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Original Article

Hospital acquired infection in a department of hematology-oncology care in the Congo

Lydie Ocini Ngolet[1*], Alexis Fortuné Bolenga Liboko[2*], Bienvenu Roland Ossibi Ibara[3*], Alexis Elira Dokekias[1*]

Departments of [1]Hematology, [2]Oncology, [3]Infectious Diseases, Teaching Hospital, 13 Auxence Ikonga Avenue, P.O Box 32, Brazzaville, Congo. [*]Equal contributors.

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Abstract: Objectives: Hospital Acquired Infection (HAI) is a major cause of morbidity and mortality in hemato-oncology. The study aims to report the incidence of hospital-acquired infections in patients with hematological malignancies and the risk factors associated with them. Material and methods: An observational study with cross-sectional data collection was carried out from January 1, 2019, to April 30, 2020, in the department of hematology of Brazzaville University Hospital. The study concerned 77 patients diagnosed with hematological malignancies admitted for a course of chemotherapy. Written consent was obtained from each participant. Participants were divided into two groups: with HAI (n=50) and without HAI (n=27). They were compared using the chi-square test and Student's T-test. Univariate and multivariate analyses of the association of HAI with all the risk factors were performed for analysis of the 2 x k contingency tables and repeated using logistic regression. Results: The cumulative incidence was 64.9% with a 95% confidence interval of [53.8-74.7]. The time to onset of HAIs was 10.6±6.50 days. The incidence of HAI was significantly greater in acute myelogenous leukemia (80%), grade 4 neutropenia (80%). The risk factors were hospitalization stay of over 14 days (OR: 1.09), the regimen: daunorubicin-aracytine (OR: 5.96), the hemoglobin level on admission (OR: 0.72), and the neutropenia of grade 4 (OR: 7.9). The most common clinically identified focus of infection was peripheral venous infections. The fatality rate was 10%. Conclusion: The determination of HAI and the identification of its risk factors make it possible to establish prevention strategies.

Keywords: Hospital-acquired infections, cancer, Brazzaville

Introduction

Many challenges remain to be met in the management of hematological malignancies in Sub-Saharan Africa. The Capacity diagnosis is limited, and the cost of the chemotherapy is not accessible for the population [1]. Complications induced by aggressive chemotherapies are barriers to optimal treatment. Indeed, the aggressiveness of chemotherapies is responsible for a profound immunodeficiency that increases the risk of hospital-acquired infection (HAI) that leads to prolonged hospitalization, generates medical expenses to families, and death [2]. This risk is exacerbated by the lack of hygiene, standard, complementary infection prevention measures, control practice, and protective hospital environments [3]. Despite that fact, no data about the topic is, to our knowledge, available in the Congo. Considering the absence of HAIs information in patients with blood cancer, this study aims to address the HAI in the hematology department and the risk factors associated with it.

Material and methods

The Brazzaville teaching hospital is the biggest health facility in the country. The hematology unit is a 23 bed service that manages all patients with blood disorders, blood cancers included. We conducted an observational study with cross-sectional data collection for 16 months (January 1, 2019, to April 30, 2020).

Inclusion criteria: all patients diagnosed with blood cancers and admitted during the study period for a chemotherapy treatment without infections or latent infections.

Non-inclusion criteria: Patients admitted with an infection or positive malaria test. Patients

Table 1. Grade of Neutropenia

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Neutrophil polynuclear count	2	1.5-1.9	1-1.4	0.5-0.9	<0.5

for whom medical records were not completed.

For each patient included, demographic and clinical information such as age, type of blood cancer, clinical, biological features at their admission, and type of chemotherapy (length of corticosteroid treatment and antimicrobial prophylaxis) were recorded.

When a hospital-acquired infection (HAI) was diagnosed, we collected diagnosis information and laboratory data (leucocyte count, neutropenia grading, hemoglobin, and platelet rate). Treatment information of HAI such as length of stay, antibiotics therapy, and outcome.

