Safety and Efficacy of Outpatient Management Strategy for Low-Risk Febrile Neutropenia in Pediatric Oncology: A Tertiary Care Experience in Egypt

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Abstract:

Background: Low-risk febrile neutropenia (LRFN) can be managed at home safely, which also enhances quality of life and lowers medical costs. The objectives we set were to outline and evaluate the management of LRFN patients.

Methods: This prospective study enrolled 99 episodes (87 patients) of LRFN pediatric cancer patients between May 2021 and July 2022. Patients were categorized into group I (home based management protocol) and group II (in-patient care strategy).

Results: The median age of patients in this study was 8 years. 72.4%, were males. Hematological malignancies were reported in 55.2% episodes. Onset of neutropenia occurred after a median of 8 days and persisted for a median of 6 days. Fever and presence of a focus of infection were reported in 37.4% and 32.3% of the episodes, respectively. Respiratory tract infections (62.5%) were the main focus of infections recorded in the study. 82% of patients received oral antibiotics as an outpatient management approach. Seventeen % of patients received intravenous mono-therapy in the hospital. Recovery was recorded in 90 episodes (90.9%) (95.1% in group I and 70.6% in group II), while failure of treatment was reported in 4 patients, and 3 in-patient cases shifted to high risk, and 2 in-patient cases that developed complications (typhilitis and convulsions). The risk factors for adverse effects were lower CBC parameters (TLC, ANC, AMC, and PLT), hospital admission and raised CRP.

Conclusion: Outpatient management strategy recorded higher recovery rate than in patient management strategy.

Keywords: Low Risk; Fever, Neutropenia, Pediatric; cancer; outpatient management

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Introduction:

Cancer is one of the most serious diseases all over the world. According to WHO 2021, an estimated 400,000 children and adolescents between the ages of 1 day and 19 years are predicted to develop cancer each year. [1]

Egypt is a middle-income country in which 40% of the individuals are under the age of 18 (38.9 million in 2018) with an age-standardized incidence rate of cancer approaching 166.6 per 100,000 person. [2]

Fever and Neutropenia (FN) is the most serious hematologic complication of chemotherapy and the leading cause of morbidity and mortality in oncology patients receiving intensive chemotherapy, which in turn is associated with significant economic and social burden on the health care system. It is linked to the possibility of infections that could be fatal in many cases, as well as chemotherapy dose reductions and delaying the course of treatment, which could affect its efficacy. [3]

Children with cancer and FN are a heterogeneous group with varying risk of infection and mortality are stratified into high risk for development of infection and more prone to development of complications and sepsis with higher risk of mortality.Those were grouped into High Risk Fever Neutropenia patients (HRFN) while patient that have low risk for complication are Low Risk Fever Neutropenia patients (LRFN). [4]

Outpatient management is a recognized treatment for LRFN patients aiming to reduce hospital stays with improvement of patients' quality of. Life. It diminishes the overall cost of treatment and save hospital beds as well, but most importantly it decreases possibility of hospital acquired infections (HAIs).[5, 6] However,

outpatient management application is individualized and not standardized without uniform criteria for the population implicated as it differs according to the institutional guidelines and facilities. [7] In South Egypt cancer Institute (SECI), protocol of management of LRFN previously depended on intravenous antibiotic treatment and hospitalization. [8]

This study aimed to outline the schedule for management of LRFN in pediatric oncology department in SECI, assess the outcome of the outpatient oral antibiotic treatment in LRFN patients compared to the hospitalized LRFN patient that don't fulfill the criteria to be discharged and treated with intravenous antibiotic and to assess the factors affecting morbidity and mortality among the targeted population.

Patients and Methods:

Patients:

This prospective study was carried out at the Pediatric Oncology and Hematological Malignancy Department, South Egypt Cancer Institute (SECI) (the only university tertiary centers of pediatric oncology in Upper Egypt), Assiut University, between May 2021 and July 2022. The study was approved by the local ethical committee of SECI (IRB No: 561). Informed written consents were taken from the patients' caregivers before being included in this study.

