or in hemodynamic instability is present [23]. IDSA also recommends the use of vancomycin in FN cancer patients when there is evidence of MRSA [23]. The Rwanda Pediatric guidelines recommend using 3rd generation cephalosporins in pediatric patients with sepsis [24]. Local hospitals generally use third-generation cephalosporins and gentamicin, while private hospitals use piperacillin-Tazobactam and Amikacin or a combination of carbapenem and vancomycin for patients with FN with oncology conditions.

Identifying the causative microorganisms guides antibiotherapy choices, thus improving the quality of life in children with neutropenic fever [5,7,9]. Rwanda still treats FN empirically based on study findings from HICs. There are no local epidemiologic studies on FN in Rwanda. This study aimed to describe the bacterial etiology and antibiotic sensitivity of febrile neutropenia in children with and without hemato-oncology diseases at three tertiary Rwandan hospitals over 5 years.

METHODS

Study design

A retrospective cohort study was used for a period of 5 years (January 2016 to December 2021).

All children aged below 15 years diagnosed with neutropenic fever who consulted the respective hospitals during the study period were included.

Study settings

Three paediatric tertiary centres (hospitals) which provide paediatric hematology-oncology services in Rwanda were included: University Teaching Hospital of Kigali (CHUK), Rwanda Military Hospital (RMH), and King Faisal Hospital, Kigali (KFH).

The CHUK is the largest academic tertiary referral hospital in Rwanda, located in the capital city of Kigali, and has a pediatric hemato-oncologist on staff. There are 86 paediatric beds, of which 10 are for hemato-oncology. The RMH is a public tertiary care level hospital in Kigali with a national centre for Radiotherapy and specialized personnel in oncology and radiotherapy, with 81 pediatric beds. The KFH is a private hospital in Kigali that provides paediatric oncology services, including chemotherapy with two oncologists on staff.

All the hospitals have a level three laboratory, but none have an automated system. Only RMH had an accredited laboratory during the data collection period. For bacterial culture, culture medium was used, and plates were observed for 7 days. Antibiotic susceptibility testing was carried out by using disk diffusion (Kirby-Bauer testing) and interpreted as per Clinical and Laboratory Standards Institute (CLSI) standards.

Study participants

The inclusion criteria were patients who presented with fever and low absolute neutrophil count, defined as a temperature greater than 38 degrees Celsius and ANC <1500 cells/microliter, respectively, and had a blood culture drawn.

The exclusion criteria were children with Neutropenia without fever and children with FN for whom blood cultures were not obtained.

Data collection procedures

Data were collected in 3 referral hospitals of Rwanda, as mentioned above, and all children who met the inclusion criteria were included in the study. A structured questionnaire was used to gather all required information from patients' records regarding participants' socio-demographic and medical history, including underlying diseases, vital signs, especially temperature, empirical treatment on admission, and treatment adjusted after the antibiogram report. The full blood count (FBC), microbiological results, and antibiograms

were retrieved from laboratory records.

Data analysis

Data from questionnaires were checked for completeness and inconsistencies, and then entered into the Epidata version 3.1 (The Epidata Association, Odense, Denmark). Stata version 13 (Stata Corp LLC, College Station, TX) was used for data analysis. Descriptive data were presented as follows: categorical data were presented using frequencies and percentages in tables and charts. Continuous data were summarized by mean and median values depending on their distribution. Chi-square test and logistic regression (binary logistic regression and multivariable logistic regression analysis) were utilised to study the relationship between the outcomes and possible predictors. Statistical significance for associations was taken at the level $p < 0.05$.

The Institutional Review Board (IRB) of the University of Rwanda, College of Medicine Health Science, reviewed and approved the study and its implementation through its ethics committee. No informed consent was used as it is secondary data collection, but confidential agreements were signed between the researcher and the hospital management. To ensure the confidentiality of the research data, no patient names were collected. Codes replaced patient identification.

RESULTS

A total of 32518 medical records of children admitted over the 5-year period at the study sites were reviewed, and these included 250 children with haemato-oncological disease. A total of 138 children under 15 years of age with FN were identified; 92 with haemato-oncological disease and 46 with other conditions (Figure 1).

The overall prevalence of febrile neutropenia was 0.42% (420 per 10,000 children). The prevalence of febrile neutropenia in haemato-oncology was 36% (92/250).

