

# Characteristics and risk factors for admission in children undergoing hematopoietic cell transplantation in a pediatric emergency department

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September 25, 2021

## Abstract

We describe 68 hematopoietic cell transplantation (HCT) patients who visited our pediatric emergency department during 2014-2015 (188 encounters). Fever was the main complaint in 74 (34.8%) encounters. Diagnostic tests were performed in 147 (78.2%) episodes [100% of patients with unstable Pediatric Assessment Triangle (PAT) and 75.7% with stable PAT (P value 0.02)] and treatment was required in 93 (49.5%) episodes [15 (78.9%) with unstable PAT and 78 (46.2%) with stable PAT (P value <0.001)]. Risk factors for admission were unstable PAT [relative risk (RR) 3.4 (2.6-4.6), P value <0.001] and [?]100 days since HCT [RR 2.1 (1.4-3.1), P value <0.001].

## INTRODUCTION

Since 1968, when the first hematopoietic cell transplantation (HCT) was successfully performed in a child with severe combined immunodeficiency<sup>1</sup>, new sources have been used to harvest stem cells<sup>2, 3, 4</sup>. While this revolution in the field has improved the overall success rate, some patients undergoing this treatment present various secondary complications<sup>5, 6, 7</sup>. All of these complications significantly increase the number of visits to pediatric emergency departments (PEDs).

The objective of this study was to analyze the chief complaints, medical care required, and other factors associated with admission among HCT patients. We further aimed to determine the degree with which care delivery adhered to the quality criteria established for the PED<sup>8</sup>, comparing these results against the general population.

## METHODS

We carried out a descriptive, retrospective study of HCT patients who presented to our PED in Hospital Infantil Universitario Niño Jesús, from January 1, 2014 to December 31, 2015. Our hospital performs 40 to 50 HCT procedures each year.

The study sample comprised HCT patients between the ages of 0 and 18 years. Multiple presentations per patient were allowed.

The following data were retrieved from the electronic medical charts: date of birth, gender, time since HCT [categorized as (i) pre-engraftment (<30 days after HCT), (II) early post-engraftment (30-100 days after

HCT), and (iii) late post-engraftment (>100 days after HCT)], number of PED visits, Pediatric Assessment Triangle (PAT) applied in the PED, chief complaint, length of PED stay, diagnostic tests performed (e.g., blood, imaging), treatment received in the PED (e.g., airway or respiratory antibiotic support, cardiovascular support, intravenous fluids, blood transfusion), admission, return visit (unplanned emergency visit for any diagnosis within 72 hours of discharge from the PED), and admission rate for the second visit (unplanned acute readmission for any diagnosis within 72 hours of discharge from the PED). Patient identities and data were anonymized.

Data were analyzed with Stata software, version 15.0. Normally distributed variables are reported as mean and standard deviation, non-normally distributed data as median and interquartile range. Categorical variables are expressed as percentages. Two-tailed t tests were used to compare mean values between groups,  $\chi^2$  tests to compare proportions. A p value <0.05 was considered statistically significant.

## RESULTS

During the period studied there were 134,335 visits to the PED. Among the 302 patients undergoing HCT followed-up during the 2-year period, 59 (19.5%) children, who received a total of 68 HCT sessions, had 213 care encounters in the PED (188 excluding nursing procedures), which represented 0.2% of all PED episodes. Demographic characteristics and clinical data are shown in Table 1. The median number of encounters per patient was 3 (interquartile range 2-4); 15 (25.4%) patients presented to the PED once, 32 (54.2%) visited twice, and 12 (20.3%) three or more times. Of the 188 episodes analyzed, 118 (62.8%) corresponded to patients who had received allogeneic HCT and 70 (37.2%) had undergone autologous HCT. Chief complaints in the PED visit were as follows: fever [with or without respiratory, digestive, otorhinolaryngologic (ORL), neurologic, cutaneous, osteoarticular, and urinary symptoms] in 74 (39.4%) patients, respiratory/ORL symptoms in 55 (29.2%), graft-versus-host disease complications in 49 (26.1%), and neurologic symptoms in 10 (5.3%).