The diagnosis criteria of HAI were based on the definition below.

Definitions

We labeled HAI, when it occurred during or after the course of chemotherapy and when they were neither present nor incubation at the chemotherapy. A 48 hours delay is generally taken.

Infection was diagnosed when an oral temperature greater than 38.2 degree Celsius from a single reading or an oral temperature of at least 38 degree Celsius sustained over 1 hour or reported from two consecutive readings in 2 hours.

Clinically documented infection was defined when the fever was associated with local inflammation.

Microbiologically documented infection was defined when a pathogen was identified in the context of fever. Undetermined infection was defined when the fever was not associated with any local inflammation and pathogens not identified.

We used the Common Toxicity Criteria established by the US National Cancer's classification to classify neutropenia (**Table 1**) [4].

All informed patients consented to participate in the study. This study was approved by the Institutional Ethics Review Committee (CERSSA; Ref: 2019/01/058).

Statistical analysis

The data were analyzed by the software R version 4.0.2. The count data are presented as frequency (percentage) and the differences between groups were assessed using the chi-square test. Quantitative variables were presented as the mean ± standard deviation and the comparison of these means was made with the Student's t-test. The incidence of HAI with its 95% confidence interval was calculated.

To assess risk factors associated with hospital-acquired infections (HAIs), the variables with *p*-values ≤0.05 in the univariate test were further analyzed in a multivariate analysis using a multiple logistic regression model. Maximum likelihood estimates of Odds-ratio (OR) with their 95% confidence intervals were calculated. A *P*-value of ≤0.05 was regarded as a statistically significant difference.

Results

From January 1, 2009, to June 1, 2020, 77 admissions were recorded for 40 patients. These included 19 men (47.5%) and 21 women (52.5%) with an average age of 38 years (extremes 4 and 81 years). The sex ratio was 0.90. The total number of hospitalization days was 1360 days; the average length of hospitalization was 28.9±13.8 days. The time to onset of HAI was 10.6±6.50 days.

Patients with acute leukemia were the most frequently admitted. The distribution of patients by the number of admissions and type of hematologic malignancies are detailed in **Table 2**.

Frequency and incidence of hospital-acquired infections

The number of HAIs during the study period was 50 for 31 patients. The frequency of HAIs was 64.93%. The average number of HAIs per patient was 1.6 ranging from 1 to 4 episodes per patient. The cumulative incidence was 64.9% with a 95% confidence interval of [53.8-74.7]. The incidence rate was 37/1000 days of hospitalization. The incidence of HAIs was 30% with a 95% confidence interval of [19.1-43.8]. It varied significantly according to the

Table 2. Distribution of Patients by Number of Admissions and Type of Hematologic Malignancies

Type of hematologic malignancy	Number of admissions	Percentage
ALL	24	31.17
AML	20	26.97
Lymphoma and CLL	16	20.78
MM	17	22.08
Total	77	100

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, CLL: chronic lymphocytic lymphoma, MM: multiple myeloma.

Table 3. Distribution of incidence of hospital acquired infections by clinical and biological features

		Number of HAIs	Incidence %	P
Hematologic malignancies				0.032
ALL	24	18	75.0	
AML	19	15	80	
Lymphoma and CLL	12	7	58.3	
MM	17	9	52.9	
Number of admissions				0.049
1	40	31	77.5	
2	22	12	54.5	
>2	15	7	46.7	
Neutropenia grade during HAI				0.013
0	6	2	33	
1	10	4	40	
2	4	5	50	
3	5	3	60	
4	30	24	80	
Admission length				0.024
<14 days	8	1	12.5	
≥14 days	13	9	69.2	
Nuclear polynuclear count at the admission				0.940
>1 G/L	20	12	60	
<1 G/L	37	24	64.9	

