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Assessment of colonization and infection epidemiology in patients undergoing autologous hematopoietic stem cell transplantation: a single-center study

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Abstract

Introduction: Infections are one of the main causes of early death after autologous hematopoietic stem cell transplantation (auto-HSCT).

Material and methods: We present a single-center retrospective analysis of colonization and infection epidemiology in 115 patients with median age 63 years (range 21–72), who underwent auto-HSCT in 2017 or 2018 in the course of multiple myeloma [79.1% (n = 91)], Hodgkin lymphoma [18.3% (n = 21)] and non-Hodgkin lymphoma [2.6% (n = 3)].

Results: Colonization was observed in 40.9% of patients before auto-HSCT, the most common location being the urinary tract — 54.3%. Multi-drug resistant bacteria (MDR) accounted for 20.9% of positive colonization cultures before auto-HSCT.

In the post-transplantation period, infections occurred in 77.4% of patients after auto-HSCT. Bacteremia was observed in 43.5% of patients and it was mostly caused by methicillin-resistant coagulase-negative *Staphylococcus epidermidis* (MRCNSE) — 27.6%. Infection of the skin near the central vascular catheter was found in 18.3% of patients, urinary tract infections in 11.3%, and gastrointestinal infections in 20.9%. MDR pathogens accounted for 65.2%. The most common of these was methicillin-resistant coagulase-negative *Staphylococcus* (MRCNS) — 73.9%. Fungal and viral infections were reported in 21.7% and 7%, respectively. The median duration of empirical and targeted antibiotic therapy was 5 (range 1–20) and 7 (range 4–31) days, respectively. Death due to septic shock occurred in 2/115 (1.7%) patients during the neutropenia period.

Conclusions: Evaluation of the epidemiology of colonization and infection in patients undergoing auto-HSCT can be an effective tool in providing control and therapy for infections in HSCT recipients. Such knowledge is also essential in monitoring potential pathogen transmission and helping to improve local infection management standards.

Key words: colonization, infections, auto-HSCT

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Introduction

In 2017, the European Society for Blood and Marrow Transplantation (EBMT) reported c.45,500 hematopoietic stem cell transplantations (HSCTs). The number of patients who received autologous hematopoietic stem cell transplantation (auto-HSCT), most commonly used in the treatment of multiple myeloma and lymphoma, was approximately 24,000 (58%), whereas allogeneic hematopoietic stem cell transplantations (allo-HSCT),

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used primarily for the treatment of acute leukemia and non-Hodgkin lymphoma, were performed in approximately 17,000 patients (42%) [1].

The number of transplantations is constantly increasing, and is currently over 1.4 million. However, this procedure is still associated with a high risk of treatment-related mortality (TRM). The main causes of TRM are infections, organ toxicity, and graft-versus-host disease (GvHD) [2].

The Center for International Blood and Marrow Transplant Research (CIBMTR) estimates that for auto-HSCT, infections are responsible for 29% of deaths up to 100 days after HSCT, and for 5% in the late post-transplantation period [3].

More than half of the infections causing death after HSCT are associated with unspecified etiology. Of the known factors, bacteria make up about 15%, fungi 11%, viruses 9%, parasites 1%, and infections of mixed origin account for 5% [2]. The EBMT analysis for the period 1980–2001 revealed a significant increase in the median time of 5-year survival after HSCT, which is mainly related to a decreased number of lethal infectious complications [2, 4].

Infections after auto-HSCT are connected with a specific cascade of immunological dysfunction associated with a decrease in the number of circulating mature B cells followed by a reduction in immunoglobulin levels. Restoration of the individual components of the immune system occurs with different dynamics in which innate immunity (neutrophils, monocytes, and natural killer cells) typically precedes adaptive immunity (T- and B-lymphocytes). Complete immune reconstitution can take from several months up to two years after HSCT [5]. Although infections and immune dysfunction in the auto-HSCT setting are not as severe as in allo-HSCT, a related etiology and chronological order of infections typical of HSCT may also be observed.