During the study period, 287 episodes (106 patients) with both hematological and solid tumors (age:1-18 years, with established neutropenia after receiving myelosuppressive chemotherapy, were enrolled. Ninety-nine episodes (87 patients) of LRFN fulfilled the criteria, while HRFN patients and patients not fulfilling the inclusion criteria were excluded.

Definitions:

Fever is defined as a single oral temperature of 38.3ºC (101º F) or a temperature greater than 38.0ºC (100.4º F) sustained for more than 1 hour in a patient with neutropenia.

Neutropenia is defined as an absolute neutrophil count (ANC) of less than 500/µL, or less than 1000/µL with an anticipated decline to less than 500/µL in the next 48-hour period.

LRFN patients are those with an anticipated brief (≤ 7 days duration) period of neutropenia and ANC >1000 cells/mm³ with no serious medical comorbid conditions.

Inclusion criteria:

Patients with LRFN enrolled were: older than one year, younger than 18 year, clinically well-appearing, vitally stable with no comorbid conditions as assessed by the evaluating physician, [denovo cases with Acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) on maintenance therapy (> week 20 in high and stander risk disease, > week 9 in low risk disease in modified st. Jude total XV treatment protocol)[9], Hodgkin lymphoma or solid tumors on standard chemotherapy].

Exclusion criteria:

Patients with AML, NHL, Patients in relapse or with uncontrolled disease receiving intensive or salvage chemotherapy treatment except high risk solid tumors patients on remission receiving standard chemotherapy treatment , Hematopoietic stem cell transplant (HSCT) patient, patient with solid tumor underwent surgery within 2 weeks, patients with history of overwhelming sepsis, history of MDR infection (multi-drug resistance) or ICU admission within the last 6 month and patients with Down syndrome were excluded.

Methods:

Evaluation:

For each patient enrolled in the study, demographic data analyzed included age, gender and diagnosis, Detailed history including chemotherapy, administration first and last day, previous sepsis, ICU admission, infection, complete physical examination and routine laboratory investigations including complete blood counts (CBC) with determination of absolute neutrophil counts (ANC) were mandatory, liver and kidney function tests, C- reactive protein (CRP), serum electrolytes (sodium, potassium, magnesium, phosphorus level) and blood cultures at presentation and repeated as needed.

Analysis of the neutropenic episodes:

Concerning the onset, amplitude, duration and grade of neutropenia (mild neutropenia when the ANC is 1000- 1500 cells/µl, moderate neutropenia when the ANC of 500-1000 cells/µl, severe neutropenia refers to an ANC <500/µl and profound neutropenia refers to an ANC <100 cells/µl), time to recovery from neutropenia, presence of associated fever and its duration and days of hospitalization.

Grouping:

LRFN patients were identified and classified into 2 groups according to eligibility criteria

Group (I) (Home based management protocol): the included patients were: patents lived less than 1hour/40miles from SECI, with available safe transportation and working telephone, compliance to oral antibiotic, without significant focus of infection (that requires admission), good care and hygiene and no history of shaking chills at the current episode.

Group (II) (In-patient care strategy): patients not fulfilling criteria for outpatient regimen of treatment, patients with history of intolerance to oral treatment and afebrile patients with severe neutropenia were included in to our study if the patient lived far away within more than 1 hour from SECI (SECI present its service to many patients allover upper Egypt).

Treatment strategy and follow-up:

As demonstrated by Figure 1) showing algorithm 1, the strategy included the following:

Group (I): will receive oral antibiotic combination of fluoroquinolones (ciprofloxacin) PO (10-20 mg/kg/day) with amoxicillin clavulanate PO (45 mg/kg/day PO q12h).

Group (II): will receive monotherapy third-generation cephalosporin (ceftazidime) IV, daily dosage: 150 mg/kg/dose and amikacin 15 mg/kg/day once daily was added if indicated.

Follow-up of the patients and re-assessment:

Group I and II will be assessed and evaluated by full history, physical examination, CBC, C-reactive protein (CRP), and blood culture.

For group I: will be assessed every 72 hours.