Table 4. Distribution of hospital acquired infections by site

Infection sites	Number	Percentage (%)
Undetermined infections	17	34
Peripheral venous tract	14	28
Lower respiratory tract*	7	14
Gastrointestinal	6	12
Stomatitis	3	6
Urinary tract	2	4
Skin**	1	2
Total	50	100

*2 cases of tuberculosis and 1 case of Covid-19. **Zoster.

type of hematological malignancy of blood cancer. It was 80% in acute myeloblastic leukemia, 75% in acute lymphoblastic leukemia, 58.3% and 52.9% respectively in chronic lymphoid neoplasia/lymphoma and multiple myeloma. The Incidence was also correlated with the severity of the neutropenia and the length of hospitalization. It was 69.2% when the patient was admitted for 14 days at least and 80% when the neutropenia was grade 4. The neutrophil polynuclear count at admission was not associated with the development of HAIs **Table 3**.

Site of hospital-acquired infections

Infections were undetermined in 34% of cases. They were clinically documented in 66% of cases. We counted 14 infections (28%) that originated from the peripheral venous tract. The diagnosis was based on cellulitis, skin abscess, or pus discharge from the peripheral venous tract. Seven cases of lower respiratory tract infections (14%) were diagnosed through standard radiography (chest x-ray). Among them, 2 cases of pulmonary tuberculosis and 1 case of Sars-cov-2 infection were identified. Other infectious were digestive (12%), stomatological (6%), and urinary tract infection (4%). One case of shingles (2%) was observed (**Table 4**).

Infections were microbiologically documented in 4% of the cases by a culture of urines that identified E. Coli.

Molecular biology had diagnosed 2 cases of pulmonary tuberculosis and 1 case of coronavirus disease 2019.

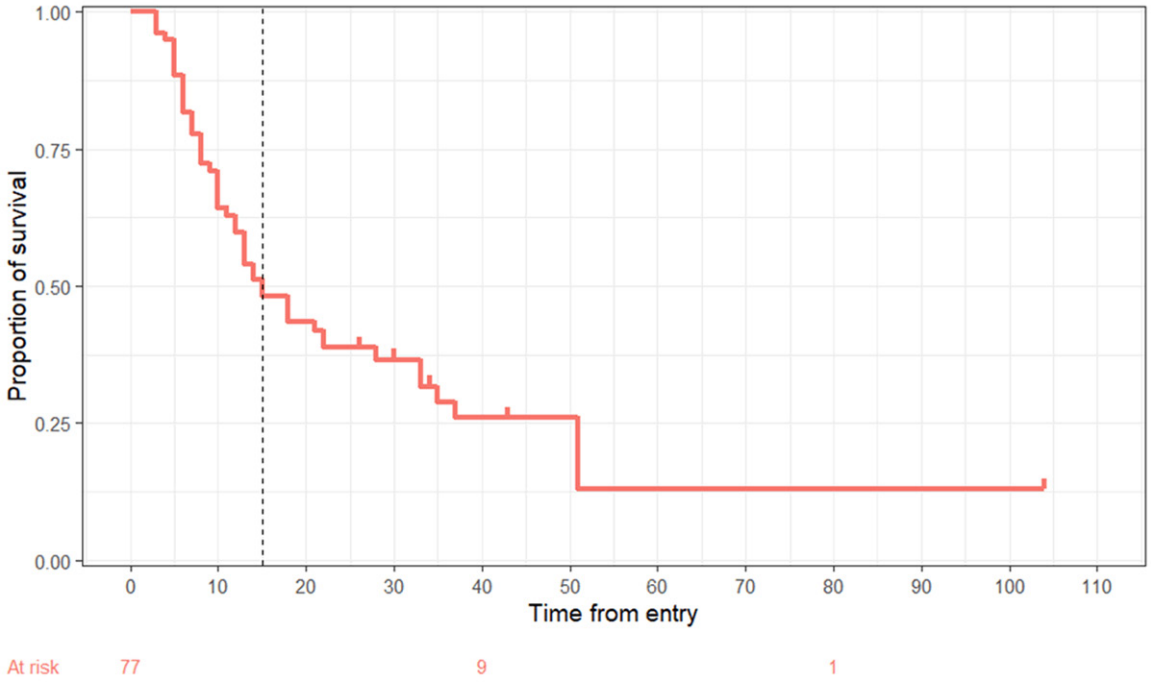

Figure 1. Trend for hospital acquired infections during hospitalization.