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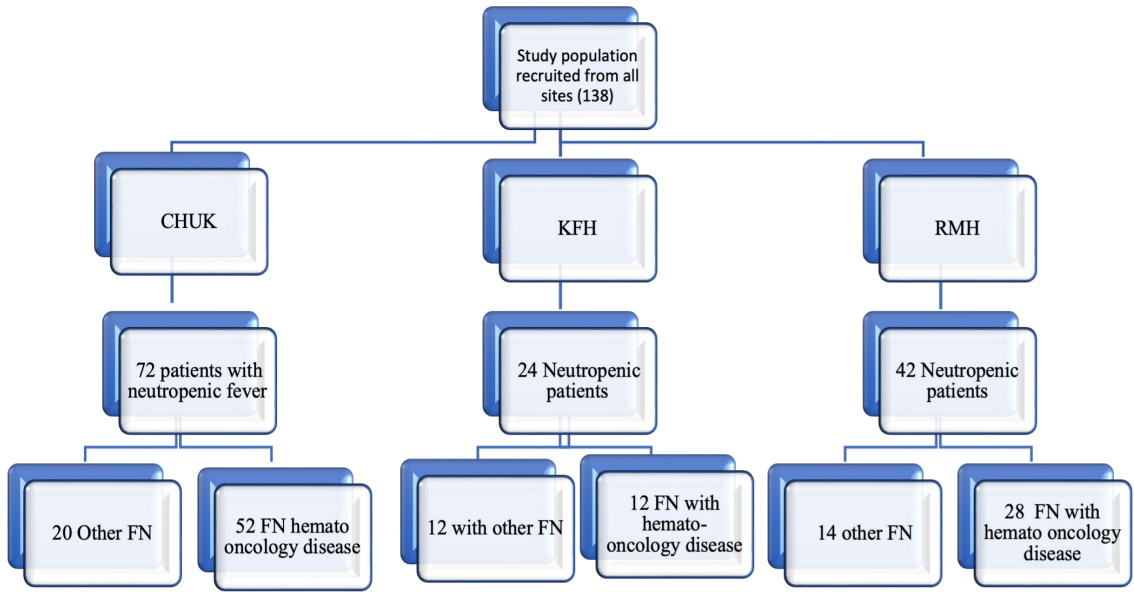


Figure 1: Flow chart for study participants' recruitment

Table 1: Sociodemographic and clinical characteristics of participants

Characteristics	N	%
Age (Mean ± SD)	7.92 ± 4.15 years	
Age range		
1-5 years	47	34.06
6-11 years	55	39.86
12-15 years	36	26.09
Gender		
Male	76	55.07
Female	62	44.93
Residence		
Kigali	45	32.61
South	29	21.01
East	24	17.39
West	21	15.22
North	18	13.04
Outside of Rwanda	1	0.72
ANC		
Severe	94	68.11
Moderate	30	21.74
mild	14	10.14

Severe: ANC lower than 500 cells/microL, Moderate: ANC between 500-1000 cells/microL, Mild: ANC more than 1000 cells/microL

Sociodemographic and clinical characteristics of children with febrile neutropenia

The mean age of patients with FN was 7.9 years (SD 4.15), ranging from 1 year to 15 years. Fifty-five percent (55%) of the participants were males, and 32.6% of the total number of patients resided in Kigali City, and 68% of the patients had severe neutropenia (Table 1).

Distribution of diagnoses among participants with febrile neutropenia

Haemato-oncologic diagnoses made up (67%) of all causes of FN, with acute lymphoblastic leukemia (ALL) being the most common at 50% (46/92). Non-haemato-oncologic causes were (33), with the most common diagnoses being malnutrition (75%) and sepsis (50%).

Microbes identified in children with febrile neutropenia

Of 138 children with febrile neutropenia, 52 (37%) yielded positive blood cultures. Of the 52 isolates, 18 (34.7%) were gram-positive and 34 (65.3%) were gram-negative. Twenty-nine patients with oncologic conditions had positive blood cultures, and 23 of these positive blood cultures were among those with non-oncologic disease. The only gram-positive organism isolated was Staphylococcus aureus. The prevalence of a gram-positive isolate was 8 (27.5%) among the 29 haemato-oncology patients with a bacterial isolate.