In the first phase (phase I), lasting from the beginning of conditioning to the engraftment, neutropenia and mucosal damage occur leading to predominant bacterial, fungal (*Candida spp.* and *Aspergillus spp.*) and herpes virus infections [herpes simplex virus (HSV), human herpesvirus 6 (HHV-6)]. During this period, the infections are usually located in the blood and airways. Phase II, which starts upon the engraftment and lasts for a period of 100 days after HSCT, is related to lymphopenia. Gram (–) bacteria infections and often severe, invasive fungal infections with *Aspergillus spp.* and *Pneumocystis jiroveci* (PJ) are dominant in this phase. Besides, reactivation or new infections with cytomegalovirus (CMV), Epstein-Bárr virus (EBV), and polyoma- and adenovirus may be observed. In late phase III, which starts more than 100 days after HSCT, infections with encapsulated bacteria prevail, and they include *Streptococcus pneumoniae, Haemophilus influenzae,* or *Neisseria meningitidis*. Fungal infections (*Aspergillus spp., Candida spp.,* PJ) may also occur. Phase II/III may also be characterized by infection of varicella zoster virus (VZV). There is always a correlation between the amount of helper CD4+ T lymphocytes and the etiology of the infection [6].

A variety of risk factors for infections after auto-HSCT have been defined, including duration and severity of neutropenia induced by treatment [<7 vs. >7 days; absolute neutrophil count (ANC) <0.5 G/L], virological status, and type of cancer [2, 7–9]. Apart from the above, local epidemiology of microorganisms in the transplantation center, as well as colonization of the patient and applied anti-infection prophylaxis have a significant impact on transplant-related infections.

This study aimed to assess the colonization with pathogenic microorganisms and the incidence of infections during the peritransplantation period, as well as the effectiveness of applied prophylaxis in patients who underwent auto-HSCT in the Department of Hematology at the Medical University of Łódź, Poland.

Material and methods

A retrospective analysis of medical records was used in our study. Colonization with pathogens was assessed in each patient during the pre-transplantation period based on an analysis of microbiological cultures of material collected from the throat, nasal cavity, and anal area, as well as urine culture. The tests were taken by a trained nursing team. Each patient gave their informed consent for access to clinical data.

All 115 patients [men 54.8% (n = 63); women 45.2% (n = 52)] with median age 63 years (range 21–72) underwent auto-HSCT transplantation between 1 January 2017 and 31 December 2018 in the Department of Hematology of the Medical University of Łódź. The patients treated with auto-HSCT were diagnosed with multiple myeloma [79.1% (n = 91)], Hodgkin lymphoma [18.3% (n = 21)] or non-Hodgkin lymphoma [2.6% (n = 3)]. The types of conditioning treatment regimens are presented in Table I.

The median duration of hospitalization was 29 days (range 17–50). Prophylactic antimicrobial, antiviral and antifungal treatment was applied in all patients from the beginning of chemotherapy to reaching ANC >0.5 G/L and immune reconstitution. The prophylaxis for all patients consisted of ciprofloxacin 500 mg twice daily (bid) and fluconazole 400 mg once daily during the peritransplantation period; cotrimoxazole 960 mg three times a week since neutrophil recovery until six months after HSCT; acyclovir 800 mg bid during the peritransplantation period and after engraftment 200 mg three times a day for six months after HSCT.

In addition, all patients underwent environmental prophylaxis, manifesting with increased restriction of aseptic and antiseptic regimens in the Bone Marrow Transplantation Ward, including air-conditioned isolation rooms with high-efficiency particulate arrestance (HEPA) air, limited

Table I. Types of conditioning regimen

Diagnosis	Type of conditioning regimen	Number of patients N [%]
Multiple myeloma	Melphalan 200 mg/m^2	50 (43.5)
	Melphalan 140 mg/m^2	26 (22.6)
	Melphalan 100 mg/m^2	15 (13.0)
Hodgkin lymphoma	BEAM	19 (16.5)
	BeEAM	2 (1.7)
Non-Hodgkin lymphoma	BEAM	1 (0.9)
	BeEAM	1 (0.9)
	TEAM	1 (0.9)

BEAM — carmustine (BCNU), etoposide, cytarabine, melphalan; BeEAM — bendamustine, etoposide, cytarabine, melphalan; TEAM — thiotepa, etoposide, cytarabine, melphalan

contact with visitors, an adequate diet, and strict personal hygiene.