Risk factors of healthcare-associated infections

Exposure to certain factors has increased the risk of developing HAIs. The duration of hospitalization was significantly longer in patients who developed HAIs. Each day spent in hospital significantly increased the risk of developing HAIs by 1.72 times. Thus, at 14 days of hospitalization, the probability of developing HAIs was 50% and 87.5% after 50 days of hospitalization (**Figure 1**).

The risk of infection varied according to the type of chemotherapy regimen used. It was 5.96 times greater during the Daunorubicin-Aracytin (DA) regimen indicated for acute myeloblastic leukemia and 2.03 greater during the regimen Cyclophosphamid-Vincristin-Daunorubicin-Dexamethasone (CVAD) indicated for Acute Lymphoblastic Leukemia. The risk to develop HAI was low for the regimens Bortezomid-Alkeran-Vincristin-Daunorubicin-Dexamethasone (BMVAD) and Doxorubicin-Bleomycin, Vinblastine-Deticene (ABVD). Sixty-six-point twenty-three percent of patients (66.23%) had antimicrobial prophylaxis. Prophylaxis was given to 72.72% of patients with acute leukemia while only 3.03 and 9.09% of patients with lymphoma/CLL and multiple myeloma had been given one. Antimicrobial prophylaxis was not a risk factor for HAI. We found no significant correlation between corticosteroid therapy and the risk of developing HCAI. The depth of chemo-induced neutropenia was significantly correlated with the risk of developing HCAI. The risk of HAI decreased by 58% when the number of PNN increased by 1 G/L. Sixty-six point sixty-seven (66.67%) of patients with grade 4 neutropenia developed HCAI. The risk to develop a HAI was 7.9 times greater when the neutropenia was grade 4.

The risk decreased by 60% when the hemoglobin level increased by 1 g/dL. Lymphocyte and monocyte count at baseline were not associated with the risk of developing HAIs (**Table 5**).

Evolution

Antibiotic therapy was instituted in all patients. It was combined with antiviral treatment in 1 patient. The most frequently administered antibiotic therapy was ceftriaxone and gentallin (20 cases), oxacillin and gentallin (14 cases), quinolone and metronidazole (12 cases), amoxicillin-clavulanic acid and quinolone (8 cases), imipenem and quinolone (2 cases), ceftazidime and gentallin (2 cases). Apyrexia was obtained on average within 2.5 days (extremes 2 and 7

