Management Costs of Febrile Neutropenia in Oncology Patients in Colombia

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Abstract

Purpose: To describe the clinical characteristics, resource utilization, and direct cost of febrile neutropenia (FN) in a healthcare institution in Colombia for patients seen between 2017-2019.

Methods: A descriptive and retrospective study of a cohort of patients hospitalized due to FN. Costs were extracted from the review of medical records from diagnosis of FN until discharge or death, and official sources were used to estimate the cost.

Results: Forty-four FN episodes were included. Median age was 61 years (IQR: 53-72). Solid tumors accounted for 68.8%. In first-line treatment were 14 (31.8%), same in proportion in adjuvant/neoadjuvant, and 5 (11.4%) in second-line. FN occurred in 15 (34.0%) high-risk patients. Mean LOS per episode was 5.1 ± 2.5 days. All patients were discharged alive. The median overall cost was $925 ± $783 per episode, with hospital stay being the main driver-cost.

Conclusion: FN occurred mainly in advanced-stage solid tumors and in low-risk group. Higher costs in this cohort were found in long length of stay and high-risk patients.

Introduction

Febrile neutropenia (FN) continues to be an oncology emergency, which may result in serious consequences, such as complication infection, organ failure, admission to intensive care unit (ICU), and highly associated to mortality [1–3]. Although the main cause of neutropenia corresponds to chemotherapy in cancer patients, there are other conditions that may lead to neutropenia, such as solid tumors affecting the bone marrow; certain cases of lymphoproliferative neoplasms (e.g. granular lymphocytic lymphoma, hairy cell leukemia, and chronic lymphocytic leukemia); radiation if administered at various sites of active bone marrow proliferation; and less frequently, autoimmune, rare genetic, congenital, or monoclonal pathological etiologies [2].

The occurrence of FN varies considerably depending on the type of cancer, age, performance status, comorbidities, chemotherapy agents, and regimen, among other factors [4]. From the review of hospitalization due to FN, 53% of cases were solid tumors, and 42% were lymphoma or leukemia [3]. FN incidence has been reported in 60–85% of adults [5] with hematological cancers and chemotherapy, and in 23.8% of patients with small cell or non-small cell lung cancer receiving platinum-based chemotherapy. However, in non-small cell lung cancer with squamous cell carcinoma patients, FN occurred in more than 50% [6].

FN was also reported in 9.2–12.9% of patients with breast cancer receiving adjuvant therapy. In these cases, hospitalization rates were 5.2–11.4% [7], and in 9–47% [8] of patients with non-Hodgkin lymphoma under treatment with chemotherapy. Therefore, FN incidence is important while it may fluctuate depending on the condition of the population.

The main complications of neutropenia correspond to complicated infections, prolonged hospital stay, and death [9]. Moreover, FN may have a long-term clinical impact because it requires adjustments in chemotherapy treatment, including dose reduction, delay in treatment, discontinuation of chemotherapy, switch to less toxic alternatives, or less effective treatment regimens. which can translate into decreased response and lower survival rates [10, 11].

The episodes of FN in the United States are estimated to account for 5.2% of all cancer-related hospitalizations and 8.3% of cost from all cancer-related hospitalizations [12]. Forty-percent of FN events that required hospitalization had ≤ 5 days of stay, 42% had 6–10 days of days, 12% had 11–15 days of stay, and 6% had ≥ 16 days of stay [9]. One study showed that hospital stay is an important cost-driver of healthcare utilization and related costs (76.8%), followed by antibacterial treatment (8.5%), laboratories (6.0%) and blood bank (5.9%) [13]. As such, the costs associated with FN have been estimated to vary depending of the type of cancer [14].

The scarce evidence available on incidence, risk factors, population, and economic impact of FN in Colombia continues to be a shortcoming. A study was conducted, only in Colombia, assessing the epidemiology of FN cases in adult patients with hematological malignancy [5]. Due to the lack of data available on FN, the purpose of this study is to provide information related to the contribution of different cost component, as well as demographic and clinical factors associated with this condition, which have not been yet analyzed in detail in the country.

Methods

Study Design and Patient Population

This retrospective and descriptive cohort study of FN episodes used data from Clínica SOMA, a healthcare institution in Medellín (Colombia), from 2017 to 2019. The study population consisted of all patients aged ≥ 18 years who were hospitalized with diagnosis of any type of cancer and FN. The date of hospitalization with diagnosis of FN was considered as index date. Patients were followed up until discharge from hospital or death, and FN episodes were classified as high-risk or low-risk according to the Multinational Association of Supportive Care in Cancer (MASCC) Risk Index score.

During this period, all medical resources were measured. These were categorized according to type of service (i.e. hospital, antibiotic, therapeutic, and diagnostic test). Likewise, the epidemiological characteristics and type of tumor will be obtained, and episodes will be classified according to the identified cause and data associated with mortality.

Since a specify diagnostic code for FN does not exist, FN definition was made according to the Colombian Cancer Institute “absolute neutrophil count ≤ 500 cells/mL or ≤ 1,000 cells/mL, with a downward trend over 48 hours after measurement.” [15].

