

Original Research Article

Assessment of the management and outcome of neutropenia in paediatric haemato-oncology inpatients at Kenyatta National Hospital

Beatrice K. Amadi¹, Godfrey M. Limungi^{2*}, Eunice M. Kezia¹, Abel O. Khisa³

¹Department of Pediatrics, Kenyatta National Hospital, Nairobi, Kenya

²Doctoral School of Health Sciences, Faculty of Health Sciences, University of Pécs, Pécs, Hungary

³International Rescue Committee, Nairobi, Kenya

Received: 17 July 2023

Revised: 10 August 2023

Accepted: 09 October 2023

*Correspondence:

Dr. Godfrey M. Limungi,

E-mail: glimungi@kmtc.ac.ke

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Neutropenia is a common complication among the haemato-oncology pediatric patients. Children who develop such complications are prone to bacterial infections which further predispose them to death. This study aimed at improving the practice of management of neutropenia in children with the view of reducing pediatric haemato-oncology mortality.

Methods: We retrospectively reviewed medical records of paediatric haemato-oncology inpatients aged 13 years and below, who developed neutropenia during treatment at Kenyatta National Hospital. A data abstraction form was used to collect data from 113 medical records of patients admitted between 1st January 2020 and 31st December 2020. Data were analyzed using R to obtain descriptive and inferential statistics using a 95% confidence interval.

Results: Boys constituted most of the cases assessed. The median (IQR) age at admission was 6 (4, 10) years. Leukaemias were more common than lymphomas. Acute lymphocytic leukaemia (59%) and Hodgkin's lymphoma (4%) were the most and least frequently diagnosed haemato-oncology cancers. Most patients were diagnosed during the induction stage, 47 (42%) and had febrile neutropenia 59 (52%). Vaccination and bone marrow suppression histories were poorly documented. Thirty-three (29%) patients were reported to have succumbed during their treatment. G-CSF prescription was statistically significantly associated ($p=0.045$) with the survival status (death or alive) of patients, particularly at the induction stage ($p=0.007$).

Conclusions: Neutropenia management in KNH is done as per protocol, with room to improve on history taking. Although 29% of the children succumbed within the course of treatment, the majority (71%) of the patients were discharged.

Keywords: Management, Neutropenia, Outcome, Pediatric haemato-oncology

INTRODUCTION

Dale (2016) reports neutrophil counts $<1500/\mu\text{l}$ ($<1.5 \times 10^9/\text{l}$) as neutropenia, with counts less than $<1500/\mu\text{l}$ ($0.5 \times 10^9/\text{l}$) termed as severe and a risk factor for bacterial infection.¹ Punnapuzha et al define a single oral temperature $\geq 101^\circ\text{F}$ or a temperature $\geq 100.4^\circ\text{F}$ (38.0°C) recorded over an hour and associated with less than 1500 cells/microliter of neutrophils as febrile neutropenia

(FN).² Mohammed et al in their study on febrile neutropenia management in paediatric cancer patients at Ethiopian tertiary care teaching hospital reported significant mortality and morbidity resulting from febrile neutropenia and hospital admission in children with cancer is due to the associated morbidity.³ Haemato-oncology patients receiving chemotherapy are at greater risk for febrile neutropenia with increased morbidity and mortality.^{4,5} Untreated FN accounts for between 2 and

21% mortality based on a study done by Davis and Wilson.⁶ This then calls for prompt management of febrile neutropenia in terms of risk stratification and antibiotic therapy administration within the first 60 minutes following admission.⁷ According to Cashen and Van Tine, the treatment of neutropenia entails empiric broad-spectrum antibiotics and granulocyte colony-stimulating factor (G-CSF).⁸

Neutropenia is significantly associated with morbidity and mortality and is a cause of hospital admission in children with cancer.³ Kenyatta National Hospital admitted 116 paediatric haemato-oncology patients in 2020 out of whom 31 died (36.4%).⁹ Although febrile neutropenia post-chemotherapy poses a high risk for morbidity and mortality in paediatric oncology patients, documentation of clinical evaluation findings is inadequate and the pattern of antibiotic prescription for neutropenic and non-neutropenic patients greatly varies.⁵

This study aimed to assess the practice in the management of neutropenia in children with haemato-oncology cancers admitted at Kenyatta National Hospital with the aim of improving practice and policy pertaining to the management of neutropenia in this population.

