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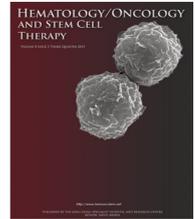
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# Current practice of oral care for hematopoietic stem cell transplant patients: A survey of the Eastern Mediterranean Blood and Marrow transplantation group

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**KEYWORDS**

Hematopoietic stem cell;  
Mucositis;  
Oral care;  
Transplant

**Abstract**

**Introduction:** The oral cavity is one of the most common sites impacted by hematopoietic stem cell transplantation (HSCT) with acute complications including mucositis, bleeding, salivary gland dysfunction, infection, and taste alteration. These complications may result in significant morbidity and can negatively impact outcomes such as length of stay and overall costs. As such, oral care during HSCT for prevention and management of oral toxicities is a standard component of transplant protocols at all centers. The objective of this study was to evaluate the current oral care practices for patients during HSCT at different transplant centers within the Eastern Mediterranean region.

**Material and methods:** An internet-based survey was directed to 30 transplant centers in the Eastern Mediterranean region. The survey included five sections asking questions related to (1) transplant center demographics; (2) current oral care protocol used at the center and type of collaboration (if any) with a dental service; (3) use of standardized oral assessment tools and grading systems for mucositis; (4) consultations for management of oral complications; and (5) oral health needs at each center. Data are presented as averages and percentages.

**Results:** A total of 16 responses from 11 countries were collected and analyzed, indicating a response rate of 53%. Eight centers reported that a dentist was part of the HSCT team, with four reporting oral medicine specialists specifically being part of the team. Almost all centers (15/16; 93%) had an affiliated dental service to facilitate pre-HSCT dental clearance with an established dental clearance protocol at 14 centers (87%). Dental extraction was associated with the highest concern for bleeding and the need for platelet transfusion. With respect to infection risk, antibiotic prophylaxis was considered in the setting of low neutrophil counts with restorative dentistry and extraction. All centers provide daily reinforcement of oral hygiene regimen. The most frequently used mouth oral rinses included sodium bicarbonate (68%) and chlorhexidine gluconate (62%), in addition to ice chips for dry mouth (62%). The most frequently used mucositis assessment tools were the World Health Organization scale (7/16; 43%) and visual analogue scale for pain (6/16; 37%). Mucositis pain was managed with lidocaine solution (68.8%), magic mouth wash (68.8%) and/or systemic pain medications (75%).

**Conclusions:** Scope and implementation of oral care protocols prior to and during HSCT varied between transplant centers. The lack of a universal protocol may contribute to gaps in oral healthcare needs and management for this group of patients. Further dissemination of and education around available oral care guidelines is warranted.

Clinical relevance.

Considering oral care during HSCT a standard component of transplant protocols, the current study highlights the common oral care practices for patients at centers within the Eastern Mediterranean region.

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**Introduction**

The oral cavity is one of the most common sites impacted by hematopoietic stem cell transplantation (HSCT) and associated conditioning regimens, and in the context of allogeneic HSCT, graft versus host disease prophylaxis regimens [1]. Potential complications include oral mucositis (OM), bleeding, salivary gland dysfunction, and taste alteration [2]. Furthermore, as the mouth is colonized by the microflora, including potentially pathogenic organisms, opportunistic infections become a major concern [3–5]. These complications may result in significant morbidity and can negatively impact outcomes such as length of hospital stay and overall costs [6,7]. As such, oral care during HSCT for prevention and management of oral toxicities is considered a standard component of transplant protocols at all centers [8–10].

Basic oral care recommendations for hematologic malignancy patients undergoing HSCT were published in 2015 in a position paper from the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) and the European Society for Blood and Marrow Transplantation (EBMT) [1]. These recommendations were developed by experts in the field of oral medicine, hematological malignancies, and HSCT using available literature and expert opinion to guide healthcare providers who manage these patients. However, it is unclear up to what extent these recommendations are followed among different transplant centers and to what extent there is variability of practice between HSCT centers.

The objective of this study was to evaluate oral care practices for patients during HSCT at different transplant centers in the Eastern Mediterranean region.

