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ELEVENTH ANNUAL MEETING

ASSESSMENT OF PROGNOSTIC FACTORS, COLONIZATION AND INFECTION EPIDEMIOLOGY IN PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION

Conditioning therapy and long-term immunosuppressive treatment in allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients make them highly susceptible to infectious complications [1]. Additionally, these are patients often colonized with multidrug-resistant (MDR) pathogens [2].

AIM

To analyze the colonization with pathogens and the incidence of infections after allo-HSCT. Moreover, we described the relationship of colonization and infections, the effectiveness of the anti-infection prophylaxis, as well as the assessment of treatment outcomes in allo-HSCT recipients.

METHOD

- We conducted a single-center retrospective analysis of colonization and infection epidemiology in 44 patients undergoing matched related donor allo-HSCT between 2012-2022 in the Department of Hematology in Lodz, Poland.
- We collected clinical data [Table 1], laboratory, and microbiological findings.
- For statistical analysis, we used Cox proportional hazard models, the Kaplan-Meier method, log-rank, and Chi^2 tests.

Table 1. Indications for allo-HSCT and conditioning regimens.

Diagnosis	n (%)	Type of conditioning regimen in a particular diagnosis	n (%)
AML	23 (52.3)	Flu/Bu 4	8 (34.8)
		BuCy 2	7 (30.4)
		TBi/Cy	3 (13.1)
		Flu/Bu 2	2 (8.8)
		Flu/Bu 4+ATG	1 (4.3)
		Flu/Bu 2+ATG	1 (4.3)
		Cy/ATG	1 (4.3)
ALL	8 (18.1)	TBI/Cy+ATG	5 (62.5)
		BuCy 2	2 (25)
		Cy/ATG	1 (12.5)
AA	4 (9.1)	Cy/ATG	4 (100)
MDS	2 (4.5)	Treo/Flu/ATG	1 (50)
		Treo/Cy	1 (50)
T-PLL	2 (4.5)	Flu/Bu 4	2 (100)
CML	1 (2.3)	Flu/Bu 4	1 (100)
aCML	1 (2.3)	Flu/Bu 4	1 (100)
HL	1 (2.3)	Flu/Bu 2	1 (100)
MPAL	1 (2.3)	BuCy 2	1 (100)
T-LBL	1 (2.3)	TBI/Cy	1 (100)

allo-HSCT - allogeneic hematopoietic stem cell transplantation; AML – acute myeloid leukemia; ALL – acute lymphoblastic leukemia; AA – aplastic anemia; MDS – myelodysplastic syndrome; T-PLL – T-cell prolymphocytic leukemia; CML – chronic myeloid leukemia; aCML – atypical chronic myeloid leukemia; HL – Hodgkin lymphoma; MPAL – mixed phenotype acute leukemia; T-LBL – T-cell lymphoblastic lymphoma; Bu – busulfan; Cy – cyclophosphamide; Flu – fludarabine; TBI – total body irradiation; ATG – anti-thymocyte globulin.

RESULTS

- Baseline colonization was observed in 84.1% of patients.
- The most common location was the anal region (55.4%).
- MDR pathogens accounted for 50.7% of all positive colonization cultures [Table 2].

Table 2. Etiology of colonizing pathogens before allo-HSCT.

Location of colonization	Etiology of colonization	Positive colonization culture, n (%)
Anal area		49 (100)
	Escherichia coli ESBL (+)	8 (16.3)
	Escherichia coli ESBL (-)	3 (6.1)
	Klebsiella pneumoniae ESBL (+)	14 (28.6)
	Enterobacter cloacae ESBL (+)	2 (4)
	Enterococcus faecium	7 (14.3)
	Enterococcus faecalis	7 (14.3)
	Enterococcus faecium GRE	3 (6.1)
	Candida krusei	1 (2.1)
	Candida glabrata	1 (2.1)
	Candida albicans	2 (4)
	Staphylococcus haemolitycus	1 (2.1)
Urinary tract		20 (100)
	Enterococcus spp.	7 (35)
	Coagulase-negative staphylococci	5 (25)
	Enterobacteriaceae	1 (5)
	Escherichia coli ESBL (-)	1 (5)
	Escherichia coli ESBL (+)	3 (15)
	Klebsiella pneumoniae ESBL (+)	1 (5)
	Streptococcus agalactiae	1 (5)
	Serratia marcescens	1 (5)
Nasal cavity		5 (100)
	Staphylococcus aureus MSSA	3 (60)
	Klebsiella pneumoniae ESBL (+)	1 (20)
	Streptococcus pneumoniae	1 (20)
Pharynx		3 (100)
	Klebsiella penumoniae ESBL (+)	1 (33.3)
	Enterococcus faecium	1 (33.3)
	Escherichia coli ESBL (+)	1 (33.3)

ESBL - extended-spectrum beta-lactamases;
GRE - glycopeptide-resistant enterococci;
MSSA - methicillin-sensitive Staphylococcus aureus.
allo-HSCT - allogeneic hematopoietic stem cell transplantation.

- Bacteremia occurred in 47.7%, of which 39.4% was caused by methicillin-resistant coagulase-negative *Staphylococcus epidermidis*.
- Fungal infections and viral reactivations were reported in 31.8% and 29.5%, respectively.