METHODS

Study design

A cross-sectional study was conducted retrospectively and quantitative data were obtained on the assessment and management of neutropenia in pediatric haemato-oncology inpatients at Kenyatta National Hospital oncology wards between January 2020 and December 2020.

Study area

The study area comprised the pediatric oncology wards 1E and 3D of Kenyatta National Hospital, which is the tertiary referral hospital in Kenya as well as a teaching and research hospital comprising of 1800 bed capacity. It is located off Ngong Road along Hospital Road in Nairobi County. Specialized pediatric oncology quality health care is among the services provided at the hospital. The pediatric oncology ward 1E is located on 1st floor of the old hospital building while ward 3D is located on the third floor of the hospital's tower block. The pediatric oncology patients were admitted through the pediatric outpatient haemato-oncology clinic (POPC) and the pediatric emergency unit (PEU).

Study population

The study targeted all pediatric oncology inpatients aged ≤ 13 years with haematological cancers (leukaemias: acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML) and chronic myeloid leukaemia (CML). Lymphomas: Burkett's, Hodgkin's and non-

Hodgkin's), at Kenyatta National Hospital between 1st January 2020 and 31st December 2020.

Inclusion criteria

Patients aged ≤ 13 years during the study period, who started their induction courses of treatment at Kenyatta National Hospital, and were diagnosed with neutropenia (ANC of $<1500 \mu\text{l}$ (1.5×10^9 cells per litre)).

Exclusion criteria

All patients who satisfied the inclusion criteria above but whose medical records were inaccessible or illegible or were missing the desired information such as the total blood counts, treatment sheets, vital signs especially temperature and doctor's review notes related to neutropenia diagnosis were excluded.

Sampling technique

The study utilized a census sampling method where 113 children with haematological cancers at Kenyatta National Hospital from January-December 2020 were recruited.

Data collection instruments

Patients' medical records were reviewed and data was collected using a pre-coded data abstraction form. We developed the tool based on the study objectives so as to capture information which included vital signs, history, physical examination, laboratory investigations, radiological examination, prescription patterns of drugs used in neutropenia management (antibiotic combination therapy, antifungal therapy, haematopoietic growth factors) and clinical outcomes of management of neutropenia (discharged, died).

Data collection procedure

Data were collected after permission to review the patients' medical records was granted by the head of clinical services at the hospital. All files of patients ≤ 13 years admitted between 1st January 2020 and 31st December 2020 were retrieved and those that meet the inclusion criteria were used. Useful data were extracted from such files to the data abstraction form. This was done on a daily basis by the researchers and research assistants for one month.

Data management and analysis

Privacy and confidentiality were ensured through anonymity and careful handling of the data abstraction tool. Incompleteness and inconsistency were checked and corrections were done immediately before data were transferred to R 4.3.1 (through R Studio) for analysis to obtain descriptive statistics (mean, percentages, and proportions) and inferential statistics.

Ethical considerations

The approval to conduct the study was obtained from Kenyatta National Hospital/University of Nairobi (KNH/UoN) Ethics and Research Committee and a waiver of consent was sought for the use of medical records of the potential participants for both the pre-test and the study. An application for permission to collect data was sought at KNH research centre and pediatrics departments prior to data collection. Confidentiality of data was maintained through anonymity of data. Filled data abstraction forms were stored under key and lock to ensure that only researchers could access them. The study was non-invasive as it involved medical records of the patients hence confidentiality and anonymity were assured to prevent psychological harm to clients whose medical records were used.