Table 2: Distribution of the diagnoses among children with febrile neutropenia

Diagnosis	N	%
Hemato-oncologic causes	92	67
ALL	46	50
AML	12	13.04
Burkitt lymphoma	6	6.52
Anaplastic LC Lymphoma	2	2.17
Non-Hodgkin's lymphoma	1	1.08
Chronic myeloid leukemia	1	1.08
Aplastic anemia	15	16.3
Solid tumor	9	9.8
Wilms tumor	6	66.67
Brain tumor	2	22.22
Ewing sarcoma	1	11.11
Non haemato-oncologic causes	46	33
Infectious	30	65
Sepsis	15	50.00
Typhoid fever	6	20.00
Pneumonia	5	16.67
Other	4	13.33
Non-infectious	16	35
Malnutrition	12	75
Nephrotic syndrome	4	25

AML: Acute Myeloid Leukemia, ALL: Acute lymphoblastic leukemia

Ten (43.5%) among the 23 other patients also had bacterial isolates.

The prevalence of a gram-negative isolate was 21 (72.5%) among the 29 haemato-oncology patients

with a bacterial isolate and 13 (55.5%) among the 23 non-haemato-oncology patients with bacterial isolates. These differences between patients with haemato-oncologic conditions and those without are not significant ($p=0.23$).

Escherichia coli and *Staphylococcus aureus* were the most common in malignancy-related cases, while *Salmonella typhi* and *S. aureus* were the most common in non-malignant causes of FN (Table 3).

Antibiotic sensitivity

Gram-negative bacilli showed wide resistance to 3rd-generation cephalosporins; only *E. coli* was 100% ceftriaxone (Table 4). *Salmonella typhi* had 50% resistance to ceftriaxone and piperacillin-tazobactam, 33% resistance to carbapenems and amikacin, while 83% were susceptible to cefotaxime and ciprofloxacin, and 100% of *Salmonella* were susceptible to gentamicin. *E. coli* was 100% susceptible to carbapenems, while *Klebsiella* spp showed 82% sensitivity to carbapenems. 100% of *Acinetobacter* showed susceptibility to amikacin and polymyxin B, but only 50% of *Acinetobacter* were sensitive to gentamicin, ciprofloxacin, and piperacillin-tazobactam.

75% of *Pseudomonas* showed susceptibility to ceftazidime, 33% of *Pseudomonas* showed resistance to carbapenems, amikacin, and ciprofloxacin. Only 33% of *S. aureus* was MSSA, but 11% of MRSA was resistant to vancomycin.

Of 138 patients who were recruited with neutropenic fever, 29 died within 30 days of hospitalization, giving an overall case fatality of 21%. Among 92 febrile neutropenic patients with hemato-oncologic disease, 19 patients died within 30 days of admission with a case fatality of 20%.

Table 3: Utilization of cervical cancer screening modalities (n = 198)

Diagnosis	<i>S. typhi</i>	<i>E. coli</i>	<i>Klebsiella</i> spp.	<i>S. aureus</i>	<i>Acinetobacter baumannii</i>	<i>Pseudomonas Aeruginosa</i>	Total
Malignancy causes							
Hematological	0	10	5	8	2	2	27
Solid tumors	0	1	1	0	0	0	2
Non-malignancy causes							
Infectious	6	1	2	8	0	1	18
Non-infectious	0	0	3	2	0	0	5
Total	6	12	11	18	2	3	52

Table 4: Antibiotic sensitivity of organisms isolated from children with fever and neutropenia

Antibiotics sensitive to	Isolated microorganisms					
	Salmonella typhi* n=6	E. coli* n=12	Klebsiella spp.* n=11	S. aureus n=18	Acinetobacter baumannii n=2	Pseudomonas aeruginosa* n=3
Oxacillin	0	0	0	33	0	0
Amoxiclav	17	0	0	6	0	0
Cephalotin	17	0	0	11	0	0
Cefotaxime	83	16	0	0	0	0
Cephalotin	17	0	0	11	0	0
Gentamycin	100	8	36	0	50	67
Amikacin	67	67	45	0	100	67
Chloramphenicol	17	16	18	0	0	0
Tetracycline	0	8	0	55	0	0
Colistin	0	0	0	33	0	0
Erythromycin	0	0	0	50	0	0
Cotrimoxazole	0	0	9	0	0	0
Ciprofloxacin	83	58	27	33	50	67
Imipenem	67	100	82	n/a	n/a	67
Clindamycin	0	0	0	72	0	0
Ceftazidime	75	25	25	0	0	75
Cefuroxime	0	0	0	6	0	0
Ceftriaxone	50	0	9	0	0	0
Piperacillin-tazobactam	50**	n/a	50**	n/a	50**	n/a
Vancomycin	n/a	n/a	n/a	89	n/a	n/a
Meropenem	67	100	82	n/a	n/a	67
Polymyxin B	50	8	9	22	100	33