## Material and methods

An internet-based survey was used to elicit information on oral care protocols at HSCT centers as part of the Eastern Mediterranean Blood and Marrow Transplantation (EMBMT) group, which include 30 centers in all countries from the eastern Mediterranean region [11]. The member countries of EBMT include Afghanistan, Bahrain, Djibouti, Egypt, the Islamic Republic of Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, the Occupied Palestinian territory, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, Turkey, and Yemen [12]. The survey was in English language and built in SurveyMonkey® (San Mateo, CA, USA). It included a total of 32 close-ended questions divided over five sections asking about: (1) transplant center demographics; (2) pre-HSCT dental clearance; (3) current oral care protocol used at the center and type of collaboration (if any) with dental service; (4) use of standardized oral assessment tools and grading systems for mucositis; and (5) consultations for management of oral complications. For the purpose of the survey, in-house dental service was defined as providing dental care within the medical center and affiliated dental service was defined as dental practice that is not based in the medical facility yet provides dental treatment to patients referred from medical facilities under certain agreement and guidelines.

Prior to the distribution of the survey, validation of the survey questions was completed through face validity by field experts to evaluate the survey questions for the ability to capture intended aims and check for errors such as confusing language and leading statements. The survey was then pilot-tested through enrollment of five dentists and five HSCT physicians, and collection of answers, comments, and feedback. Pilot data were analyzed using principal components analysis for statistical correlations and used to modify five questions in total [13].

The final survey was emailed to the HSCT program directors at the 30 centers within EMBMT with a request to participate in this study starting January 2019. Follow-up emails were sent 2 and 4 weeks after the initial email to those who did not reply. Extracted data were analyzed and presented as averages and percentages. In addition, *t*-test was used for centers comparisons and statistical significance.

## Ethical approval statement

A human research ethical approval was obtained through King Abdulaziz University (Faculty of Dentistry), Jeddah, Saudi Arabia.

## Results

### Transplant centers demographics

Respondents from a total of 16 HSCT centers from 11 countries participated and completed the survey with a response rate of 53.3% (Table 1). Overall, 75% of centers had five or

fewer transplant attending physicians as part of the team. The median number of transplant procedures performed annually was 28 (range, 1–100), with approximately half performed less than 30 autologous (9/16, 56.3%) and less than 30 allogeneic (8/16, 50%) transplants annually. A dentist was included in the HSCT team at half of the centers ( $n = 8$ ), with four centers staffed specifically with Oral Medicine specialists. Overall, 14 HSCT centers would refer patients for dental clearance prior to HSCT either to in-house dental service (10/14; 71.4%) or affiliated dental practice (3/14; 21.4%) or left for the patient to choose (1/14; 7.1%). The remaining two centers did not include pre-HSCT dental clearance as part of their protocol.

### Pre-HSCT dental clearance

Dental prophylaxis (plaque and calculus debridement) was specifically part of the pre-HSCT preparation protocol at 13 centers (81.3%; Table 2). This dental procedure was more likely to take place at centers that have a dentist as part of the team ( $p = 0.46$ ) (Table 2). During the pre-HSCT dental clearance, centers were more inclined to prescribe antibiotic prophylaxis in the setting of neutropenia (8/16; 50%) prior to invasive dental procedures (7/16; 43.8%), and for patients with central venous catheters (6/16; 37.5%). This include patients with neutropenia and absolute neutrophil count of less than 500 cells/ $\mu\text{L}$  who are about to receive dental prophylaxis (9/16; 56.3%), restorative dentistry (10/16; 62.5%), or extractions (8/16; 50%). For bleeding risk, five centers (31.3%) were more likely to order platelet transfusion prior to dental prophylaxis and restorative dentistry when platelet counts fall to less than 20 K/ $\mu\text{L}$ . At the same time, 10 centers (62.5%) would order platelet transfusion prior to dental extraction when platelet count falls to less than 50 K/ $\mu\text{L}$ .