In all patients, a central vascular catheter was implanted before the transplantation procedure. In the case of fever in patients with no clinically apparent signs of infection, lack of colonization with pathogens, and/or previous infection with a resistant pathogen, one of two empirical treatment options were used: cephalosporine with activity against *Pseudomonas* (cefepime or ceftazidime) or piperacillin with tazobactam. Patients with a complicated clinical course were administered carbapenem combined with glycopeptide/oxazolidine or beta-lactam antibiotic acting against *Pseudomonas* together with aminoglycoside combined with glycopeptide/oxazolidine. In the case of a severe non-colonized condition, the patient was administered carbapenem together with aminoglycoside and glycopeptide/oxazolidine [10].

The presence of colonization and/or a history of infection with a resistant pathogen were the reasons for implementing an adequate antibiotic therapy.

The recommendations were modified according to the results of microbiological cultures and imaging examinations, and the treatment was continued for at least 72 hours after the fever and other symptoms of infection had subsided, and the granulocyte system (ANC >0.5 G/L)had regenerated for two days. Patients with fever lasting more than 72–96 hours despite the introduction of broad-spectrum antibiotic therapy, were applied an empirical antifungal treatment with the amphotericin B lipid complex or caspofungin [10].

Bacteremia was defined as a positive result of microbiological culture from a single sample, or in the case of Gram (+) bacteria infections from a double blood sample, taken from a febrile patient.

The analysis evaluated the frequency and type of colonization and its influence on post-transplantation infections, as well as the incidence of infections and the pathogens responsible for them.

Results

Evaluation of colonization

Colonization with a pathogen was revealed in 47/115 (40.9%) patients, and in 16 (13.9%) patients the analyzed area was colonized by more than one pathogen.

The total number of pathogens responsible for colonization was 70 (67 positive bacterial cultures, three positive fungal cultures). Bacteria were responsible for 67 positive cultures of all colonizing pathogens, of which 14/67 (20.9%) were multidrug-resistant (MDR) bacteria. Extended-spectrum beta-lactamases (ESBL) was the most common type of resistance; it accounted for 13/14 (92.9%) of all resistance types.

The most commonly colonized area was the urinary tract 38/70 (54.3%), followed by the anal area 15/70 (21.4%), then the nose 11/70 (15.7%), and then the throat 6/70 (8.6%).

The analyzed group demonstrated 38 positive cultures in the urinary tract, with *Enterococcus spp.* (12/38; 31.6%) being the most frequent pathogen. In 15 positive cultures from the anal area, Escherichia coli strain producing ESBL was most frequently found (8/15; 53.3%). Positive throat and nasal cultures were observed in six and 11 cases, respectively, and the most common bacteria was methicillin-sensitive *Staphylococcus aureus* (MSSA), of which the frequency of occurrence was 2/6 (33.3%) in the throat and 11/11 (100%) in the nasal cavity (Table II).

Infection evaluation

Post-transplantation infections occurred in 89/115 (77.4%) of patients. Among patients with fever, of which the median duration was three days, microbiologically documented infections were found in 58/89 (65.1%) patients, fever of unknown origin in 28/89 (31.5%), and clinically documented infections in 3/89 (3.4%).

The total number of pathogens responsible for infection was 174 (141 positive bacterial cultures, 25 positive fungal cultures, and eight viral infections). So, on average, there were 1.5 (174/115) infection factors per patient after auto-HSCT.

Bacterial infections

There were 141 microbiologically confirmed positive bacterial cultures in patients after auto-HSCT. Gram-positive bacteria predominated, accounting for 117/141 (82.9%). MDR pathogens accounted for 92/141 (65.2%). The most common type of bacterial resistance was MRCNS, making up 68/92 (73.9%).

