JHWCR
Journal of Health, Wellness, and Community Research
Volume III, Issue IV
Open Access, Double Blind Peer Reviewed.
Web: https://jhwcr.com, **ISSN**: 3007-0570
https://doi.org/10.61919/dyepxp89

Article

Impact of Filgrastim Versus Pegfilgrastim on Hospital Stay and Mortality Among Chemotherapy-Induced Febrile Neutropenia Patients

Samar Minallah[1], Amer Rehman Farooqi[1], Zainab Shakeel[1], Ayesha Khan[1], Hafsah Iqbal[1], Kashif Sajjad[1]

1 Shaukat Khanum Memorial Cancer Hospital, Peshawar, Pakistan

Correspondence
kgmcmbbs3@gmail.com

Cite this Article

Received	2025-04-07
Revised	2025-04-26
Accepted	2025-04-28
Published	2025-05-13
Conflict of Interest	None declared
Ethical Approval	Respective Ethical Review Board
Informed Consent	Obtained from all participants
Data/supplements	Available on request.
Funding	None
Authors' Contributions	SM, ARF, ZS, AK, HI, and KS contributed to concept, design, data collection, analysis, and manuscript drafting.

ABSTRACT

Background: Febrile neutropenia (FN) is a life-threatening complication of chemotherapy that often necessitates hospitalization and may increase mortality. While granulocyte colony-stimulating factors (G-CSFs) like filgrastim and pegfilgrastim are used to mitigate FN risk, limited comparative data exists in resource-limited settings, particularly in Pakistan. **Objective**: To compare the impact of filgrastim versus pegfilgrastim on hospital stay duration and mortality among patients with chemotherapy-induced febrile neutropenia. **Methods**: This prospective cohort study enrolled 199 adult patients (n = 199) with chemotherapy-induced FN at Shaukat Khanum Memorial Cancer Hospital, Peshawar, from September 2023 to May 2024. Inclusion criteria were adults diagnosed with FN requiring G-CSF therapy; those with G-CSF contraindications, pregnancy, or unrelated active infections were excluded. Patients received either filgrastim (300 mcg/day for five days) or pegfilgrastim (6 mg single dose). Clinical characteristics, neutrophil counts, and outcomes were recorded. Ethical approval was granted by the hospital IRB in accordance with the Declaration of Helsinki. Data were analyzed using SPSS v25; chi-square and Mann-Whitney U tests were applied to assess statistical significance. **Results**: Pegfilgrastim significantly reduced hospital stay (0 vs. 7 days; $p < 0.0001$) and was associated with fewer cases of severe neutropenia (0 vs. 7; $p < 0.0001$). All three reported deaths occurred in the filgrastim group, though not statistically significant ($p = 0.118$). Clinically, pegfilgrastim showed superior hematological recovery and fewer hospitalizations. **Conclusion**: Pegfilgrastim demonstrated greater clinical efficacy than filgrastim by reducing hospital stay and neutropenia severity without increasing mortality, making it a more effective FN management strategy in low-resource oncology settings.

Keywords: Febrile Neutropenia, Chemotherapy, Filgrastim, Pegfilgrastim, Granulocyte Colony-Stimulating Factor, Hospital Stay, Mortality

INTRODUCTION

Febrile neutropenia (FN) is a life-threatening complication frequently encountered in patients undergoing myelosuppressive chemotherapy, characterized by an abnormally low neutrophil count coupled with fever. This condition not only imposes significant morbidity and mortality risks but also disrupts planned chemotherapy schedules, leading to dose reductions or treatment delays that may compromise therapeutic efficacy and patient outcomes (1). Severe neutropenia, defined by absolute neutrophil counts below 0.5×10^9/L, predisposes individuals to opportunistic infections, necessitating urgent medical intervention and prolonged hospitalization. The repercussions of FN extend beyond the clinical, encompassing increased healthcare costs and decreased quality of life due to extended hospital stays and aggressive antimicrobial therapy (2,3). Mortality related to FN remains high, especially in vulnerable populations such as the elderly and those with comorbidities, with some studies reporting rates as high as 40% during acute episodes (4). Longitudinal analyses further highlight that mortality risk persists beyond the initial infectious event, underscoring the chronic impact of FN on cancer patients (5).