n/a: not tested, *Only 4 isolates were tested for ceftazidime sensitivity, **Only 2 isolates were tested to piperacillin/tazobactam

Factors associated with mortality among patients with neutropenic fever

Of 138 patients who were recruited with neutropenic fever, 29 died within 30 days of hospitalization, giving an overall case fatality of 21%. Among 92 febrile neutropenic patients with hemato-oncologic disease, 19 patients died within 30 days of admission, with a case fatality of 20%. Patients with severe neutropenia had an increased risk of death compared to those with mild or moderate neutropenia (OR=3.62; 95% CI: 1.17-11.16; p=0.025). The majority of deaths were due to acute lymphoblastic leukemia and malnutrition (Table 5).

DISCUSSION

This study demonstrated that *E. coli* was the most common organism causing bacteremia in febrile neutropenic pediatric patients, with high resistance to 3rd generation cephalosporins and gentamicin.

During the 5-year period, the mean age of patients recruited in the study was 7.9 years (SD=4.15), ranging from 1 year to 15 years. Fifty-five percent of the participants were male, and 68% of the patients had severe neutropenia, similarly reported by another study [25].

This study revealed that 67% had hematological-oncology diseases, while 33% had other conditions.

Table 5: Factors associated with mortality among children with neutropenic fever

Predictors	30 days outcome		OR (95% CI)	P value
	Died	Alive		
Age				
1-5 years	11 (23.40%)	36 (76.60%)	1.35 (0.44-4.14)	0.599
6-11 years	12 (21.82%)	43 (78.18%)	1.54 (0.52-4.53)	0.426
12-15 years	6 (16.67%)	30 (83.33%)	Ref	
Sex				
Male	19 (25.00%)	57 (75.00%)	1.43 (0.62-3.33)	0.395
Female	10 (16.13%)	52 (83.87%)	Ref	
Blood culture result				
Positive	14 (25.93%)	40 (74.07%)	1.34 (0.58-3.08)	0.48
Negative	15 (17.86%)	69 (82.14%)	Ref	
Gram				
Positive	4 (20%)	16 (80.00%)	Ref	
Negative	9 (26.47%)	25 (73.53%)	1.44 (0.37-5.47)	0.592
Hematological malignancies				
Yes	17 (25.00%)	51 (75.00%)	Ref	
No	12 (17.14%)	58 (82.86%)	1.61 (0.70-3.69)	0.26
Solid tumors				
Yes	2 (22.2250)	7 (77.78%)	1.08 (0.21-5.49)	0.927
No	27 (20.93%)	102 (79.07%)	Ref	
ANC				
Severe	25 (26.60%)	69 (73.40%)	3.62 (1.17-11.16)	0.025
Moderate/Mild	4 (9.09%)	40 (90.91%)	Ref	
Isolated germ				
Salmonella	1 (16.67%)	5 (83.33%)	Ref	
E. Coli	5 (41.67%)	7 (58.33%)	3.5 (0.31-40.7)	0.306
Klebsiella	3 (27.27%)	8 (72.73%)	1.87 (0.15-23.4)	0.625
Staphylococcus aureus	4 (22.22%)	14 (77.78%)	1.42 (0.13-16.02)	
Acinetobacter	0 (0.00%)	2 (100%)	-	
Pseudomonas	0 (0.00%)	3 (100%)	-	

ALL was the most common hemato-oncologic condition at 50%. This can be explained by the high incidence of ALL in Rwanda [26]. Similar findings have been observed elsewhere [6,7,20,27].

The overall prevalence of febrile neutropenia in our study was 0.42%. Prevalence in hemato-oncology was 36%, similar to other studies, which report prevalence ranging from 11% to 38% [28]. This high incidence of FN in hemato-oncology patients raised awareness of the severity of FN in those patients; thus, screening and isolation from

the general ward are recommended.