Bacteremia occurred in 50/115 (43.5%) and catheter-induced infections were found in 30/115 (26.1%) patients. In 27/115 (23.5%) patients, bacteremia was caused by more than one pathogen. In total, 87 positive blood cultures were noted. Methicillin-resistant coagulase-negative

Table II. Etiology of colonizing pathogens before autologous hematopoietic stem cell transplantation (auto-HSCT) depending on location*

Location of colonization	Etiology of colonization	Positive cultures N [%]
Urinary tract	*Enterococcus spp.*	12 (31.5)
	Lactobacillus spp.	7 (18.4)
	Coagulase-negative *staphylococcus*	5 (13.2)
	Enterobacteriaceae	5 (13.2)
	Escherichia coli ESBL (–)	4 (10.5)
	Klebsiella pneumoniae ESBL (+)	2 (5.3)
	Streptococcus agalactiae	2 (5.3)
	Proteus mirabilis ESBL (–)	1 (2.6)
	Total	38 (100)
Anal area	*Escherichia coli* ESBL (+)	8 (53.3)
	Klebsiella pneumoniae ESBL (+)	2 (13.3)
	Bacteroides vulgates	1 (6.7)
	Enterobacter cloacae ESBL (+)	1 (6.7)
	Enterococcus raffinosus	1 (6.7)
	Enterococcus faecium	1 (6.7)
	Aspergillus fumigates	1 (6.7)
	Total	15 (100)
Nasal cavity	*Staphylococcus aureus* MSSA	11 (100)
	Total	11 (100)
Pharynx	*Staphylococcus aureus* MSSA	2 (33.3)
	Staphylococcus aureus MRSA	1 (16.7)
	Candida albicans	1 (16.7)
	Candida krusei	1 (16.7)
	Streptococcus viridians	1 (16.7)
	Total	6 (100)

*In 16 (13.9%) patients before auto-HSCT, location was colonized by >1 pathogen; ESBL — extended-spectrum beta-lactamases; MSSA — methicillin-sensitive *Staphylococcus aureus*; MRSA — methicillin-resistant *Staphylococcus aureus*

Staphylococcus epidermidis (MRCNSE) was the most common pathogen, accounting for 24/87 (27.6%) of the etiological factors responsible for blood infections.

The skin in the central vascular catheter was infected in 21/115 (18.3%) patients. There were 30 positive cultures and the main etiological agent was MRCNSE, which accounted for 16/30 (53.3%) of pathogens infecting this area.

Urinary tract infections occurred in 13/115 (11.3%) patients and the most common etiological agent was *Escherichia coli* ESBL (–). It accounted for 6/15 (40%) of positive cultures.

Positive stool cultures were observed in 24/115 (20.9%) patients. Bacteria accounted for nine positive stool cultures, and fungi accounted for 25. *Clostridium difficile* (8/9; 88.9%) was the predominant bacterial pathogen in this group (Table III).

Only 3/47 (6.4%) colonized patients developed in total three infections with the pathogen responsible for their previous colonization. These infections affected the urinary tract and they were connected with earlier colonization of the anus. *Klebsiella pneumoniae* ESBL (+) was responsible for 2/3 (66.7%) of all infections with the colonizing pathogen, and *Escherichia coli* ESBL (+) for 1/3 (33.3%).

Fungal infections

Fungal infections occurred in 25/115 (21.7%) patients. 25 positive cultures of fungal pathogens were reported in the gastrointestinal tract. *Candida albicans* was observed most often — 11/25 (44%) (Table III).

Viral infections

Viral infections occurred in 8/115 (7%) patients after auto-HSCT. HSV was found in 5/115 (4.3%) and viral respiratory tract infection was reported in 2.6% (3/115) of patients.

The median duration of empirical and targeted antibiotic therapy was 5 (range 1–20) and 7 (range 4–31) days, respectively.