To mitigate the adverse effects of chemotherapy-induced neutropenia (CIN), the use of granulocyte colony-stimulating factors (G-CSFs) such as filgrastim and pegfilgrastim has been widely adopted. These agents stimulate the production and activation of neutrophils, thereby reducing the frequency, duration, and severity of FN episodes. Filgrastim, the conventional form, typically requires daily subcutaneous administration, whereas pegfilgrastim, a PEGylated long-acting

variant, offers the convenience of a single injection per chemotherapy cycle. Despite their pharmacological similarities, clinical guidelines in high-income countries often consider both agents equally effective based on randomized controlled trials demonstrating non-inferiority (6,7). However, recent comparative studies challenge this equivalence. Sharma et al. reported a statistically significant reduction in FN incidence, hospital admissions, and associated costs among patients receiving pegfilgrastim compared to filgrastim (8). These findings suggest that the long-acting formulation may provide not only clinical but also economic advantages, especially in oncology settings where resource optimization is critical (9).

In the context of low- and middle-income countries (LMICs) like Pakistan, the stakes are even higher. Access to supportive oncology care is inconsistent, and treatment decisions are often influenced by availability, cost, and institutional protocols rather than strict clinical guidelines. There exists a notable gap in localized data comparing the effectiveness of filgrastim and pegfilgrastim in such environments, particularly in terms of outcomes like hospital stay duration and mortality. Given the high burden of cancer in regions like Khyber Pakhtunkhwa and the concentration of tertiary care facilities such as Shaukat Khanum Memorial Cancer Hospital, evaluating real-world outcomes of these interventions is essential for evidence-based resource allocation. Moreover, cancer types, patient comorbidities, and risk stratification based on chemotherapy regimens in this setting may differ markedly from those in Western populations, warranting locally contextualized research. Previous studies have not sufficiently addressed how G-CSF choice influences clinical outcomes in heterogeneous cohorts across varying chemotherapy risk levels, leaving clinicians with limited empirical guidance.

Therefore, this study aims to address a significant knowledge gap by comparing the impact of filgrastim and pegfilgrastim on hospital stay length and mortality among patients with chemotherapy-induced febrile neutropenia in a tertiary care setting in Peshawar. By evaluating these two widely used G-CSFs under real-world conditions, the study seeks to inform clinical decision-making, optimize patient management strategies, and support the development of institutional protocols tailored to resource-constrained healthcare environments. The underlying hypothesis posits that pegfilgrastim, due to its sustained pharmacodynamic activity, will be associated with a shorter hospital stay and reduced mortality compared to filgrastim.

MATERIALS AND METHODS

This prospective cohort study was conducted at the Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital, Peshawar, from September 2023 to May 2024. Adult patients of either gender who developed febrile neutropenia (FN) as a complication of chemotherapy were included after meeting defined eligibility criteria. Inclusion criteria comprised patients aged 18 years and older who had an absolute neutrophil count (ANC) of <500 cells/mm^3 accompanied by a fever of ≥38.3°C once or ≥38.0°C sustained over one hour, confirmed through laboratory tests. Patients were excluded if they had known hypersensitivity to granulocyte colony-stimulating factors (G-CSFs), contraindications to G-CSF therapy, prior exposure to bleomycin, were pregnant or breastfeeding, or presented with unrelated active infections requiring urgent medical attention. Participants were enrolled using a non-probability consecutive sampling technique. All eligible patients provided written informed consent before inclusion, and patient confidentiality was ensured throughout the study. The study protocol adhered to the principles of the Declaration of Helsinki and received ethical approval from the hospital's institutional review board.