If the patient is clinically stable, CBC rising or stable, fever pattern is improving, the culture is negative, and CRP is negative or declining, continue as home-based approach.

If the patient developed any vital instability, CBC is declining; fever or focus of infection is not controlled, positive culture or CRP is rising or becomes positive Hospitalization and shift to HRFN treatment protocol.

For group II: will be assessed every 48 hours

If the patient is clinically stable, CBC rising, culture is negative, and CRP negative or declining, Discharge on oral antibiotic (step-wise approach) with the consideration of early discharge within 48 hours.

If the patient is still neutropenic and clinically stable, fever subsided or improving, culture is negative and CRP is negative or declining, Continue on the same antibiotic therapy.

If the patient shows deterioration of the clinical condition, persistent neutropenia or fever, ANC drops below 100, CRP is rising or becomes positive, or become febrile, Shift to HRFN treatment protocol.

Criteria of discontinuation of antibiotic and/or discharge from hospital:

Recovery from neutropenia: ANC≥300 and rising.

Afebrile for ≥ 24 hours.

Resolution of the infection and any clinical morbidity.

The last blood culture is negative for more than 48 hours, and CRP is declining or negative.

The outcome:

The outcome of each episode was assessed regarding recovery or failure of treatment (development of complication, readmission for in-patient group II discharged on step-wise approach of neutropenia if there was recurrence of the fever or reappearance of any symptoms or signs of infection in the same episode ± affection of the oral treatment intake, shift to HRFN protocol infection-related mortality and morbidity, ICU admission) and prognostic factors affecting their outcome.

Statistical analysis:

All statistical calculations was done using SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) version 22. Data were statistically described in terms of mean ± standard deviation (±SD), or median and range when not normally distributed, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables was done using Mann Whitney U test or Kruskal Wallis test as the data were not normally distributed. Wilcoxon sign rank test was used for comparing paired quantitative data overtime. For comparing categorical data, Chi square ($\chi 2$) test was performed. Fisher Exact test was used instead when the expected frequency is less than 5. P-value is always 2 tailed set significant at 0.05 levels.

Results:

Patient characteristics and grouping were illustrated in Table 1 the main criteria for the selected patients Majority of patients were males (72.4%) with a median age 8 years old. Hematological malignancies were reported in most of the cases in 48 episodes (55.2%), mainly ALL, accounting for 35.6% of the patients. Most of the patients with hematological diseases were stratified into low risk (LR) and standard risk (SR) disease in 14.6% and 43.8%, respectively.

Solid tumors represented (44.8%) with the majority were Ewing sarcoma (ES) in (12.6%) patients. About 60% of the patients had low risk and intermediate-risk disease.

LRFN patients were classified into 2 groups according to eligibility criteria to group I represented by [82/99 (82.8%)] episodes and group II by [17/99 (17.2%)] episodes.

Analysis of neutropenic episodes As demonstrated by table 2: The onset of neutropenia occurred after a median of 8 days of receiving the last cycle of chemotherapy and persisted for a median of 6 days, with no significant difference between group I and group II regarding the onset of neutropenia (p=0.786).

The median duration of hospital admission recorded were 7 days in group II.

Moderate neutropenia occurred in (32.3%) while severe neutropenia occurred in (67.7%) of the episodes, mainly in group II patients with a significant difference from group I (p=0.046).

Neutropenic episodes were associated with fever in (37.4%) {35.4% of group I and 47.1% of group II} that persisted for a median duration of 4 days with no significant difference.

Concomitant infections were reported in (35.4%) of the episodes, mainly in group II (70.5 %) versus (28%) in group I, with statistically significant difference in between (p=0.046). The majority of the cases had respiratory tract infection (RTI) in (20.2%) of episodes {15.9 % of group I and 41.2% of group II}.

Outcome:

Recovery:

Among the study groups, recovery from neutropenia was recorded in 90.9% of the episodes. Most of them belonged to group I by 95% with statistically significant difference from group II (p=0.007).