Diagnostic tests were performed in 147 (78.2%) encounters: 100% (19) of those patients found to be unstable on PAT and 75.7% (128) with stable PAT (P value 0.02). In 93 (49.5%) episodes the children required treatment, 15 (78.9%) of whom were patients with unstable PAT and 78 (46.2%) with stable PAT (P value <0.001). The therapeutic interventions performed in these episodes were as follows: intravenous antibiotic therapy in 23 (24.7%), fluid bolus in 21 (22.6%), blood transfusion in 9 (9.7%), airway support in 3 (3.2%), and cardiovascular support in 2 (2.2%). According to the elapsed time between HCT and PED visit, diagnostic tests were performed in [?]100 days in 47 (79.7%) patients and in 95 (73.6%) >100 days (P value 0.37); in terms of those requiring treatment, 29 (49.2%) of these patients were children with [?]100 days since HCT and 52 (40.3%) in >100 days (P value 0.26). According to the HCT type, diagnostic tests were performed in 39 (76.5%) patients with allogeneic HCT and in 12 (70.6%) with autologous HCT (P value 0.63); 38 (74.6%) of patients with allogeneic HCT and 9 (53.0%) with autologous HCT (P value 0.07) required treatment.

Risk factors for admission are shown in Table 2.

## DISCUSSION

Only 20% of HCT patients followed-up in this study presented to the PED. These individuals tended to visit the PED more than 100 days after HCT, and fever was their main complaint. Despite having a stable PAT, most of these patients required diagnostic and therapeutic interventions.

As in other articles<sup>7, 8, 9</sup>, fever was the leading cause of PED presentation, accounting for 1 out of every 3 care episodes. The median age of HCT patients was higher than the rest of the patients receiving care in the PED. Leukemia was the most common oncohematological disease, thus coinciding with other patient series<sup>10, 11</sup>. The most prevalent HCT type in our series was haploidentical allogeneic and the median time from HCT until PED presentation was more than 100 days in agreement with the existing literature<sup>10</sup>.

Although the HCT patients in our cohort represented a small percentage of the overall PED visits, the care they required placed a high burden on staff, as the children spent more time on average in the PED and

required numerous diagnostic and therapeutic interventions. This was even more the case for patients who had an unstable PAT assessment upon arrival to the PED.

The admission rate for HCT patients was six times higher than the overall rate, though no correlation was found between admission and HCT type. Unstable PAT and [?]100 days from HCT to PED presentation were the main risk factors for admission in these patients, raising the likelihood of PED presentation to three times and twice the risk, respectively, of stable patients and those for whom >100 days had elapsed since HCT. Unplanned return visits<sup>8</sup> were above what is recommended in a PED<sup>12</sup>, possibly owing to the fact that the oncologic day hospital was only open on weekdays. In contrast, the admission rate for the second visit was below the established limit<sup>8</sup>, which suggests that these patients were correctly cared for in the PED.

Our study has several limitations, starting with the retrospective, single-center design used. Second, many patients with a history of HCT are from outside the region of Madrid and may have returned to their place of residence after 3 months post-transplantation, which means that some may not be represented in the registry, as only the most severe patients are likely to remain nearby for care after transplantation. Despite these limitations, we believe the data used in this study faithfully represent our HCT patients.

Despite representing a minimal percentage of visits to the PED, HCT-patient care posed a significant care burden due to the very significant number of care encounters required, complementary tests administered, and the treatments performed. Establishing an independent PED care circuit that provides care on both weekends and weekdays would benefit these patients. According to our data, the need for admission was more accurately predicted by altered states according to the PAT system and the days since transplantation than the HCT type.

## CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest

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