The study aimed to evaluate and compare the clinical effectiveness of filgrastim and pegfilgrastim in patients with chemotherapy-induced FN. The primary outcomes assessed were hospital stay duration and all-cause mortality. Secondary outcomes included post-treatment ANC levels, severity of neutropenia, white blood cell (WBC) counts including leukopenia and leukocytosis, and signs of sepsis such as fever, tachycardia, and respiratory abnormalities. Participants were categorized into two groups based on the G-CSF therapy administered. Group A received filgrastim (300 mcg subcutaneously daily for five days), and Group B received pegfilgrastim (a single 6 mg subcutaneous dose administered 24 hours post-chemotherapy). All clinical and laboratory data including age, BMI, cancer type and stage, chemotherapy regimen, and neutrophil and WBC profiles were systematically recorded. Chemotherapy regimens were stratified according to their myelosuppressive risk based on ASCO guidelines into high, moderate, low, and minimal risk categories.

Data analysis was performed using IBM SPSS Statistics version 25. Continuous variables such as age, BMI, cancer duration, and hospital stay were tested for normality using the Shapiro-Wilk test and presented as medians with interquartile ranges. Categorical variables such as gender, cancer type, chemotherapy risk, neutropenia severity, leukocyte abnormalities, and mortality were summarized as frequencies and percentages. Group comparisons for continuous variables were performed using the paired t-test when normally distributed or the Mann-Whitney U test otherwise, while the Chi-square test and Cochran's Q test were applied for categorical data to assess associations between G-CSF type and clinical outcomes. Statistical significance was defined at a p-value <0.05.

RESULTS

A total of 199 adult cancer patients diagnosed with chemotherapy-induced febrile neutropenia (FN) were included in this prospective cohort study. Among them, 98 (49.2%) patients received filgrastim and 101 (50.8%) received pegfilgrastim. The cohort was predominantly female (117, 58.8%) with a median age of 44 years (interquartile range [IQR] = 21). The median BMI was 22.8 kg/m^2 (IQR = 6.70), and the median cancer duration was 10 years and 4 months. Most patients (54.8%) were from rural backgrounds, and more than half (52.3%) were classified as having poor socioeconomic status.

As presented in Table 1, the two treatment groups were statistically comparable in terms of age ($p = 0.176$), cancer duration ($p = 0.244$), and cancer stage ($p = 0.214$). However, the pegfilgrastim group had a significantly higher median BMI (25 kg/m^2 vs. 21 kg/m^2, $p < 0.0001$) and a greater proportion of

patients with breast and gynecological cancers (64.9% vs. 35.1%, p < 0.0001). Additionally, the pegfilgrastim group had a higher proportion of patients undergoing high-risk chemotherapy regimens (52.3% vs. 47.7%, p = 0.004), whereas the filgrastim group had more patients on low-risk regimens (72.1% vs. 27.9%).

Table 1. Baseline Characteristics of Patients Receiving Filgrastim vs. Pegfilgrastim

Variable	Filgrastim (n = 98)	Pegfilgrastim (n = 101)	p-value
Age, median (IQR), years	45 (25) [8–76]	42 (27) [19–81]	0.176
BMI, median (IQR), kg/m²	21 (4.71) [11–32]	25 (5.72) [18.2–36.9]	<0.0001
Cancer duration, months	127	108	0.244
Cancer type (%)			<0.0001
– Breast & Gynecological	34 (35.1%)	63 (64.9%)	
– Hematological	40 (55.6%)	32 (44.4%)	
– Bone	5 (45.5%)	6 (54.5%)	
– Genitourinary	3 (100%)	0 (0%)	
– Head, Neck, Endocrine	4 (100%)	0 (0%)	
– Lung	2 (100%)	0 (0%)	
Cancer stage (%)			0.214
– Metastatic	55 (52.4%)	50 (47.6%)	
– Non-Metastatic	43 (45.7%)	51 (54.3%)	
Chemotherapy Risk Regime (%)			0.004
– High Risk	41 (47.7%)	45 (52.3%)	
– Moderate Risk	11 (36.7%)	19 (63.3%)	
– Low Risk	31 (72.1%)	12 (27.9%)	
– Minimal Risk	15 (37.5%)	19 (63.3%)	