RESULTS

Clinical presentation assessment of neutropenia patients

The study assessed records from 113 haemato-oncology patients diagnosed with neutropenia. Boys constituted the majority of the cases assessed, 67 (59%). The median (IQR) age at admission into the haemato-oncology ward was 6.0 (4.0, 10.0). Acute lymphocytic leukaemia, 67 (59%) was the most common haematologic cancer diagnosed whereas Hodgkin's lymphoma, 5 (4%) was the least frequently diagnosed. Most patients were at the induction stage, 47 (42%). The majority of the patients assessed had febrile neutropenia 59 (52%) (Table 1).

Documentation of the neutropenia history and vitals was also assessed in the study. Vaccination and bone marrow suppression histories were poorly documented with only 45 (40%) and 40 (35%) patients respectively.

Temperature, pulse, respiration and blood pressure were better documented as observed in 113 (100%), 112 (99%), 112 (99%), and 79 (70%) respectively (Table 2).

Table 1: Distribution of child characteristics.

Characteristic	N (%) (n=113)
Age at admission (in years)	
N	113.0
Median (IQR)	6.0 (4.0, 10.0)
Child sex	
Female	46 (41)
Male	67 (59)
Haemato-oncology cancers diagnosed	
Acute lymphocytic leukaemia	67 (59)
Acute myeloid leukaemia	9 (8.0)
Burkitt's lymphoma	17 (15)
Hodgkin's lymphoma	5 (4.4)
Non-Hodgkin's lymphoma	15 (13)
Neutropenia stage at admission	
Consolidation	24 (21)
Induction	47 (42)
Maintenance	42 (37)
Height (in cm)	
N	100.0
Median (IQR)	118.0 (107.0, 133.0)
(Missing)	13
Weight (in kg)	
N	112.0
Median (IQR)	20.5 (15.0, 27.0)
(Missing)	1
Type of neutropenia	
Febrile	59 (52)
Non-febrile	54 (48)

Table 2: Documentation of vaccination history.

Characteristics	N (%) (n=113)
Vaccination history is up-to-date	
No (records missing/incomplete)	68 (60)
Yes	45 (40)
History of use of bone marrow suppressants documented	
No (records missing/incomplete)	73 (65)
Yes	40 (35)
Temperature recorded	
Documented	113 (100)
Pulse recorded	
Documented	112 (99)
Not documented	1 (0.9)
Respiration recorded	
Documented	112 (99)
Not documented	1 (0.9)
Blood pressure recorded	
Documented	79 (70)
Not documented	34 (30)

Table 3: Levels of documentation of data on laboratory and radiological investigations.

Characteristic	N (%) (n=113)
Blood slide for malaria	
Not requested	91 (81)
Requested	22 (19)
Full haemogram	
Not requested	1 (0.9)
Requested	112 (99)
Clinical chemistry tests e.g. UECS, LFTS	
Not requested	0 (0)
Requested	113 (100)
Microbiology cultures	
Not requested	47 (42)
Requested	66 (58)
Molecular biology cytogenetics	
Not requested	110 (97)
Requested	3 (2.7)
Chest x-ray	
Not requested	73 (65)
Requested	40 (35)
Chest CT-scan	
Not requested	107 (95)
Requested	6 (5.3)

Table 4: Prescription patterns among patients.

G-CSF prescribed	Total, N (%)
No	28 (25)
Yes	85 (75)
Total	113 (100)
Antibiotic prescribed	
Combination therapy	82 (73)
Monotherapy	31 (27)
Total	113 (100)
Prescription period	
<5 days	31 (28)
5-7 days	76 (67)
Not specified	6 (5)
Total	113 (100)

Patients were also checked for various laboratory and radiological investigations done on them. The number and proportion of patients for whom blood slide for malaria, full hemogram, clinical chemistry tests, microbiology cultures, molecular biology cytogenetics, chest x-ray, and chest CT-scan requested were 22 (19%), 112 (99%), 113 (100%), 66 (58%), 3 (2.7%), 40 (35%), and 6 (5.3%) respectively as shown in Table 3.