Cost Data

The costs per episode were calculated by multiplying the number of units of each resource by the cost per unit. Only the services attributable to FN were included. Costs were reported using the local currency and converted to United States dollars (US $), at the exchange rate 3,278 Colombian pesos per US$. The healthcare provider perspective was adopted.

Data Source

The main source of data will be the patients' clinical records, including demographics, clinical data, and resource use per episode, while the cost per patient was calculated using the official government manual and drug price information system, which were based on mean values of those datasets.

Statistical Analyses

All sociodemographic, clinical, and cost variables will be summarized using descriptive statistics according to their distribution, through measures of central tendency and measures of dispersion for quantitative variables and absolute and relative frequencies. For qualitative ones, the distribution will be evaluated using the Shapiro-Wilk test. These analyses will be carried out for the all population and by subgroups. Measures of resources were analyzed using observed values and are reported as means and/or percentages.

Results

Patient demographics and disease characteristics

A total of 44 FN episodes were included in the study. The mean age of the patient population was 61 years (IQR: 53–72). None of the patients died during hospitalization. Table 1 shows demographics and cancer types. Most of patients belonged to the contributory regime. Solid tumors accounted for 68.8%, with colorectal (20.0%), breast (16.7%), and lung (13.3%) cancers being the most frequent within this group. In terms of oncology treatments, 14 (31.8%) patients were in first-line, 14 (31.8%) were in the adjuvant/neoadjuvant setting; and 5 (11.4%) were in second-line. All patients were discharged alive. According to MASCC score, 15 (34.1%) episodes occurred in the high-risk group, and 29 (65.9%) episodes occurred in the low-risk group.

Table 1
Patient Demographics and Disease Characteristics

Demographics/ Characteristic	No. of Patients (%)		
	Total	High-Risk Group	Low-Risk Group
Sex			
Women	23 (52.3)	8 (53.3)	15 (51.7)
Men	21 (48.7)	7 (46.7)	14 (48.3)
Mean age (IQR)	61 years (IQR: 53–72)		
Cancer type			
Hematologic malignancies	14 (31.8)	7 (46.7)	7 (24.1)
Non-Hodgkin lymphoma	10 (71.4)	6 (85.7)	4 (57.1)
Chronic lymphocytic leukemia	2 (14.3)	0 (0.0)	2 (28.6)
Hodgkin lymphoma	1 (7.1)	0 (0.0)	1 (14.3)
Solid tumors	**30 (68.18)**	**8 (53.3)**	**22 (75.9)**
Colon cancer	6 (20.0)	0 (0.0)	6 (27.3)
Breast cancer	5 (16.7)	0 (0.0)	5 (22.7)
Lung cancer	4 (13.3)	2 (25)	2 (9.1)
Stomach cancer	3 (10.0)	1 (12.5)	2 (9.1)
Cervix cancer	2 (6.7)	0 (0.0)	2 (9.1)
Pancreatic cancer	2 (6.7)	1 (12.5)	1 (4.5)
Rectum cancer	2 (6.7)	2 (25)	0 (0.0)
Synovial sarcoma	2 (6.7)	0 (0.0)	1 (9.1)
Anal cancer	1 (3.3)	1 (12.5)	0 (0.0)
Bone cancer	1 (3.3)	0 (0.0)	1 (4.5)
Leiomyosarcoma	1 (3.3)	0 (0.0)	1 (4.5)
Ovarian cancer	1 (3.3)	1 (12.5)	0 (0.0)

Table 2
Disease Treatment Based on MASCC Risk Group

	High-Risk Patients	Low-Risk Patients
First-line	7 (46.7%)	7 (24.1%)
Second-line	2 (13.3%)	3 (10.3%)
Adjuvant and neoadjuvant	2 (13.3%)	12 (41.4%)
Other	4 (26.7%)	7 (24.1%)

Healthcare Utilization and Total Medical Costs

The hospital mean (± SD) of length of stay (LOS) was 5.7 ± 29 days and, the mean cost (± SD) per FN episode was $967 ± 783. Six patients (13.7%) were admitted to the ICU, with a mean duration of 3.8 days (range: 3.0–5.0), contributing to LOS 17.4% of bed days. Patients with hematologic tumors have mean LOS 6.0 ± 3.4 and mean cost of $1,105 ± 972, which was similar among patients with solid tumors, LOS 5.5 ± 2.7 and mean cost of −$840 ± 679. Within the risk groups, the cost was higher in high-risk patients ($ 1,207 ± $ 1,035) as compared to low-risk patients ($ 779 ± $ 583). The mean cost during adjuvant or neoadjuvant treatment was $688 ± 586, first-line $946 ± 895, second-line $1,388 ± 609, and other lines $987 ± 898.

Hospital stay (included ICU and ward) accounted for 66.8% of total cost. Laboratory tests accounted for 14.2%; blood bank, 3.0%; medication, 8.2%; diagnostic test, 4.8%; and physicians accounted for the remaining 3.0%.