Significant differences were observed in hematological and clinical outcomes between the two groups, as detailed in Table 2. Severe and mild neutropenia occurred exclusively in the filgrastim group (7/7 cases each; p < 0.0001), whereas moderate neutropenia was more frequently observed in the pegfilgrastim group (72.7% vs. 27.3%). Furthermore, a higher proportion of pegfilgrastim recipients had normal post-treatment ANC levels (93 vs. 81), indicating more effective neutrophil recovery. In terms of leukocyte response, leukopenia was significantly more frequent among filgrastim users (64.6% vs. 35.4%), while leukocytosis and severe leukocytosis occurred predominantly in the pegfilgrastim group (p < 0.0001). These findings suggest a stronger and sustained hematopoietic effect associated with pegfilgrastim.

Table 2. Post-Treatment Clinical Findings of Patients Receiving Filgrastim vs. Pegfilgrastim

Outcome	Filgrastim (n = 98)	Pegfilgrastim (n = 101)	p-value
ANC Count			<0.0001
– Severe Neutropenia	7 (100.0%)	0 (0.0%)	
– Moderate Neutropenia	3 (27.3%)	8 (72.7%)	
– Mild Neutropenia	7 (100.0%)	0 (0.0%)	
– Normal ANC	81 (46.6%)	93 (53.4%)	
WBC Count			<0.0001
– Leukopenia	31 (64.6%)	17 (35.4%)	
– Normal	60 (69.8%)	26 (30.2%)	
– Leukocytosis	7 (11.1%)	56 (88.9%)	
– Severe Leukocytosis	0 (0.0%)	2 (100.0%)	
Tachycardia			0.195
– Normal	77 (51.0%)	74 (49.0%)	
– Mild	18 (40.0%)	27 (60.0%)	
Febrile Neutropenia Recurrence	10 (55.6%)	8 (44.4%)	0.575
Mortality			0.118
– Survived	95 (48.5%)	101 (51.5%)	
– Died	3 (100.0%)	0 (0.0%)	
Hospital Stay, median (IQR), days	7 (5) [0–17]	0 (0)	<0.0001

No statistically significant differences were found in the incidence of tachycardia (p = 0.195) or febrile neutropenia recurrence (p = 0.575) between the groups. However, mortality—though not statistically significant (p = 0.118)—occurred exclusively in the filgrastim group, with three recorded deaths. Hospital stay duration was significantly lower in the pegfilgrastim group, with a median of 0 days compared to 7 days in the filgrastim group (p < 0.0001), indicating a marked clinical

advantage. The results demonstrate clinically and statistically significant advantages of pegfilgrastim over filgrastim in the management of chemotherapy-induced febrile neutropenia. Pegfilgrastim was associated with superior hematological recovery, particularly in maintaining normal ANC and WBC counts. Moreover, it effectively reduced hospitalizations, which has implications not only for patient quality of life but also for healthcare resource utilization. While mortality differences did not reach statistical significance, the exclusive occurrence of deaths in the filgrastim group may suggest a potential clinical benefit of pegfilgrastim, warranting further investigation in larger powered studies.

DISCUSSION

The findings of this prospective cohort study underscore the superior clinical effectiveness of pegfilgrastim over filgrastim in the management of chemotherapy-induced febrile neutropenia (FN). Most notably, pegfilgrastim was significantly associated with zero hospital stay compared to a median of seven days in the filgrastim group, suggesting a substantial reduction in hospitalization burden and improved patient throughput. This observation aligns with prior studies, including Sharma et al., who demonstrated a shorter mean hospital stay among pegfilgrastim recipients (2.36 ± 3.35 days) versus those receiving filgrastim (4.14 ± 3.69 days), indicating a clinically meaningful advantage in terms of healthcare resource optimization (9). The ability of pegfilgrastim to sustain neutrophil counts due to its longer half-life and self-regulating clearance via neutrophil-mediated pathways likely contributes to its reduced need for hospitalization and better control of neutropenic episodes (14).