Additionally, on checking the prescription pattern during care, 85 patients had G-CSF prescribed, combination therapy was more common, 82 (73%), whereas the majority, 76 (67%), of the patients received prescriptions of between 5-7 days long as shown in Table 4.

Clinical outcomes among neutropenia patients

In this study, we observed that the majority of patients 80 (71%) were discharged alive whereas 33 (29%) were reported to have succumbed in the course of their treatment. Among the deceased patients, more than one-third of girls died compared to only one-quarter of boys. Non-Hodgkin's lymphoma had the highest survival rates (93%) whereas acute myeloid leukaemia had the worst (22%), as indicated in Table 5.

It was also noted through Pearson's Chi-square test of independence that G-CSF prescription was statistically significantly associated with being discharged alive ($p=0.045$), as shown in Table 6.

Table 5: Distribution of patient characteristics by outcomes.

Characteristic	Deceased, n=33 N (%)	Discharged alive, n=80 N (%)
Age at admission (in years)		
N	33.0	80.0
Median (IQR)	7.0 (5.0, 11.0)	6.0 (4.0, 10.0)
Child sex		
Female	16 (35)	30 (65)
Male	17 (25)	50 (75)
Diagnosis on admission		
Acute lymphocytic leukaemia	20 (30)	47 (70)
Acute myeloid leukaemia	7 (78)	2 (22)
Burkitt's lymphoma	3 (18)	14 (82)
Hodgkin's lymphoma	2 (40)	3 (60)
Non-Hodgkin's lymphoma	1 (6.7)	14 (93)
Neutropenia stage at admission		
Consolidation	7 (29)	17 (71)
Induction	22 (47)	25 (53)
Maintenance	4 (9.5)	38 (90)
Height (in cm)		
N	28.0	72.0
Median (IQR)	121.0 (114.0, 135.0)	115.0 (103.8, 130.5)
(Missing)	5	8
Weight (in kgs)		
N	33.0	79.0
Median (IQR)	21.0 (16.0, 25.0)	20.0 (15.0, 28.0)
(Missing)	0	1
Type of neutropenia		
Febrile	20 (34)	39 (66)
Non-febrile	13 (24)	41 (76)

Table 6: G-CSF and antibiotics prescription versus patient outcomes.

	Patient outcome			P value ¹
	Deceased N (%)	Discharged alive N (%)	Total N (%)	
G-CSF prescribed				
No	4 (12)	24 (30)	28 (25)	0.045
Yes	29 (88)	56 (70)	85 (75)	
Total	33 (100)	80 (100)	113 (100)	
Antibiotic prescribed				
Combination therapy	27 (82)	55 (69)	82 (73)	0.2
Monotherapy	6 (18)	25 (31)	31 (27)	
Total	33 (100)	80 (100)	113 (100)	

¹Pearson's Chi-squared test

DISCUSSION

Characteristics and clinical presentation assessment of neutropenia patients

The study assessed records from 113 haemato-oncology patients diagnosed with neutropenia. Boys constituted

59% of the cases assessed. The median (IQR) age at admission into the haemato-oncology ward was 6 years. Leukaemias were the most common class of cancers with more than two-thirds of the patients reported. This finding was consistent with the reports by Mutua and Mwika that Leukaemias were the most prevalent childhood cancer in KNH, at 30%.¹⁰ The differences in proportion between their observation and those of our study could be

explained by the choice to focus on just a subgroup of the population (neutropenia patients), although it could also be a sign of the ever-increasing burden of leukaemias among children in the hospital, in the region and in the nation at large. In terms of the most prevalent immunophenotypes for leukaemias, patients with acute lymphocytic leukaemia were much more (59%) than those with acute myeloid leukaemia (8%). This seems to be a marked departure from the rates reported by Kabera and Macharia.¹¹ In their study, the authors highlighted AML to be twice the number of those with ALL. Most of the patients were at the induction stage, 47 (42%) when neutropenia was first detected. This was expected since this is the first step in the management of pediatric haemato-oncology cancers where the bone marrow is hard hit with chemotherapeutic agents. The majority of the patients assessed had febrile neutropenia. This finding was consistent with reports by de Castro et al and Palukuri et al, although while the latter involved adult patients suffering from breast cancers, the former study was undertaken in Spain indicating differences in context and methodology.^{12,13}