Table 5. Risk factors distribution of hospital acquired infections

	No HAI *n=27*	HAI *n=50*	OR [IC 95%]	*p*-value
Length of admission (day)	12.7 (15.1)	28.9 (13.8)	1.09 [1.00-1.18]	0.022
Weight (kg)	56.9±11.8	48.8±16.4	0.96 [0.92-1.01]	0.068
Body surface (kg/m^2)	1.66±0.19	1.39±0.33	0.02 [0.00-0.82]	0.005
ABVD	5 (18.5%)	2 (4.00%)	0.20 [0.02-1.03]	0.048
CVAD	7 (25.9%)	21 (42.0%)	2.03 [0.74-6.08]	0.250
RCHOP	1 (3.70%)	4 (8.00%)	2.04 [0.27-58.0]	0.652
BMVAD	6 (22.2%)	5 (10.0%)	0.40 [0.10-1.50]	0.179
DA	2 (7.41%)	17 (34.0%)	5.96 [1.50-43.7]	0.021
Total amount of corticosteroid administered (mg)	1098±283	288±324	0.99 [0.99-1.00]	<0.001
Length of corticosteroid treatment (day)	16.0±9.50	17.6±20.1	1.01 [0.97-1.05]	0.720
Alkeran (mg)	13.0±1.41	41.0±26.4	1.45 [0.77-2.74]	0.020
Antimicrobial prophylaxis				
Yes	16 (59.3%)	10 (20.0%)	-	
No	11 (40.7%)	40 (80.0%)	5.82 [2.07-16.4]	0.001
Hemoglobin rate at the admission (G/dL)	9.40 (2.14)	7.64 (2.39)	0.72 [0.56-0.93]	0.007
ANC count at the admission (G/L)	1.00 (0.70)	0.55 (0.70)	0.42 [0.18-0.96]	0.035
Lymphocyte count at the admission au (G/L)	3.75±1.75	3.03±9.72	0.99 [0.92-1.07]	0.758
Monocyte count at the admission (G/L)	3.3±1.3	0.29±0.22	1.55 [0.52-4.68]	0.158
Hemoglobin rate at the beginning of HAIs (g/dL)	9.5 2±0.80	8.20±1.46	0.40 [0.19-0.84]	0.001
Grade of neutropenia at the beginning of HAI				0.002
0	4 (22.2%)	2 (5.56%)	-	
1	5 (27.8%)	4 (11.1%)	1.6 [0.19-16.3]	0.660
2	0 (0.00%)	4 (11.1%)	-	
3	3 (16.7%)	2 (5.56%)	1.33 [0.1-17.64]	0.819
4	6 (33.3%)	24 (66.7%)	7.9 [1.26-68.84]	0.033

days). Seven (7) patients had died during the infectious episode. The case-fatality rate was 10%.

Discussion

That first study materializes our hypothesis. The frequency of hospital-acquired infections (HAIs) is high. Fifty patients (64.93%) developed an average of 1.6 HAIs within 10.6±6.50 days. HAIs prevalence or incidence varies among units, hospitals, and countries. In oncology units, they varied from 10 to 40.7% [5-7]. Even though none of our patients have undergone any invasive procedures, our percentage was two times higher when we compare it with the intensive care units in hospitals that are sharing the same sanitary and environmental issues as us [5, 6, 8]. Surveys from oncology units in Morocco and Mexico have shown lower HAIs' incidences. However, the number of infectious episodes was more important related probably to the presence of invasive devices and aggressive regimens [5, 6].

This work has identified the most relevant risk factors of HAIs in our unit. Some studies have shown that the duration of hospitalization was significantly correlated with the incidence of HAIs [6, 10, 11]. It was 62.2% when the length of stay was at least 14 days versus 12.5% when it was less than 14 days. A closer analysis has noticed that one day in hospital increased the risk of developing HAIs by 1.09 (1.09 [95% CI 1.00; 1.18], P=0.022). Our patients spent an average of 28.9±13.8 days. It is comparable for patients admitted in intensive care units in various hospitals in Africa: 29.1±23.4 days [8-10]. Moreover, oncology units have recorded shorter hospitalization episodes with an average of respectively 7 and 12 days [5, 6].

Aggressive regimens amplify the risk to develop HAIs [10]. The daunorubicin-aracytin proto-

col indicated in AML is, in our survey, an obvious risk factor for HCAIs [5]. Even though we have reduced the doses of the regimen (DA). Chemotherapy's toxicity remained high. The risk to develop HAIs was in our study 5.96 times more important than other regimens. Thus, the HAIs incidence of AML patients was the highest at 80% [5, 13-16]. Alkeran drug has been also identified to increase the risk of developing HAIs. That risk was dose-dependent. Patients with HAI have received an average dose of 41±26.4 mg while those without received a lower one: 13±1.41 mg (P=0.020).