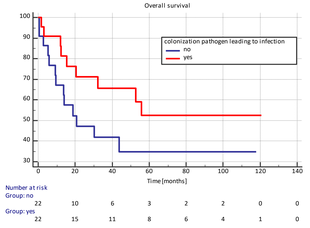
- In the post-transplantation period, infections were reported in 86.4% of patients.
- 59.5% of colonized patients developed infection with the pathogen responsible for the colonization [Table 3]. Among colonized patients, these infections were more common (*P=0.04*).

Table 3. Location and etiology of infections caused by colonizing pathogen.

Number of patients colonized before allo-HSCT				n=37
Number of patients with at least one infection with colonizing pathogen (%)				22/37 (59.5%)
Etiology	Location of colonization		Location of infection	Number of infections with colonizing pathogens
Escherichia coli ESBL (+)	anus	→	urinary tract	8
	anus	→	vascular bed	2
	anus	→	gastrointestinal tract	1
Enterococcus faecium	anus	→	urinary tract	7
	anus	→	vascular bed	1
Klebsiella pneumoniae ESBL (+)	anus	→	urinary tract	2
	anus	→	vascular bed	1
	anus	→	gastrointestinal tract	1
	urinary tract	→	urinary tract	1
	urinary tract	→	vascular bed	1
Staphylococcus epidermidis MRCSNE	urinary tract	→	vascular bed	2
	anus	→	urinary tract	1
Enterococcus faecalis	anus	→	vascular bed	1
	anus	→	urinary tract	1
Candida krusei	anus	→	urinary tract	1

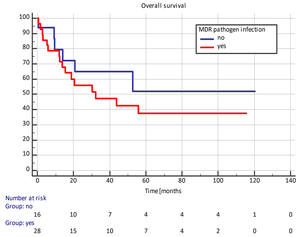
allo-HSCT - allogeneic hematopoietic stem cell transplantation;
ESBL - extended-spectrum beta-lactamases;
MRCNSE - methicillin-resistant coagulase-negative Staphylococcus epidermidis.

Figure 1. Kaplan-Meier estimation of overall survival in patients with infection caused by pathogen present in colonization vs others. Log-rank p=0.1.



- Patients colonized initially with at least 1 pathogen had significantly longer fever duration (mean=4.2 days, SD=2.96) compared to non-colonized patients (mean=1.7 days, SD=2.14) (*P=0.01*).
- The median overall survival (mOS) was 52.8 months (95% CI, 19-56 months).
- No difference was observed in OS between colonized and non-colonized patients (log-rank test: *P=0.33*).
- The MDR infection developed in 28 patients and accounted for 58.1% of all infections. The most common resistance mechanism was extended-spectrum beta-lactamase, 50.8%. MDR pathogens did not impact OS [Figure 2].

Figure 2. Kaplan-Meier estimation of overall survival in patients with MDR infection comparing to patients without MDR infection. Log-rank p=0.34.



- In multivariate Cox regression, the significant independent predictors for shorter OS were age (continuous variable), EBV reactivation, and pneumonia. [Table 4, Figures 3-4].

Table 4. Multivariate Cox proportional-hazard regression for OS in allo-HSCT recipients.

	Coefficient	p	HR	95% CI	
				lower	upper
Age at alloHSCT	0.05	0.05	1.05	1.00	1.10
Hospitalisation days	0.06	0.07	1.06	0.99	1.13
EBV reactivation	1.42	0.02	4.14	1.26	13.66
Pneumonia	1.55	0.03	4.71	1.20	18.53

allo-HSCT - allogeneic hematopoietic stem cell transplantation;
EBV – Epstein-Barr virus; HR – hazard ratio; CI – confidence interval.

Figure 3. Kaplan-Meier estimation of overall survival in patients with EBV reactivation comparing to patients without EBV reactivation. Log-rank p=0.03.

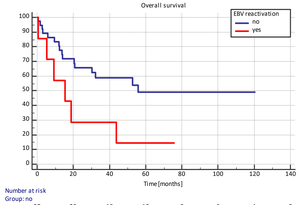
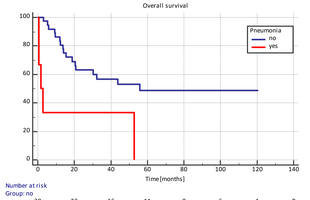


Figure 4. Kaplan-Meier estimation of overall survival in patients with pneumonia and without pneumonia. Log-rank p=0.004.



- Death occurred in 13.6% of patients within 100 days after allo-HSCT, 66.7% of them in the course of bacteremia.

CONCLUSIONS

- **Assessment of colonization may be an effective tool for predicting potential infection etiology.**
- **It can contribute to prompter targeted treatment implementation and possibly influence improved outcome.**
- **Variables like age, EBV reactivation, and pneumonia have been proven to shorten OS.**
- **More research is needed to confirm these observations.**

REFERENCES

1. Auletta JJ, Kou J, Chen M, Shaw BE. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021.
2. Lindsay J, Kerridge I, Wilcox L, et al. Infection-Related Mortality in Adults and Children Undergoing Allogeneic Hematopoietic Cell Transplantation: An Australian Registry Report. Transplant Cell Ther. 2021;27(9):798.e1-798.e10.

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