Regarding group II, there were (6/12) recovered episodes. Five of them were registered to be managed by a step-wise approach, and one episode was managed by early-discharged after approximately 48 hours of

admission with a favorable outcome, and no readmission was reported.

Treatment failure:

Failure of treatment was recorded in 9 episodes, 4 episodes in group I and 5 episodes group II. Most of them 7 needed a shift to HRFN protocol (4 episodes in group I and 3 episodes in group II). Only 2 episodes belonging to group II had developed complications (11.8% of group II episodes) {a case of typhilitis and a case of convulsion due to superior sagittal sinus thrombosis which is considered as non-neutropenic complication}.

Prognostic factors affecting the outcome:

Univariate analysis of all the 99 episodes showed that lower values of CBC elements at the presentation were significant predictor for treatment failure in the patients as TLC: (P=0.004), ANC: (P=0.001), MONO: (p=0.04) and PLT: (p=0.03), also positive CRP (P=0.022), in patient management in group II recording 55.6% of the cases that developed adverse effect versus 44.4% in outpatient management group I (P=0.007) . However, age, sex, residency, presence of focus of infection, and diagnosis, no significant effect was recorded on the outcome. shown in Table (3).

On analysis of the predictive ability of CRP for prediction of treatment failure among the studied cases by using the ROC curve analysis showed that the best cut off point recorded for a value of 0.045 (ng /ml); the areas under the curve (AUC) was 95.9% (95%CI: 0.924 – 0.993, P<0.001) with a sensitivity and specificity and accuracy of 90.0% and the best cut off point recorded for (CRP = 18) thus cases with CRP ≥ 18 were at higher risk for treatment failure.

Multivariate logistic regression analysis showed that only raised CRP is a significant predictor of treatment failure among the studied cases, that for every one unit increase in CRP level the probability of treatment failure was increased by 8.0% (OR=1.080, 95% CI 1.001 – 1.164.4, P=0.046).

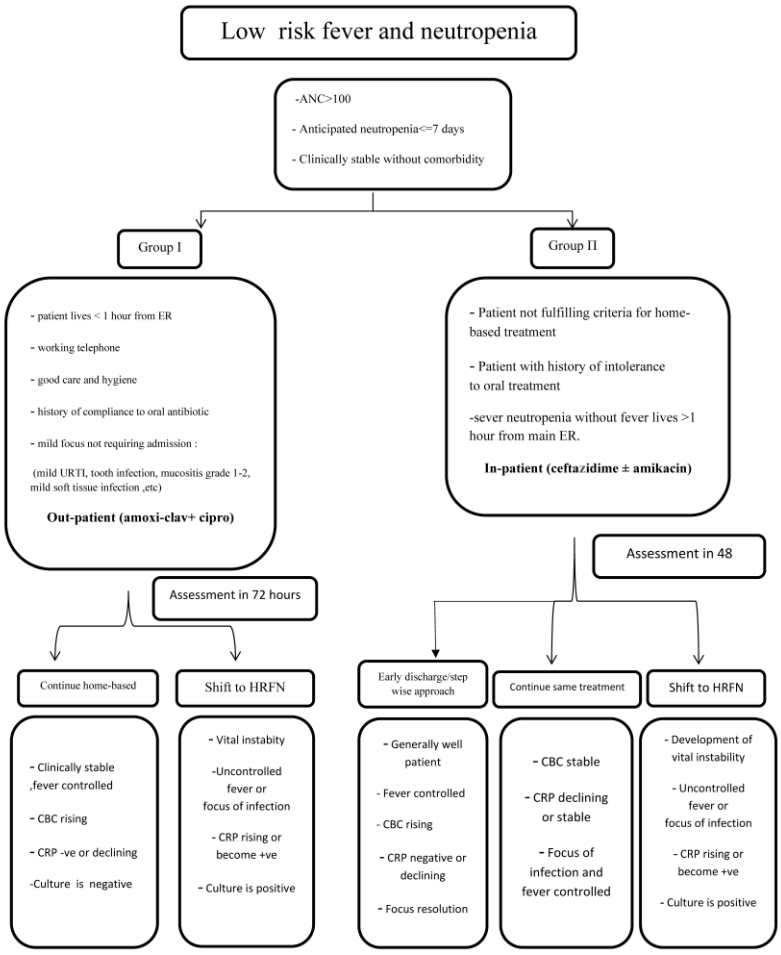

Figure (1): Algorithm shows assessment of patients with low risk fever and neutropenia