Overall, 37.6% of febrile neutropenic patients had a positive blood culture. Gram-negative bacteria were most commonly isolated at 65.4%. Salmonella and Staphylococcus aureus were the most commonly isolated microorganisms in non-hematological causes of FN. This differs from a systematic review, where the most common micro-organisms identified in non-hemato-oncology children were mostly viral - RSV, EBV, Parvovirus, and HHV6 [28]. The same results with

viral predominance were observed in other studies [15,25,29]. However, our setting lacks virologic testing, so we may be missing viral diagnoses.

The rate of bacteremia among those with hematologic conditions was 37.6%. Literature reports a 20-30% rate of bacterial infection among patients with FN [14,30]. Comparable results have been observed elsewhere [21,31,32], but lower in South Africa and Uganda studies, 13.8% and 14.1% respectively [6,33]. *E. coli* was the most common bacterium isolated, similar to other studies [7,20,34,35]. Our findings confirm the previously observed predominance of gram-negative infections among pediatric patients at CHUK [36].

Studies from resource-limited countries have also shown gram-negative bacteria to be the main etiology of bloodstream infection [6,21,22,34]. Empiric antibiotic use in peripheral facilities before referral may select for the gram-negative organisms. Gram-positive bacteria were reported as the main micro-organisms isolated in resource-rich settings, probably due to the use of semi-permanent central venous catheters and skin contamination during sampling [18,33].

The small percentages of Gram-positive bacteremia observed in our study might be linked to dissimilarities in the manner of our clinical practice compared to resource-rich settings, including the unavailability of long-term indwelling catheters, which are the primary source of Gram-positive bacteremia [37,38].

Our study has shown that Gram-negative bacteria were resistant primarily to 3rd generation cephalosporins. 67% of *S. aureus* was mainly MRSA. It is concerning that 11% of *S. aureus* isolates were resistant to vancomycin. Only three-quarters of isolated *Pseudomonas* showed sensitivity to FN's commonly used empirical antibiotic (Ceftazidime). *E. coli* and *Klebsiella* spp showed 100% and 82% sensitivity to carbapenems, respectively, similar to a systematic review of 10 studies where *E. coli* and *Klebsiella* spp showed over 90% susceptibility to carbapenems [35]. IDSA supports the use of carbapenems and vancomycin in FN cancer patients with high risk [23]. Our study confirms wide resistance of gram negatives to 3rd generation cephalosporins, which was also observed in a local study conducted by Rogo et al. [36]. Our study has shown a high prevalence of MRSA at 67% but also showed emerging resistance to vancomycin, confirming the existing data where 60% of tested

S. aureus were MRSA in a study by Ishimwe et al. [36]. By comparison, our more recently collected data showed increased MRSA and increased resistance to cefotaxime and gentamicin compared to the 2018 study by Ishimwe et al. [36].

FN is associated with high mortality and morbidity. The 30-day all-cause mortality in our study was 21% in all febrile neutropenic patients. The mortality observed in non-cancer patients can be explained by poor outcomes associated with malnutrition in general pediatric patients in our population. Recent data reports a high prevalence of malnutrition in Rwanda, with 38% of children under 5 years being malnourished. The 30-day all-cause mortality rate in cancer patients with FN was 19%. Our mortality rate was similar to another study where the overall mortality rate within 30 days after the onset of bacteraemia was found to be 24% [30]. A study in low-income countries reported mortality of 33% which is high compared to mortality observed in the USA, which was 9.5% [6,39]. This can be explained by the unavailability of data on the epidemiology of microorganisms causing FN in resource-limited countries. Patients with severe neutropenia have an increased risk of dying compared to those with mild or moderate neutropenia (OR=3.62; 95% CI: 1.17-11.16; p=0.025). No other factors were associated with mortality in our study, and this can likely be explained by the relatively small sample size.

The study had a limitation of the inability to conduct our study at Butaro district hospital, which is a national cancer center, because they were not doing blood culture during the given study period, and this could have added a valuable contribution to our study, as many children with cancer passed through there for chemotherapy.