After auto-HSCT, death occurred in 2/115 (1.7%) patients (aged 21 and 54) during the neutropenia period. Deaths were caused by septic shock caused by *Enterobacter cloacae* MDR and *Escherichia coli* ESBL (+) bacteremia, and affected patients with lymphomas in partial response to previous chemotherapy. These bacteria were not responsible for the colonization of these patients before auto-HSCT.

Discussion

Despite the development of modern preventive strategies, and a better understanding of mechanisms of immunosuppression, post-transplantation infections remain a problem. Infections connected with HSCT are the most common cause of early death in the post-transplantation period after auto-HSCT [3].

In our study, we conducted a comprehensive analysis of the colonization of patients undergoing auto-HSCT and its influence on post-transplantation infections. Moreover, we determined the frequency and type of infections involved in the post-transplantation period.

In the literature review, no study has analyzed the etiology and frequency of colonization of all sites which are subject to standardized microbiological evaluation before HSCT. In our study, we observed colonization with at least one pathogen in 40.9% of patients before auto-HSCT. The urinary tract appeared to be the most colonized region — 54.3%.

In our study, MDR bacteria accounted for 20.9% of positive colonization cultures before auto-HSCT. MDR bacteria most frequently colonized the anal region and this occurred in 11/115 (9.6%) patients before auto-HSCT. The analysis by Girmenia et al. which assessed the presence of Gram (–) colonization of the gastrointestinal tract at 54 Italian centers in 1,625 patients before auto-HSCT MDR reached 9% [11].

Table III. Etiology of infection after autologous hematopoietic stem cell transplantation in relation to number of positive cultures

Location of infection	Type of infection	Etiology of infection	Positive cultures N (%)
Bacteremia			
	Gram-positive bacteria	*Staphylococcus epidermidis* MRCNSE	24 (27.6)
		Staphylococcus hominis MRCNS	14 (16.1)
		Staphylococcus haemolyticus MRCNS	13 (14.9)
		Staphylococcus spp. MLS_B (+)	11 (12.6)
		Staphylococcus epidermidis MSCNS	8 (9.2)
		Streptococcus parasanguinis	1 (1.1)
		Enterococcus faecium GRE, HLGR	1 (1.1)
		Enterococcus faecium	1 (1.1)
		Corynebacterium afermentans	1 (1.1)
		Bacillus spp.	1 (1.1)
		Bacillus cereus	1 (1.1)
		Clostridium difficile	1 (1.1)
	Gram-negative bacteria	*Escherichia coli* ESBL (–)	6 (6.5)
		Escherichia coli ESBL (+)	1 (1.1)
		Enterobacter cloacale ESBL (+)	1 (1.1)
		Enterobacter cloacae MDR	1 (1.1)
		Acinetobacter ursingii	1 (1.1)
	Total		87 (100)
Skin of central line area			
	Gram-positive bacteria	*Staphylococcus epidermidis* MRCNSE	16 (53.3)
		Staphylococcus epidermidis MSCNS	6 (20)
		Staphylococcus spp. MLS_B (+)	3 (10)
		Staphylococcus hominis MRCNS	1 (3.3)
		Staphylococcus warneri MSCNS	1 (3.3)
		Enterococcus spp.	1 (3.3)
	Gram-negative bacteria	*Escherichia coli* ESBL (–)	2 (6.7)
	Total		30 (100)
Urinary tract			
	Gram-positive bacteria	*Enterococcus faecium*	2 (13.3)
		Enterococcus spp.	1 (6.7)
		Enterococcus faecalis	1 (6.7)
	Gram-negative bacteria	*Escherichia coli* ESBL (–)	6 (40)
		Escherichia coli ESBL (+)	3 (20)
		Klebsiella pneumoniae ESBL (+)	2 (13.3)
	Total		15 (100)
Gastrointestinal tract			
	Gram-positive bacteria	*Clostridium difficile*	8 (23.5)
	Gram-negative bacteria	*Klebsiella pneumoniae* ESBL (+)	1 (2.9)
	Fungi	*Candida albicans*	11 (32.4)
		Candida glabrata	7 (20.6)
		Saccharomyces cerevisiae	3 (8.8)
		Candida pararugosa	1 (2.9)
		Candida dubliniensis	1 (2.9)
		Candida parapsilosis	1 (2.9)
		Candida tropicalis	1 (2.9)
	Total		34 (100)