Documentation of the neutropenia history and vitals was also assessed in the study. Vaccination history and bone marrow suppression history were poorly documented with only 45 (40%) and 40 (35%) patients respectively. Temperature, pulse, respiration and blood pressure were better documented as observed in 113 (100%), 112 (99%), 112 (99%), and 79 (70%) respectively.

The documentation of most vital signs and symptoms was done satisfactorily, particularly with temperature, pulse, respiration and blood pressure recorded in the majority of the patients. History of vaccination and of bone marrow suppressant use was not always captured as evident in less than half of the patients having these documented.

Regarding, laboratory examinations, UECs and full haemograms were the most requested tests. Microbiology cultures were also requested in most patients, whereas malaria, chest x-ray and CT scans, and molecular cytogenetics were hardly requested.

Most patients were prescribed for G-CSFs. Combination therapy was also observed among patients, whereas the majority, and received prescriptions of between 5-7 days long. The prescription period was only indicative of the attention accorded to patients since the study included only inpatients who would, therefore, require daily monitoring regardless. There was no association between survival status and combination therapy.

There was an association between G-CSF prescription and survival status, among patients with leukaemia. This association was consistent with expectations from the American Cancer Society (ACS) (n.d.)'s documentation that the origin of most myelodysplastic syndromes (MDS) is a shortage of blood cells. According to ACS (n.d.), G-CSFs can improve white blood cell production and are

not used routinely to prevent infections, but they can help some MDS patients whose main problem is a shortage of white blood cells and who have frequent infections.¹⁴ The use of G-CSF is carefully selected based on the type of diagnosis and the stage of treatment. G-CSF administration during induction chemotherapy courses in leukaemia risks bone marrow stimulation to produce more abnormal or leukemic cells, instead of normal cells. As a result, the condition worsens, hence a poor prognosis. The study also reported that significantly more leukaemia patients were deceased having been put on G-CSF at induction compared to consolidation and maintenance stages. Additionally, the study findings revealed that G-CSF was effective in non-leukemic patients (such as those diagnosed with lymphomas). The practice currently advocates for the use of G-CSF in children with neutropenia in non-leukemic cancers at any stage of chemotherapy and has shown good clinical outcomes. However, G-CSF use is completely discouraged in leukaemia patients due to possible future effects and may only be used after careful consideration. Greater emphasis ought to be laid on assessment of patient status prior to prescription and administration of G-CSF, such as, through explicit contra-indication for G-CSF prescription for leukaemia patients at the induction stage.

About one-third of the patients were reported to have succumbed during their treatment. Among those who were discharged, more than half had non-febrile neutropenia with febrile neutropenia accounting for more of the deceased group. This is indicative of the devastating nature of FN as reported by Palukuri et al.¹³ Among leukaemia patients, G-CSF prescription at different stages (induction, consolidation and maintenance) of chemotherapy was significantly associated with survival. The majority of the patients who were deceased had been diagnosed while at the induction stage of treatment, whereas those diagnosed at the maintenance stage were the fewest, although this result was hugely confounded cancer diagnosis type and G-CSF prescription. Great emphasis on the nature of vigilance on management and supportive care post-induction chemotherapy to curb associated mortalities.

CONCLUSION

Neutropenia management in KNH is done as per protocol for the diagnosis and management, with room to improve on history taking. Although 29% of the children with neutropenia succumbed within the course of treatment, the majority (71%) of the patients were discharged.