CONCLUSION

This study is the first to highlight the epidemiology of FN in children in our country. Gram-negative bacteria were found to be prominent in causing FN, especially *E. coli*. Our study finds emerging resistance of gram-negative bacteria to cephalosporins, which we currently use in treating FN in children. Therefore, we recommend the use of carbapenems and vancomycin for febrile neutropenia as our study showed high sensitivity to them. And this could reduce the mortality

caused by FN in our country.

REFERENCES

- Stephens, R.S. Neutropenic Fever in the Intensive Care Unit. *Oncol. Crit. Care* 2019, 1297–1311, doi:10.1007/978-3-319-74588-6_118.
- Jesús Tornero-Molinaa, b, Fernando Sánchez-Alonsoc, Manuel Fernández-Pradaa, María-Luisa Bris-Ochaitaa, A.S.-G. y J.V.-F. Since January 2020 Elsevier Has Created a COVID-19 Resource Centre with Free Information in English and Mandarin on the Novel Coronavirus COVID-. *Ann Oncol* 2020, 19–22.
- Leibovitz, E.; Kapelushnik, J.; Alsanaa, S.; Tschernin, D.; Sergienko, R. Comparison of the Etiologic, Microbiologic, Clinical and Outcome Characteristics of Febrile vs. Non-Febrile Neutropenia in Hospitalized Immunocompetent Children. 2020.
- Lv, H.; Ning, B. Pathogenesis of Bloodstream Infection in Children with Blood Cancer. *Exp. Ther. Med.* 2013, 5, 201–204, doi:10.3892/etm.2012.738.
- Keng, M.K.; Sekeres, M.A. Febrile Neutropenia in Hematologic Malignancies. 2013, 19–27, doi:10.1007/s11899-013-0171-4.
- Lubwama, M.; Phipps, W.; Najjuka, C.F.; Kajumbula, H.; Ddungu, H.; Kambugu, J.B.; Bwanga, F. Bacteremia in Febrile Cancer Patients in Uganda. *BMC Res. Notes* 2019, 12, 4–9, doi:10.1186/s13104-019-4520-9.
- Resistance, D.; Zhang, Y.; Zheng, Y.; Dong, F.; Zhu, L.; Shi, D.; Li, X.; Li, J.; Hu, J. Epidemiology of Febrile Neutropenia Episodes with Gram-Negative Bacteria Infection in Patients Who Have Undergone Chemotherapy for Hematologic Malignancies: A Retrospective Study of 10 Years' Data from a Single Center. 2020, 903–910.
- Paul, M.; Bhatia, M.; Sasi, U. Microbiological Profile of Blood Stream Infections in Febrile Neutropenic Patients at a Tertiary Care Teaching Hospital in Rishikesh, Uttarakhand. 2020.
- Chen, C.Y.; Tsay, W.; Tang, J.L.; Tien, H.F.; Chen, Y.C.; Chang, S.C.; Hsueh, P.R. Epidemiology of Bloodstream Infections in Patients with Haematological Malignancies with and without Neutropenia. *Epidemiol. Infect.* 2010, 138, 1044–1051, doi:10.1017/S0950268809991208.
- Gonzalez, M.L.; Aristizabal, P.; Loera-Reyna, A.; Torres, D.; Ornelas-Sánchez, M.; Nuño-Vázquez, L.; Aguilera, M.; Sánchez, A.; Romano, M.; Rivera-Gómez, R.; et al. The Golden Hour: Sustainability and Clinical Outcomes of Adequate Time to Antibiotic Administration in Children with Cancer and Febrile Neutropenia in Northwestern Mexico. *JCO Glob. Oncol.* 2021, 659–670, doi:10.1200/go.20.00578.
- Shafie, S.E.; Janahi, M. Bacterial Bloodstream Infections and Antimicrobial Susceptibility Pattern in Pediatric Hematology / Oncology Patients after Anticancer Chemotherapy. 2014, 289–299.
- Wisplinghoff, H.; Seifert, H.; Wenzel, R.P.; Edmond, M.B. Current Trends in the Epidemiology of Nosocomial Bloodstream Infections in Patients with Hematological Malignancies and Solid Neoplasms in Hospitals in the United States. *Clin. Infect. Dis.* 2003, 36, 1103–1110, doi:10.1086/374339.
- Klastersky, J. Science and Pragmatism in the Treatment and Prevention of Neutropenic Infection. *J. Antimicrob. Chemother.* 1998, 41, 13–24, doi:10.1093/jac/41.suppl_4.13.
- Anoop, P.; Patil, C.N. Management of Febrile Neutropenia in Children: Current Approach and Challenges. *Pediatr. Infect. Dis.* 2021, 2, 135–139, doi:10.5005/jp-journals-10081-1257.
- Korematsu, T.; Koga, H. Transient Neutropenia in Immunocompetent Infants with Respiratory Syncytial Virus Infection. *Viruses* 2021, 13, doi:10.3390/v13020301.
- Tschernin, D.; Fruchtman, Y.; Sergienko, R.; David, O.; Leibovitz, R.; Mazar, J.; Leibovitz, E. The Etiologic, Microbiologic, Clinical and Outcome Characteristics of Immunocompetent Young Children <2 Years of Age Hospitalized with Acute Neutropenia. *Pediatr. Neonatol.* 2021, 62, 26–35, doi:10.1016/j.pedneo.2020.08.004.
- Roongpoovapatr, P.; Sunkratay, C. Causative Pathogens of Fever in Neutropenic Patients at King Chulalongkorn Memorial Hospital. *J. Med. Assoc. Thai.* 2010, 93, 776–783.
- Hakim, H.; Flynn, P.M.; Knapp, K.M.; Srivastava, D.K.; Gaur, A.H. Etiology and Clinical Course of Febrile Neutropenia in Children with Cancer. *J. Pediatr. Hematol. Oncol.* 2009, 31, 623–629, doi:10.1097/MPH.0b013e3181b1edc6.
- Castagnola, E.; Fontana, V.; Caviglia, I.; Caruso, S.; Faraci, M.; Fioredda, F.; Garrè, M.L.; Moroni, C.; Conte, M.; Losurdo, G.; 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, 1296–