Abbreviations: LRFN: low risk fever Neutropenia, HRFN: high risk fever neutropenia, ANC: absolute neutrophilic count, ER: emergency room, URTI: upper respiratory tract infection, CBC: Complete blood count, CRP: C - reactive protein

Table (1): Demographic data and patient characteristics of the studied 87 patients

Variable name		N	(%)
Age (years)	• Mean ± SD	8. 54 ± 4.48	
	• Median (range)	8 (1 – 18)	
Sex	• Male	63	(72.4)
	• Female	24	(27.6)
	• Male : Female ratio	2.6 : 1	
Residence	• Rural	60	(69.0)
	• Urban	27	(31.0)
Diagnosis	• Hematological tumors	48	(55.2)
	▪ ALL	31	(35.6)
	▪ NHL (LBL)	5	(5.7)
	▪ HL	12	(13.8)
	• Solid tumors	39	(44.8)
	▪ ES	11	(12.6)
	▪ RMS	10	(11.5)
	▪ OS	3	(3.4)
	▪ NB	6	(6.9)
	▪ WT	4	(4.6)
	▪ Brain tumors	5	(5.7)
Risk stratification for solid tumors	• Low risk	3	(7.7)
	• Intermediate risk	20	(51.3)
	• High risk	16	(41.0)
Risk stratification for hematological tumors	• Low risk	7	(14.6)
	• Intermediate risk	21	(43.8)
	• High risk	20	(41.7)

Abbreviations: **ALL:** Acute lymphocytic leukemia, **NHL (LBL)**: Non Hodgkin lymphoma lymphoblastic lymphoma, **HL**: Hogkin lymphoma ,**ES**: Ewing sarcoma, **RMS**: Rabdomyosarcoma, OS: Osteosarcoma, **NB**: Neuroblastoma, **WT**: WILMS TUMOR, **SD**: standard deviation.

Table (2): Analysis of the neutropenic episodes in the studied 99 episodes.

	Total (n=99)	Group I (n=82)	Group II (n=17)	P value*
Onset of neutropenia (days)				0.786
• Mean ± SD	9.05 ± 2.73	9.04 ± 2.71	9.12 ± 2.96	
• Median (range)	8 (4 – 15)	8 (4 – 15)	9 (4 – 15)	
Duration of neutropenia (days)				0.762
• Mean ± SD	5.93 ± 1.72	5.88 ± 1.39	6.18 ± 2.86	
• Median (range)	6 (2 – 14)	6 (2 – 9)	6 (3 – 14)	
Degree of neutropenia, n (%)				**0.046**
• Mild neutropenia	0 (0.0)	0 (0.0)	0 (0.0)	
• Moderate neutropenia	32 (32.3)	30 (36.6)	2 (11.8)	
• Severe neutropenia	67 (67.7)	52 (63.4)	15 (88.2)	
Fever, n (%)				0.364
• No	62 (62.6)	53 (64.6)	9 (52.9)	
• Yes	37 (37.4)	29 (35.4)	8 (47.1)	
• Median duration (days)	4 (1 – 8)	4 (1 – 8)	5 (2 – 8)	0.354
Focus of infection, n (%)				**0.046**
• No	64 (64.6)	60 (73.2)	5 (29.4)	
• Yes	**35 (35.4)**	**23 (28.0)**	**12 (70.5)**	
GIT infection, n (%)	12 (12.1)	8 (9.6)	4 (23.5)	0.834
• Oral mucositis	10 (10.1)	7 (8.5)	3 (25)	
• Tooth infection	2 (2)	1 (1.2)	1 (8.3)	
Chest infection, n (%)	20 (20.2)	13 (15.9)	7 (41.2)	0.112
• URTI	16 (16.2)	12 (14.6)	4 (33.3)	
○ pharyngitis	8 (8.1)	6 (7.3)	2 (11.8)	
○ tonsillitis	7 (7.1)	5 (6.1)	2 (11.8)	
○ otitis media	1 (1)	1 (1.2)	0 (0)	
• LRTI (Bronchitis)	4 (4)	1 (1.2)	3 (25)	
Soft tissue infection, n (%)	3 (3)	2 (2.4)	1 (5.9)	0.337
• Cellulitis	2 (2)	2 (2.4)	0 (0.0)	
• Abscess	1 (1)	0 (0.0)	1 (5.9)	