### Current oral care protocol

Nine centers (56.3%) have implemented a written oral care protocol and oral hygiene instructions communicated to patients either verbally (56.3%), in writing (6.3%), or both (37.5%) to be followed during HSCT (Table 3). As part of the oral care protocol, eight HSCT centers (50%) would restrict teeth brushing in the setting of thrombocytopenia and six centers (37.5%) would not restrict in the setting of neutropenia or thrombocytopenia. The use of dental floss and interdental cleaning aids was prohibited at nine HSCT centers (56.3%). The most frequently used daily mouth rinses were sodium bicarbonate (11/16; 68%) and chlorhexidine gluconate (10/16; 62.5%). Protocols related to denture wearing existed at only half of the centers (8/16; 50%), with or without limitations such as in the setting of OM. Ice chips would be used for the management of dry mouth symptoms at more than half of the centers (10/16; 62.5%). When asked about antifungal therapy as part of standard infectious disease prophylaxis, all centers reported using systemic fluconazole or voriconazole with variable dosages. However, only four centers reported details on the actual regimen used.

**Table 1** Demographics of the HSCT Centers.

Question	Response	Frequency (%)
Country	Algeria	1 (6.3)
	Egypt	1 (6.3)
	Iran	1 (6.3)
	Jordan	1 (6.3)
	Kuwait	1 (6.3)
	Lebanon	1 (6.3)
	Morocco	1 (6.3)
	Oman	2 (12.5)
	Pakistan	2 (12.5)
	Saudi Arabia	4 (25.0)
	Turkey	1 (6.3)
How many attending transplant physicians do you have at your center?	2	6 (37.5)
	3–5	6 (37.5)
	≥6	4 (25.0)
What is the total number of autologous transplants performed at your center annually?	<30	9 (56.3)
	≥30	7 (43.8)
What is the total number of allogeneic transplants performed at your center annually?	<30	8 (50.0)
	≥30	8 (50.0)

HSCT = hematopoietic stem cell transplantation.

**Table 2** Prehematopoietic Stem Cell Transplantation Dental Clearance.

Question	Response	Frequency (%)
Is there a dentist as part of the transplant team in your center?	Yes	8 (50.0)
	No	8 (50.0)
Is there an Oral Medicine specialist as part of the transplant team in your center?	Yes	4 (25.0)
	No	12 (75.0)
Is there a dental service within or affiliated with your center?	Yes	15 (93.8)
	No	1 (6.3)
Are HSCT patients referred for dental clearance prior to transplant?	Yes	14 (87.5)
	No	2 (12.5)
If you answered Yes for the previous question, where do you refer your patients for pre-HSCT dental clearance?	Dental service at center	10/14 (71.4)
	Affiliated dental service, but not located at the center	3/14 (21.4)
	Patient choice (unaffiliated dentist/dental service)	1/14 (7.1)
Are HSCT patients referred for dental prophylaxis (cleaning) prior to transplant?	Yes	13 (81.3)
	No	3 (18.8)

HSCT = hematopoietic stem cell transplantation.

### OM assessment tools and grading

When asked about OM prevention, the only specific measure noted was palifermin (four centers, 25%) (Table 4). Once a

patient develops OM, the World Health Organization (WHO) Oral Toxicity Scale and the Oral Mucositis Assessment Scale (OMAS) were the most routinely used instruments for severity assessment (43.8% and 25%, respectively). Oral pain was more likely to be assessed using the Visual Analogue