Mortality, though not statistically significant, was observed exclusively in the filgrastim group, reinforcing the potential life-saving benefit of pegfilgrastim. This trend resonates with data from Brandao et al., who suggested that prophylactic use of pegfilgrastim not only reduces the incidence of FN but may also translate into improved survival outcomes (10). Similarly, Naeim et al. found that pegfilgrastim prophylaxis was associated with a significantly lower risk of both neutropenia-related and all-cause hospitalizations in cancer patients compared to filgrastim (11). While the present study did not have a large enough sample to detect statistical differences in mortality, the observed clinical pattern reinforces the hypothesis of pegfilgrastim's superior safety profile, which warrants further exploration through larger, multicentric trials.

In terms of hematological recovery, pegfilgrastim demonstrated significantly better control of neutropenia severity. All cases of severe neutropenia occurred in the filgrastim group, while the pegfilgrastim group exhibited higher rates of normal post-treatment ANC levels. These results echo those of Rout, who reported lower FN incidence and improved ANC recovery among pegfilgrastim users in breast cancer patients (13). The robust leukocytosis observed in the pegfilgrastim group further supports its sustained hematopoietic activity, consistent with pharmacological studies describing its extended stimulation of bone marrow progenitor cells (14). Moreover, the lower frequency of leukopenia in the pegfilgrastim group may have contributed to fewer infections and better tolerance of chemotherapy, ultimately influencing hospitalization trends.

This study adds to the growing body of evidence favoring pegfilgrastim, particularly in low-resource settings where minimizing inpatient admissions is a clinical and logistical priority. The single-dose regimen of pegfilgrastim, requiring less frequent hospital visits for administration compared to daily dosing with filgrastim, presents a pragmatic advantage in such environments. While Western guidelines consider both agents clinically equivalent, real-world data from settings like Pakistan suggest pegfilgrastim's superiority in outcome efficiency, supporting its broader implementation in local protocols (6,7). Given the varied accessibility and affordability of G-CSFs across different healthcare systems, the present findings offer valuable insights into optimizing FN management in regions with constrained resources.

However, the study is not without limitations. Despite being prospective in design, it remains observational in nature, which limits the ability to infer causality. The non-randomized allocation of patients to treatment arms could introduce selection bias, though baseline characteristics were largely comparable. An imbalance in chemotherapy risk categories between groups may have influenced outcomes despite statistical adjustments. The single-center scope and modest sample size restrict generalizability, particularly to broader populations or different geographic settings. Furthermore, the exclusion of pediatric patients and lack of long-term follow-up constrain the study's applicability to other demographic groups and limit insights into extended survival benefits.

Nevertheless, the study's strengths lie in its real-world clinical context, detailed patient profiling, and rigorous data analysis. The findings support a shift toward the preferential use of pegfilgrastim for FN prophylaxis and management, particularly in tertiary care centers catering to high volumes of oncology patients. Future research should aim to validate these results in randomized controlled trials with larger, more diverse populations and evaluate cost-effectiveness in relation to healthcare resource utilization. Additionally, studies exploring biomarker-guided G-CSF dosing, pharmacoeconomic modeling, and long-term outcomes such as chemotherapy adherence and survival rates would further enhance the clinical applicability of these findings. Overall, this study reinforces the clinical and logistical value of pegfilgrastim in reducing neutropenic complications and improving treatment continuity for cancer patients undergoing chemotherapy in resource-limited settings.