Abbreviations: **SD**: standard deviation, **URTI**: upper respiratory tract infection, **LRTI:** lower respiratory tract infection. Quantitative data are presented as median (range); qualitative data are presented as number (percentage). Significance defined by $p < 0.05$

* Mann Whitney U test was used for comparing both groups.

** Chi square ($\chi 2$) test or Fisher Exact tests were used for comparing categorical data.

Table (3): Factors affecting treatment failure among the studied 99 episodes.

Variables	Total recovery (n=90)	Treatment failure (n=9)	P value*
Sex, n (%)			0.694
• Male	67 (74.4)	6 (66.7)	
• Female	23 (25.6)	3 (33.3)	
• Male : female ratio	2.91:1	2:1	
Age (years)			0.604
• Mean ± SD	8.49 ± 4.61	9.06 ± 3.88	
• Median (range)	8 (1 – 18)	10 (4 – 16)	
Residence, n (%)			1
• Rural	62 (68.9)	6 (66.7)	
• Urban	28 (31.1)	3 (33.3)	
Focus of infection, n (%)			0.144
• No	63 (70.0)	4 (44.4)	
• Yes	27 (30.0)	5 (55.6)	
Fever, n (%)			0.477
• No	55 (61.1)	7 (77.8)	
• Yes	35 (38.9)	2 (22.2)	
Diagnosis, n (%)			1
• Solid tumors	40 (44.4)	4 (44.4)	
• Hematological tumors	50 (55.6)	5 (55.6)	
Laboratory data, median (range)			
• TLC (10^3/l)	1.8 (0.5 – 6.3)	0.9 (0.5 – 1.7)	**0.004**
• ANC (10^3/l)	0.4 (0.1 – 0.9)	0.2 (0.12 – 0.30)	**0.001**
• Monocyte (10^3/l)	0.26 (0.0 – 1.9)	0.02 (0.0 – 0.42)	**0.043**
• Hemoglobin (g/l)	10.6 (6.8 – 13.4)	9.7 (7.7 – 11.4)	0.139
• Platelets (10^3/l)	204 (19 – 624)	123 (44 – 290)	**0.037**
CRP, (n=49)			**0.022****
• Negative	16 (40.0)	0 (0.0)	
• Positive	24 (60.0)	9 (100.0)	
Management, n (%)			**0.007**
• Group I	78 (86.7)	4 (44.4)	
• Group II	12 (13.3)	5 (55.6)	

Abbreviations: **TLC**: total leucocytic count; **ANC**: absolute neutrophilc count. Quantitative data are presented as median (range), qualitative data are presented as number (percentage). Significance defined by $p < 0.05$

* Mann Whitney U test was used for comparing both groups.

** Chi square ($\chi 2$) test or Fisher Exact tests were used for comparing categorical data.

Discussion:

Fever and Neutropenia is a common side effect of the myelo-suppressive chemotherapy that frequently necessitates hospitalization [10]; however, patients with LRFN can be managed safely without admission. [11]

There is no uniform algorithm of the management of LRFN in pediatric oncology patients, as it depends on facilities and the pattern of infection in each institute. [12] In SECI, the previous management of LRFN depended mainly on hospitalization, but with the development of the facilities and supportive care in our institute, we could modify the treatment approach in those patients with outpatient management.