In respect of medication costs, the antifungal use was lower: It was given to 8 patients given low-cost antifungal agents. The hematopoietic growth factor used as treatment for FN was used only in one elderly patient at high risk. The most commonly used antibiotics were cefepime hydrochloride, piperacillin/tazobactam, meropenem, and vancomycin.

Table 3
Direct Medical Costs

	Mean	SD	Range
Hospital stay	$ 618	$ 599	$ 155 – 2,374
Laboratory	$ 132	$ 102	$ 21 – 487
Blood bank	$ 81	$ 61	$ 13 – 257
Medication	$ 75	$ 68	$ 0 – 337
Diagnostic test	$ 44	$ 102	$ 0 – 618
Physicians	$ 28	$ 17	$ 16 – 88
Total	**$ 925**	**$ 783**	**$ 267 – 3,455**

Table 4
Direct Medical Costs by MASCC Risk Group

	Mean	SD	Range
Length of stay, d			
High-risk	6.1	3.2	2.0 – 13.0
Low-risk	5.4	2.7	13.0 – 92.0
Total costs			
High-risk	$ 1,207	$ 1,035	$ 318 – 3,455
Low-risk	$ 779	$ 583	$ 276 – 3,000

Discussion

This study shows the economic impact of FN jointly with the demographics and clinical characteristics of this population, showing high compliance with the clinical guidelines [16] and the administered antibiotics, antifungal, imaging, and laboratory tests. These occurred mainly in advanced-stage solid tumors and in MASCC low-risk patients. The overall mean total cost per FN episode was $967 ± $777 with a mean LOS of 5.1 days. There was a negligible variation in cost and LOS estimates among different types of patients (by risk score group or by type of cancer). The main cost-driver was hospital stay by contrasting physician visits–a component seen to be the lowest in estimating the cost of FN.

A systematic review that examined cost of FN among patients with lymphoma reported a cost estimate of FN in the United States, Singapore, Europe, Australia, Canada, and Spain. As expected, the cost varied largely among those counties from $5,819 to $13,823 (2013, US$) [17]. These findings appear to be different from those of this study, since the cost represents less than half of the cost found in this study.

However, in all studies, the LOS in hospital was the main cost driver, which is consistent with the results of this study. The ratio of ward cost per unit among the rest of the components of total cost is important. In Colombia, the cost of hematopoietic growth factor was 11 times higher than the cost associated to hospital ward. However, in other countries, the hematopoietic growth factor was 2–3 times higher than ward cost [18, 19], and even hospital ward was higher [20].

Overall LOS reported in this study was lower compared to other studies, the means of which were 8 to 9 days [12, 21, 22]. However, the study showed similar tendency among the type of cancer associated with longer LOS such as leukemias, non-Hodking lymphoma and Hodking lymphoma.

Colombian studies have estimated that the direct medical costs for colorectal and breast cancer range from $ 1,556 for early-stage disease to $ 44,744 for advance-stage disease [23, 24]. Accordingly, the FN episode cost accounted for 2% of total direct costs in advance stages, and up to 67% in early stages. The vast majority of cases in Colombia are in advanced stages of the disease [25], and therefore, FN costs comprised a marginal proportion of the healthcare costs of overall cancer.

There were some limitations to this study. Of note: Firstly, data was limited by that available in the patient's medical history. Consequently, data related to medical services provided outside of this care setting could not be obtained. Secondly, the sample size was relatively small, since the information is only part of an institution, limited to the clinical practice of such an institution. Thus, results may not be generalizable.

This study provides accurate and conservative estimates of the costs of a FN episode. Given that the costs of procedures are calculated from the description or unique code of healthcare procedures, the information in the medical records and tariff manuals, therefore. a misclassification of neutropenia patients as FN patients could not be carried out, and the costs used are benchmarks for negotiation in the country, although they may differ from those established in some institutions.

Issues raised in this paper have provided an understanding of the factors that drive FN costs stratifying care by risk group and type of cancer. This may be the starting point to design efficient care management programs and targeted strategies related to the cost of cancer care.

Further work should be done in evaluating the indirect and intangible costs, as this may represent a substantial burden for the society and families of patients, which also contributes to the economic burden of FN episodes.

Stratifying care by risk group may be helpful in identifying alternative strategies for FN treatment that may potentially result in cost savings to the healthcare system.

Conclusion

FN occurred mainly in advanced-stage solid tumors and in MASCC low-risk patients. Higher costs in this cohort were found in long LOS and/or high-risk patients.

Declarations

Author contribution: All authors contributed to the study conception and design. Material preparation, data collections were performed by Mauricio Lema, Beatriz Preciado and Diana Quiceno and Sara Mora, and the analysis was performed by Natalia Castaño and Juan Manuel Reyes. The first draft of the manuscript was written by Juan Manuel Reyes and Natalia Castaño and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

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Availability of data and material This is an observational study. The XYZ Research Ethics Committee has confirmed that no ethical approval is required. Approval was granted by Comité Ética para Investigación Clínica de la Funación CIC

Code application: (R project version)

Ethical approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Comité Ética para Investigación Clínica de la Funación CIC

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