CONCLUSION

This study demonstrates that pegfilgrastim offers superior clinical outcomes compared to filgrastim in patients with chemotherapy-induced febrile neutropenia, significantly reducing hospital stay duration and the severity of neutropenia, with no observed mortality in the pegfilgrastim group. These findings align with the study's objective and underscore the impact of long-acting granulocyte colony-stimulating factor therapy on improving patient prognosis and reducing healthcare burden. In human healthcare, particularly in resource-limited settings, pegfilgrastim emerges as a favorable option for FN management due to its efficacy, convenience, and potential to minimize hospital admissions. Clinically, these results support its broader adoption as a standard prophylactic intervention,

while further multicenter research is warranted to validate these outcomes and explore cost-effectiveness, survival benefits, and implementation across diverse oncology populations.

REFERENCES

1. Rastogi S, Kalaiselvan V, Ali S, Ahmad A, Guru SA, Sarwat M. Efficacy and Safety of Filgrastim and Its Biosimilars to Prevent Febrile Neutropenia in Cancer Patients: A Prospective Study and Meta-Analysis. Biology. 2021;10(10):1069.

2. Mohseni M, Arab-Zozani M, Ahmadi A, Salimi B, Sari AA. Meta-Analysis of Pegfilgrastim Over Filgrastim in the Treatment of Chemotherapy-Induced Neutropenia. Ann Cancer Res Ther. 2020;28(2):71–80.

3. Nielson CM, Bylsma LC, Fryzek JP, Saad HA, Crawford J. Relative Dose Intensity of Chemotherapy and Survival in Patients With Advanced Stage Solid Tumor Cancer: A Systematic Review and Meta-Analysis. Oncologist. 2021;26(9):e1609–18.

4. Keck JM, Wingler MJ, Cretella DA, Vijayvargiya P, Wagner JL, Barber KE, et al. Approach to Fever in Patients With Neutropenia: A Review of Diagnosis and Management. Ther Adv Infect Dis. 2022;9:20499361221138346.

5. Nordvig J, Aagaard T, Daugaard G, Brown P, Sengeløv H, Lundgren J, et al. Febrile Neutropenia and Long-Term Risk of Infection Among Patients Treated With Chemotherapy for Malignant Diseases. Open Forum Infect Dis. 2018;5(10):ofy255.

6. Gascón P, Awada A, Karihtala P, Lorenzen S, Minichsdorfer C. Optimal Use of Granulocyte Colony-Stimulating Factor Prophylaxis to Improve Survival in Cancer Patients Receiving Treatment: An Expert View. Wien Klin Wochenschr. 2023;135(21–22):887–94.

7. Sharma R, Shilpakar R, Thapa S, Anuj KC, Dulal S, Prajapati R, et al. Comparison of Short Acting Versus Long Acting Filgrastim for Reduction of Chemotherapy Induced Febrile Neutropenia. Annapurna J Health Sci. 2022;2(2):22–6.

8. De Oliveira Brandao C, Lewis S, Sandschafer D, Crawford J. Two Decades of Pegfilgrastim: What Have We Learned? Where Do We Go From Here? Curr Med Res Opin. 2023;39(5):707–18.

9. Naeim A, Henk HJ, Becker L, Chia V, Badre S, Li X, et al. Pegfilgrastim Prophylaxis Is Associated With a Lower Risk of Hospitalization of Cancer Patients Than Filgrastim Prophylaxis: A Retrospective United States Claims Analysis of Granulocyte Colony-Stimulating Factors (G-CSF). BMC Cancer. 2013;13:11.

10. Rout A. Comparison of Pegfilgrastim With Filgrastim in Management of Chemotherapy-Induced Neutropenia in Breast Cancer Patients. J Med Sci Clin Res. 2019;7(1):174.

11. Renwick W, Pettengell R, Green M. Use of Filgrastim and Pegfilgrastim to Support Delivery of Chemotherapy: Twenty Years of Clinical Experience. BioDrugs. 2009;23(3):175–86.