MRCNSE — methicillin-resistant coagulase-negative *Staphylococcus epidermidis*; MRCNS — methicillin-resistant coagulase-negative *Staphylococcus*; MLS_B — resistance to macrolides, lincosamides and streptogramin B; MSCNS — methicillin-susceptible coagulase-negative *Staphylococcus*; GRE — glycopeptide-resistant *Enterococci*; HLGR — high-level gentamicin-resistant; ESBL — extended-spectrum beta-lactamases; MDR — multidrug-resistance

Post-transplantation infections occurred in 77.4% of analyzed patients after auto-HSCT. In the study conducted by Gil et al. in the years 1994–2005, 92% of 314 patients after auto-HSCT demonstrated infectious complications [12]. In an analysis of 112 patients undergoing auto-HSCT between 2004 and 2009, Santos et al. recorded 57% of infections [13]. In the studies conducted on groups of patients after auto-HSCT by Salazar et al. (126 patients; 1992–1996) and Celebi et al. (45 patients; 1997–1999), much lower percentages of infections were obtained: 40% and 42%, respectively. This low percentage of infectious complications could have been related to the fact that these studies also considered infections in patients treated for solid tumors. In addition, the included patients were <60 years old, presenting a very good general condition and a lack of accompanying diseases [14, 15]. The number of infections after HSCT observed in our study is similar to results received in other transplantation centers in Poland and worldwide, where, despite applied anti-infection prevention, infections still occur in 80–100% of patients [12, 16].

In our study, bacteremia was found in 43.5% (50/115) of patients. In other studies, such as the one conducted by Salazar et al., bacteremia was described in 31% of patients after auto-HSCT, while in a study conducted by Wang et al. in the period 2005–2014, the prevalence of bacteremia reached 20% [14, 17].

It is estimated that up to 90% of blood infections with hospital pathogens are caused by the presence of a central venous catheter (CVC), 90% of which is associated with an untunnelled catheter [18]. Criteria of the US Center for Disease Control and Prevention (CDC) regarding the diagnosis of CVC-related blood infections [central line-associated bloodstream infection (CLABSI)] include a catheter which is inserted for at least two days, at least one positive catheter blood culture with the pathogen or at least two positive catheter blood cultures with a commensal pathogen, together with concurrent symptoms of systemic infection (fever >38°C, chills, hypotension). Furthermore, the symptoms must not be related to any other source of infection [19, 20].

We observed CLABSI in 26.1% (30/115) of patients after auto-HSCT. Analysis conducted by other centers, such as the study by Santos et al., revealed that CLABSI occurred in 26% of patients after auto-HSCT [13], while in a study conducted by Satlin et al., CLABSI was found in 15–40% of auto-HSCT receivers depending on the prophylaxis that was used [21]. Results obtained in our center are thus comparable to those presented by other researchers [13, 21, 22].

As far as neutropenic fever after auto-HSCT is concerned, the results vary significantly depending on the underlying disease and the treatment used, usually ranging from 50–90% [23–25]. In our analysis, febrile neutropenia complicated the post-transplantation period in 77.4% (89/115) of patients after auto-HSCT.

Exogenous hospital microorganisms, mainly Gram-positive bacteria, and endogenous bacterial flora of the gastrointestinal tract which contributes to Gram-negative infections, are an important source of bacterial infections after HSCT. In our center, in the group after auto-HSCT, Gram-positive bacteria were responsible for 82.9% of all bacterial infections, with a predominance of coagulase-negative *Staphylococci*. In the study by Gil et al. [13] in patients after auto-HSCT, Gram-positive bacteria accounted for 60% of pathogens infecting blood. Besides, coagulase-negative *Staphylococci* were also most frequently observed [12]. The higher percentage of Gram-positive bacteria (+) observed in our study is probably because in addition to blood, other infection sites, such as the gastrointestinal tract, urinary tract, and skin, were included in the assessment of bacterial count.