- 1304, doi:10.1086/522533.
20. Tural Kara, T.; Erat, T.; Yahşi, A.; Özdemir, H.; İleri, T.; Ince, E.; Taçyıldız, N.; Ünal, E.; Çiftçi, E.; Ince, E. Bloodstream Infections in Pediatric Hematology/Oncology Patients: Six Years' Experience of a Single Center in Turkey. *Turk. J. Med. Sci.* 2019, 49, 1157–1164, doi:10.3906/sag-1812-101.
21. Nkrumah, N.O.; Labi, A.K.; Acquah, M.E.; Donkor, E.S. Bloodstream Infections in Patients with Malignancies: Implications for Antibiotic Treatment in a Ghanaian Tertiary Setting. *BMC Res. Notes* 2015, 1–10, doi:10.1186/s13104-015-1701-z.
22. Jeddi, R.; Achour, M.; Amor, R.B.; Aissaoui, L.; Kacem, K.; Lakhal, R.B.; Abid, H.B.; Turki, A.; Meddeb, B.; Amor, R.B.; et al. Factors Associated with Severe Sepsis: Prospective Study of 94 Neutropenic Febrile Episodes Factors Associated with Severe Sepsis: Prospective Study of 94 Neutropenic Febrile Episodes. 2013, 8454, doi:10.1179/102453310X12583347009577.
23. Freifeld, A.G.; Bow, E.J.; Sepkowitz, K.A.; Boeckh, M.J.; Ito, J.I.; Mullen, C.A.; Raad, I.I.; Rolston, K.V.; Young, J.A.H.; Wingard, J.R. Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America. *Clin. Infect. Dis.* 2011, 52, doi:10.1093/cid/cir073.
24. Guidelines, C.T. *Clinical Treatment Guidelines*. Rwanda 2012, 67.
25. Alexandropoulou, O.; Kossiva, L.; Haliotis, F.; Giannaki, M.; Tsolia, M.; Panagiotou, I.P.; Karavanaki, K. Transient Neutropenia in Children with Febrile Illness and Associated Infectious Agents: 2 Years' Follow-Up. *Eur. J. Pediatr.* 2013, 172, 811–819, doi:10.1007/s00431-013-1965-z.
26. Rugwizangoga, B. Aspects of Infection and Leukemia in Rwanda; 2020; ISBN 978-91-7833-894-8.
27. Jungrungrueng, T.; Anugulruengkitt, S.; Lauhasurayotin, S.; Chiengthong, K.; Poparn, H.; Sosothikul, D.; Techavichit, P. The Pattern of Microorganisms and Drug Susceptibility in Pediatric Oncologic Patients with Febrile Neutropenia. *J. Pathog.* 2021, 2021, 1–9, doi:10.1155/2021/6692827.
28. Segel, G.B.; Halterman, J.S. Neutropenia in Pediatric Practice. *Pediatr. Rev.* 2008, 29, 12–24, doi:10.1542/pir.29-1-12.
29. Chaolin, H.; Yeming, W.; Xingwang, L.; Lili R.; Jianping Zhao*, Yi Hu*, Li Zhang, Guohui Fan, Jiuyang Xu, X.G.; Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, J.X.; Guangfa Wang, Rongmeng Jiang, Zhancheng Gao, Qi Jin, Jianwei Wang†, B.C. The Etiologic, Microbiologic, Clinical and Outcome Characteristics of Immunocompetent Young Children <2 Years of Age Hospitalized with Acute Neutropenia. *J. Formos. Med. Assoc.* 2020, 19–20.