The median time of onset of neutropenia occurred after 8 days from the last chemotherapy and persists for a median of 6 days in comparison to Sayed et al study that reported onset of neutropenia occurred within a median of 9 days and persists for 10 days, this could be attributed to the inclusion of HRFN episodes in their study. [8]

The analysis of neutropenic onset and duration between both groups in our study showed that there was no significance difference recorded, which is comparable to Orme et al study of LRFN in-patient versus out-patient management. [5]

Most of the cases (64.6%) had no recorded infections. The most prominent documented focus of infection in the episodes was upper respiratory tract infections in 20.2% of the cases, which is in agreement with Mohammed et al 2019 results. [13]

Among the study group, we reported recovery from neutropenia as high as 90.9% episodes, while failure of treatment (shift to HRFN protocol and development of complications) reported in (9.1%) episodes which is almost the same results of Paolino et al 2019 performed in USA reporting (90%) recovery and (10%) failure cases.[14] Unlike Cagol 2009 and his colleagues, who recorded success in the treatment of neutropenia in only 49.8%,55.2% episodes of Group I and II, respectively . This difference may be due to the inclusion of patients with advanced and metastatic tumors and cases receiving intensified chemotherapy as low-risk patients in the Cagol cohort. [15]

We recorded significant difference between the study groups in the recovery rate (95.1% in group I and 70.6% in group II) which was not recorded in Paolino et al (93% out-patient and 85% inpatient) which is explained by the difference in the study design as cases were randomized in Paolino et al 2019 study while in our cohort, group II recorded more patients with severe neutropenia and focuses of infection requiring admissions.[14] Also, we have a higher disparity between both groups' population sizes (82 episodes in group I and 17 in group II).

As patients included in the study had a lower rate of morbidity, we recorded no mortalities in our study. this is in agreement with the results of Paolino et al 2019 [14] and in contrast to Cagol et al 2009. [15]

In group II analysis of the recovery cases, 5/12 of the episodes were recorded to be managed with the step-wise approach as they were discharged after 72 hours on oral antibiotics, while one case was early discharged without oral antibiotics after 48 hours with no readmission recorded. This finding was also reported in Avilés-Robles et al 2020 cohort as 100% of cases prone to a step-wise approach (after 48-72 hours) by oral antibiotics had a favorable outcome, despite that only 93% of the in-patient group had a favorable outcome, but no statistical significance was recorded. [16]

Predictors of treatment failure in LRFN in this cohort recorded that patients with lower CBC parameters (TLC, ANC, MONO, PLT) at the presentation, positive CRP and in-patient management protocol in comparison to outpatient management protocol. This could be due to the lower CBC parameters (TLC and ANC) recorded in group II and the possibility of hospital acquired infection though we couldn't prove it statistically. More sample size is needed.

Multivariate analysis stated that only positive CRP values are found as the most significant predictor of treatment failure.

CRP was done in 49 episodes at presentation with a level estimated between (12-96 mg/dl), with no significant difference between both groups. The measured cut-off point in our cohort was (CRP >18 mg/dl). Thus, CRP > 18 is an alarm that must be taken into consideration during the identification of LRFN patients. This matches the systematic review and meta-analysis done by Phillips and his colleagues documented that positive CRP values were predictors for adverse effects in pediatric FN with an estimated cut-off point > 50 mg/dl. This is maybe due to the inclusion of HRFN patients in this meta-analysis.[17] A higher sample size is needed to estimate and establish the cut-off point.

Conclusion:

This study supports the safety of the outpatient management strategy for LRFN pediatric patients with un necessary hospitalization, with an excellent recovery rate, and no recorded major complications or mortalities were observed.

Limitations:

- The small number of episodes.
- The lack of published data concerning LRFN.
- Some lab facilities are not available in our center.
- The unavailability of an outpatient setting. Inpatient group II category could be treated in an outpatient setting instead of hospitalization.

Recommendations:

Further research using reduction of treatment in pediatric cancer patients with FN should be conducted with focusing on the inclusion of more number of patients and risk criteria modification for better selection and best timing for discharge, as well as using proper out-patient settings for better surveillance of patients and protection from untoward hospitalization.