Corticosteroids promote the development of HAIs [3, 14-17]. Our study does not comfort that finding. Both groups: infected and non-infected had similar exposure to corticosteroids (16±9.5 days versus 17.6±20.1 days, P=0.720). The overall dose of corticosteroid administered was higher in the non-infected group: 1098±283 mg versus 288±224 mg for the infected group (P<0.001). More than the total dose administered, the prolonged exposure to corticosteroid is a significant risk factor of HAIs [14].

Concerning biological factors, we have found, like Flower et al, a correlation between the depth of neutropenia and the risk of HAIs [18]. The incidence was 80% when neutropenia was grade 4, 60% grade 3, 50% grade 2, 40% grade 1 versus 33% when there was no neutropenia (P=0.023). The risk of developing HAIs was significantly greater when the count of neutrophil polynuclear was less than 0.5 G/L: 7.9 [95% CI 1.26; 68.84]) [12-17]. The association between the incidence of HAIs and the duration of neutropenia could not be analyzed because many of our patients were still neutropenic at the end of our study. Lymphopenia and monocytopenia were not, contrary to some studies, risk factors for HAIs in our study [20].

Infections of undetermined origin are the most frequent entities in departments with oncological activity [13-20]. The profile of clinically documented infections varies depending on the study. In our unit, the infections were primarily cutaneous. The starting point of infections was the peripheral venous route while it was digestive or respiratory in oncology departments in industrialized countries [5, 12, 20]. The frequency of cellulitis in our study raises the problem of non-aseptic manipulation of the peripheral venous line and the duration of the catheter in place (more than 3 days) in our department.

Lung infections were the second most common site of infection [5]. Pulmonary tuberculosis is a growing problem in this population. In the Congo, three hundred and eighty-two cases are diagnosed yearly [21]. Therefore, a screening strategy needs to be implemented before initiating any chemotherapy treatment for patients with cancer.

Digestive infection was the third most frequent infectious site (12%). Unlike Western countries, food and utensils are not decontaminated or packaged. Meals are prepared at home by families which increase the risk to develop foodborne pathogen. To limit the risk of food poisoning, we instruct families to wash kitchen utensils with hot water and rinse them with bleach. Pasteurized, fermented, canned food, delicatessen, and raw vegetables are prohibited in neutropenic subjects. Foods should be cooked no more than 3 hours before meals.

Stomatological infections have an odontogenic origin. They delayed for 1 patient the beginning of the chemotherapy. Therefore, an evaluation of the dental condition by a stomatologist or dentist should be introduced in the initial pre-therapy check-up.

The low rate of microbiologically documented infections is related to the lack of culture methods.

Antibiotic therapy has been introduced in all cases. It was probabilistic. The combination of ceftriaxone and gentamycin was the first-line treatment for infections of undetermined origin. Other antibiotics were indicated according to the site of infection. Oxacillin, for example, was administered for skin infections. The outcome was favorable in 90% of cases. Apyrexia was achieved within an average of 2.5 days (extremes 1 and 7 days). The case-fatality rate (10%) was similar to non-oncological services [8, 9].

Conclusion

This first study made it possible to assess the extent and identify certain aspects of the prob-

lem of managing hematological malignancies and to provide an attempt to explain the poor results we obtain in the treatment of acute leukemia. HAIs disrupt the chemotherapy schedules and the budget allocated to the purchase of anti-cancer drugs. They delay the initiation of cancer treatment. Infection of the peripheral venous tract is the primary cause of HAIs. Training nurses and physicians in the various components of chemotherapy with an emphasis on hygiene and the application of standard and complementary infection prevention measures are essential prerequisites for the reduction of HAIs in hematology.

Data availability

The data used to support the findings of this study are available from the corresponding author upon request.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Lydie Ocini Ngolet, Department of Hematology, Teaching Hospital, 13 Auxence Ikonga Avenue, P.O Box 32, Brazzaville, Congo. Tel: +242-05-511-9860; E-mail: lngolet@yahoo.fr

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