Over recent years, the number of MDR infections has significantly increased, thus creating numerous problems for effective antibiotic therapy. The prevalence of MDR pathogens varies depending on the location of transplant centers and their local infection epidemiology, and is strongly dependent on the type of infection prophylaxis and the treatment provided. In our study, MDR pathogens accounted for 65.2% of etiological factors of detected infections. The literature review does not contain a multi-drug resistance analysis covering multiple locations of infection and different types of resistance like those shown in our study [methicillin-resistant coagulase-negative *Staphylococcus* (MRCNS), resistance to macrolides, lincosamides and streptogramin B (MLS_B), ESBL, MDR, glycopeptide-resistant *Enterococci* (GRE), high-level gentamicin-resistant (HLGR)] simultaneously. In a multicenter analysis, Averbuch et al. evaluated the Gram-negative bacteria resistance of 241 recipients of auto-HSCT in 2014–2015. The percentage of Gram-negative MDR rods was 20% for the auto-HSCT group [26].

Invasive fungal infections are an important type of complication associated with the transplantation procedure. In our analysis, infection with at least one fungal pathogen occurred in 21.7% and it was mostly caused by *Candida spp.* — being responsible for 88% (22/25) of all fungal pathogens, headed by *C. albicans* — 44% (11/25). According to scientific reports, the incidence of infections caused by *Candida spp.*, and in particular by *C. albicans*, has decreased in recent years, due to widespread prophylactic and therapeutic activities, including the use of second-generation azoles [27]. On the other hand, intensive prophylaxis has contributed to an increase in the incidence of resistant strains, such as *C. glabrata* [28–30]. In the presented study, *C. glabrata* constituted 28% (7/25) of all detected fungal pathogens. A similar trend is observable in the study by Kontoyiannis et al. [31] conducted on 16,200 patients after auto- and allo-HSCT between 2001 and 2006: *C. glabrata* (33%) and *C. albicans* (20%) cultures predominated in the group of invasive candidiasis.

Viral infection was reported in 7% (8/115) of auto-HSCT receivers. Neither CMV nor EBV reactivation was detected. The most common viral infection was caused by HSV and this occurred in 4.3%. This percentage of cases attributed to reactivation is undoubtedly a result of a high baseline population seroprevalence of HSV which can be found in 50–96% of people [32].

In our study, 6.4% of patients who appeared to be colonized before auto-HSCT could not avoid infection with pathogens that were associated with colonization. The literature review has no analysis which would simultaneously evaluate different locations of colonization with etiology and influence on post-transplantation infections. Colonization with a pathogen may increase the risk of infection and furthermore affect the effectiveness of subsequent antibiotic therapy, thus posing a threat to the effective regeneration of the hematopoietic system. The assessment of colonization can be a useful tool to identify patients with a high risk of developing infections caused by the colonizing pathogen. The analysis of both colonization and infection should be carried out systematically in the transplantation center, providing an opportunity for proper prevention and empirical treatment.

Conclusions

Neutropenic patients are susceptible to many types of infection, including bloodstream infections and gastrointestinal infections, as well as those connected with the urinary tract and skin.

The etiology and frequency of infection depend largely on the local infection epidemiology of each center, including principles of prophylaxis and patterns of empirical and targeted antibiotic treatment.

Searching for risk factors such as those associated with colonization, helps to identify neutropenic patients at the highest risk of infection and death.

Evaluation of colonization and infection in patients undergoing auto-HSCT can be effective in monitoring potential pathogen transmission, and provides a useful tool for improving local standards for managing infections. Such knowledge is also essential to guide infection control measures and effective infection therapy in HSCT recipients.

Authors' contributions

KMK and AP were responsible for creating the study protocol; KMK, MCz and PS were responsible for patient enrolment and data acquisition; KMK and AP were responsible for writing the manuscript; AW and AP were responsible for manuscript revision and proofreading.

Conflict of interest

None.

Financial support

None.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; uniform requirements for manuscripts submitted to Biomedical journals.

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