References:

1. World health Organization. Cure All framework: WHO global initiative for childhood cancer: increasing access, advancing quality, saving lives. 2021.
2. Soliman RM, Elhaddad A, Oke J, et al. Temporal trends in childhood cancer survival in Egypt, 2007 to 2017: A large retrospective study of 14 808 children with cancer from the Children's Cancer Hospital Egypt. International journal of cancer. 2021;148(7):1562-74.
3. Boccia R, Glaspy J, Crawford J, et al. Chemotherapy-induced neutropenia and febrile neutropenia in the US: a beast of burden that needs to be tamed? The oncologist. 2022;27(8):625-36.
4. Haeusler GM, Thursky KA, Slavin MA, et al. Risk stratification in children with cancer and febrile neutropenia: a national, prospective, multicentre validation of nine clinical decision rules. EClinicalMedicine. 2020;18.
5. Orme LM, Babl FE, Barnes C, Barnett P, et al. Outpatient versus inpatient IV antibiotic management for pediatric oncology patients with low risk febrile neutropenia: a randomised trial. Pediatric blood & cancer. 2014;61(8):1427-33.
6. Dulisse B, Li X, Gayle JA, et al. A retrospective study of the clinical and economic burden during hospitalizations among cancer patients with febrile neutropenia. Journal of medical economics. 2013;16(6):720-35.
7. Lehrnbecher T, Phillips R, Alexander S, et al.

Guideline for the management of fever and neutropenia in children with cancer and/or undergoing hematopoietic stem-cell transplantation. Journal of clinical oncology. 2012;30(35):4427-38.

8. Sayed H, Amir Y, Osman A. Neutropenic Fever in Pediatric Patients with Cancer in South Egypt: A Report from a Single Institute. International Journal of Cancer and Biomedical Research. 2022;6(1):47-55.
9. Yilmaz B, Koc A, Dogru O, et al. The results of the modified St Jude Total Therapy XV Protocol in the treatment of low-and middle-income children with acute lymphoblastic leukemia. Leukemia & Lymphoma. 2023;64(7):1304-14.
10. Mack J, Spray B, Mack D, et al, editors. PEGFILGRASTIM ADMINISTRATION TIMING AND ITS EFFECT ON FEBRILE NEUTROPENIA IN PEDIATRIC PATIENTS. PEDIATRIC BLOOD & CANCER; 2019: WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.
11. Haeusler GM, Gaynor L, Teh B, et al. Home-based care of low-risk febrile neutropenia in children—an implementation study in a tertiary paediatric hospital. Supportive Care in Cancer. 2021;29:1609-17.
12. Teuffel O, Ethier M, Alibhai S, et al. Outpatient management of cancer patients with febrile neutropenia: a systematic review and meta-analysis. Annals of oncology. 2011;22(11):2358-65.
13. Mohammed HB, Yismaw MB, Fentie AM, et al. Febrile neutropenia management in pediatric cancer patients at Ethiopian Tertiary Care Teaching Hospital. BMC research notes. 2019;12:1-6.
14. Paolino J, Mariani J, Lucas A, et al. Outcomes of a clinical pathway for primary outpatient management of pediatric patients with low-risk febrile neutropenia. Pediatric blood & cancer. 2019;66(7):e27679.
15. Cagol ÂR, Castro Junior CGd, Martins MC, et al. Oral vs. intravenous empirical antimicrobial therapy in febrile neutropenic patients receiving childhood cancer chemotherapy. Jornal de Pediatria. 2009;85:531-5.
16. Avilés-Robles MJ, Reyes-López A, Otero-Mendoza FJ, et al. Safety and efficacy of step-down to oral outpatient treatment versus inpatient antimicrobial treatment in pediatric cancer patients with febrile neutropenia: A noninferiority multicenter randomized clinical trial. Pediatric Blood & Cancer. 2020;67(6):e28251.
17. Phillips RS, Wade R, Lehrnbecher T, et al. Systematic review and meta-analysis of the value of initial biomarkers in predicting adverse outcome in febrile neutropenic episodes in children and young people with cancer. BMC medicine. 2012;10:1-13.