Recommendations

Emphasis should be laid on documenting patient history as well as requesting for specialized examination such as microbiology cytogenetics which may prove pivotal for good patient outcomes. Greater emphasis ought to be laid on assessment of patient status prior to prescription and

administration of G-CSF, such as, through explicit contra-indication for G-CSF prescription for leukaemia patients at the induction stage.

More robust studies and approaches such as survival analysis that factor in the duration of G-CSF intake, and distribution of neutropenia among specific classes of cancers would be useful in building on these findings.

ACKNOWLEDGEMENTS

We acknowledge all the staff working in wards 1E and 1D at Kenyatta National Hospital for their cooperation during the entire period of data collection.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee from the Kenyatta National Hospital/University of Nairobi (KNH/UoN) Ethics and Research Committee and a waiver of consent was sought for the use of medical records of the potential participants for both the pre-test and the study

REFERENCES

- Dale D. How I diagnose and treat neutropenia. *Curr Opin Haematol*. 2016;23(1):1-4.
- Punnapuzha S, Edemobi P, Elmoheen A. Febrile Neutropenia. *StatPearls*. 2021.
- Mohammed H, Yismaw M, Fentie A, Tadesse T. Febrile neutropenia management in pediatric cancer patients at Ethiopian tertiary care teaching hospital. *BMC Res Notes*. 2019;12(1):528.
- Escrhuella-Vidal F, Laporte J, Albasanz-Puig A, Gudiol C. Update on the management of febrile neutropenia in haematologic patients. *Revist Españ Quimioter*. 2019;32(Suppl 2), 55.
- Muchela M. Patterns of antibiotic prescription during febrile episodes in pediatric patients with cancer at the Kenyatta National Hospital. University of Nairobi. 2020.
- Davis K, Wilson S. Febrile neutropenia in pediatric oncology. *Pediatr Child Health*. 2020;30(3):93-7.
- Rivera-Salgado D, Valverde-Munoz K, Ávila-Agüero M. Febrile neutropenia in cancer patients: management in the emergency room. *Revist Chilena Infectol*. 2018;35(1):62-71.
- Cashen A, Van Tine B. *The Washington Manual of Haematology and Oncology Subspecialty Consult; (Lippincott Manual Series)*. 4th edn. Kindle Edition. Washington. Wolters Kluwer Health; 2016.
- Kenyatta Health Information System (2021).
- Mutua I, Mwika P. Incidence of childhood cancers at a tertiary hospital in Kenya: 2009-2019. *Acta Sci Pediatr*. 2020;8(3).
- Macharia L, Mureithi M, Anzala O. Cancer in Kenya: types and infection-attributable. Data from the adult population of two National referral hospitals (2008-2012). *AAS Open Res*. 2019;1:25.
- de Castro Carpeño J, Gascón-Vilaplana P, Casas-Fernández-de Tejerina AM, Antón-Torres A, López-López R, Barnadas-Molins A, et al. Epidemiology and characteristics of febrile neutropenia in oncology patients from Spanish tertiary care hospitals: PINNACLE study. *Mol Clin Oncol*. 2015;3(3):725-9.
- Palukuri N, Yedla R, Bala S, Kuruva S, Chennamaneni R, Konatam M, et al. Incidence of febrile neutropenia with commonly used chemotherapy regimen in localized breast cancer. *South Asian J Cancer*. 2020;9(01):04-6.
- American Cancer Society (n.d.). Growth Factors and Similar Medicines for Myelodysplastic Syndromes. Available from: <https://www.cancer.org/cancer/myelodysplastic-syndrome/treating/growth-factors.html>. Accessed on 13 May 2023.

Cite this article as: Amadi BK, Limungi GM, Kezia EM, Khisa AO. Assessment of the management and outcome of neutropenia in paediatric haemato-oncology inpatients at Kenyatta National Hospital. *Int J Community Med Public Health* 2023;10:4040-6.