30. Baluch, A.; Shewayish, S. Neutropenic Fever. 2019, doi:10.1007/978-3-030-21859-1.
31. Paul, M.; Bhatia, M.; Sasi, U. Microbiological Profile of Blood Stream Infections in Febrile Neutropenic Patients at a Tertiary Care Teaching Hospital in Rishikesh, Uttarakhand. 2020.
32. Kumar, P.; Suman, M.; Maji, K. Micro-Organisms Associated with Febrile Neutropenia in Patients with Haematological Malignancies in a Tertiary Care Hospital in Eastern India. 2015, 31, 46–50, doi:10.1007/s12288-014-0393-1.
33. Mvalo, T.; Eley, B.; Bamford, C.; Stanley, C.; Chagomerana, M.; Hendricks, M.; Eysen, A.V.; Davidson, A. International Journal of Infectious Diseases Bloodstream Infections in Oncology Patients at Red Cross War Memorial Children's Hospital, Cape Town, from 2012 to 2014. *Int. J. Infect. Dis.* 2018, 77, 40–47, doi:10.1016/j.ijid.2018.09.012.
34. James, V.; Prakash, A.; Mehta, K.; Durugappa, T. Re-Thinking Treatment Strategies for Febrile Neutropenia in Paediatric Oncology Population: The Perspective from a Developing Country. *Infect. Agent. Cancer* 2021, 16, 1–8, doi:10.1186/s13027-021-00387-y.
35. Trecharichi, E.M.; Tumbarello, M. Antimicrobial-Resistant Gram-Negative Bacteria in Febrile Neutropenic Patients with Cancer: Current Epidemiology and Clinical Impact. *Curr. Opin. Infect. Dis.* 2014, 27, 200–210, doi:10.1097/QCO.0000000000000038.
36. Ishimwe, E.; Rogo, T. Antibiotic Resistance in Children with Bacteremia Admitted in the Largest Tertiary Hospital in Rwanda. 2018, 75, 2–5.
37. Paul, M.; Gafter-Gvili, A.; Leibovici, L.; Bishara, J.; Levy, I.; Yaniv, I.; Shalit, I.; Samra, Z.; Pitlik, S.; Konigsberger, H.; et al. The Epidemiology of Bacteremia with Febrile Neutropenia: Experience from a Single Center, 1988-2004. *Isr. Med. Assoc. J.* 2007, 9, 424–429.
38. Kanafani, Z.A.; Dakdouki, G.K.; El-Chammas, K.I.; Eid, S.; Araj, G.F.; Kanj, S.S. Bloodstream Infections in Febrile Neutropenic Patients at a Tertiary Care Center in Lebanon: A View of the Past Decade. *Int.*

J. Infect. Dis. 2007, 11, 450–453, doi:10.1016/j.ijid.2006.12.008.

39. Zhang, Y.; Zheng, Y.; Dong, F.; Ma, H.; Zhu, L.; Shi, D.; Li, X.; Li, J.; Hu, J. Epidemiology of Febrile Neutropenia Episodes with Gram-Negative

Bacteria Infection in Patients Who Have Undergone Chemotherapy for Hematologic Malignancies: A Retrospective Study of 10 Years' Data from a Single Center. *Infect. Drug Resist.* 2020, 13, 903–910, doi:10.2147/IDR.S241263.