**Table 3** Oral Care during HSCT.

Question	Response	Frequency (%)
In which of any of the following pre-HSCT dental treatment scenarios is antibiotic prophylaxis recommended? (you can choose more than one)	Antibiotic prophylaxis for patients with central venous catheter prior to an invasive dental procedure	6 (37.5)
	Antibiotic prophylaxis prior to any invasive dental procedure	7 (43.8)
	Antibiotic prophylaxis prior to any/all dental visits pre-HSCT	1 (6.3)
	Antibiotic prophylaxis in the setting of neutropenia	8 (50.0)
	We rarely prescribe antibiotics for dental purposes	4 (25.0)
	Antibiotic prophylaxis is not recommended	1 (6.3)
	Please provide the platelet count threshold at which a platelet transfusion would be indicated prior to: Dental prophylaxis (anticipate gingival bleeding)	>10,000
>20,000		5 (31.3)
>30,000		2 (12.5)
>40,000		1 (6.3)
>50,000		3 (18.8)
Platelet transfusions are not considered or coordinated in the context of pre-HSCT dental treatment		4 (25.0)
Please provide the platelet count threshold at which a platelet transfusion would be indicated prior to: Restorative dentistry (no or minimal bleeding anticipated)	>10,000	1 (6.3)
	>20,000	5 (31.3)
	>30,000	3 (18.8)
	>40,000	0 (0)
	>50,000	3 (18.8)
	Platelet transfusions are not considered or coordinated in the context of pre-HSCT dental treatment	4 (25.0)
Please provide the platelet count threshold at which a platelet transfusion would be indicated prior to: Dental extraction(s) (significant bleeding anticipated)	>10,000	1 (6.3)
	>20,000	1 (6.3)
	>30,000	2 (12.5)
	>40,000	1 (6.3)
	>50,000	10 (62.5)
	Platelet transfusions are not considered or coordinated in the context of pre-HSCT dental treatment	1 (6.3)
Please provide the absolute neutrophil count threshold at which antibiotic prophylaxis would be indicated prior to: Dental prophylaxis (anticipate gingival bleeding)	<500	9 (56.3)
	<750	0 (0)
	>1,000	5 (31.3)
	<1,000	2 (12.5)
	Not routinely done	0 (0)
Please provide the absolute neutrophil count threshold at which antibiotic prophylaxis would be indicated prior to: Restorative dentistry (no or minimal bleeding anticipated)	<500	10 (62.5)
	<750	0 (0)
	>1,000	3 (18.8)
	<1,000	2 (12.5)
	Not routinely done	1 (6.3)
Please provide the absolute neutrophil count threshold at which antibiotic prophylaxis would be indicated prior to: Dental extraction(s) (significant bleeding anticipated)	<500	8 (50.0)
	<750	1 (6.3)
	>1,000	5 (31.3)
	<1,000	1 (6.3)
	Not routinely done	1 (6.3)
Does your center have a written/documented oral care protocol?	Yes	9 (56.3)
	No	7 (43.8)

(continued on next page)

Table 3 (continued)

Question	Response	Frequency (%)	
In your center, oral hygiene instruction for the patient is provided:	Verbally	9 (56.3)	
	Written	1 (6.3)	
	Both verbally and written	6 (37.5)	
	In which of the following scenarios is traditionally tooth brushing restricted?	Tooth brushing is never restricted	6 (37.5)
		Tooth brushing is restricted with neutropenia	1 (6.3)
	Tooth brushing is restricted with thrombocytopenia	8 (50.0)	
	Tooth brushing is restricted with thrombocytopenia and neutropenia	1 (6.3)	
	Is the use of dental floss or an interdental cleaning aid permitted during HSCT?	No	9 (56.3)
Yes, recommended always without limitations		3 (18.8)	
Yes, except for pediatric patients		1 (6.3)	
Only with acceptable platelet count and no oral mucositis		1 (6.3)	
Only under supervision		1 (6.3)	
Only gentle flossing		1 (6.3)	
Which of the following (if any) mouth rinses are included as part of standard oral care regimen? (you can choose more than one answer as applicable)		Saline 0.9%	6 (37.5)
	Chlorhexidine 0.12%	10 (62.5)	
	Dibasic sodium phosphate (Caphosol®)	4 (25.0)	
	Sodium bicarbonate 1%	11 (68.8)	
	Nystatin 100,000 IU	3 (18.8)	
	Povidone iodine 0.1%	1 (6.3)	
	Hexetidine (Rinsidin®) 0.1%	1 (6.3)	
	Lidocaine solution 2%	1 (6.3)	
What is the protocol for patients with dentures during the course of HSCT?	Patient is allowed to use the denture at all times without limitations	4 (25.1)	
	Patient is allowed to use the denture but with limitations	4 (25.0)	
	Patient is allowed to use the denture except when there is oral mucositis	1 (6.3)	
	No protocol available	8 (50.0)	
	Which of the following are used for dry mouth management during HSCT? (you can choose more than one answer as applicable)	Biotene® products	2 (12.6)
Dibasic sodium phosphate (Caphosol®)		4 (25.0)	
Fluoride rinse		2 (12.5)	
Ice chips		10 (62.5)	
Ice cream		1 (6.3)	
No specific measures are available		4 (25.0)	

HSCT = hematopoietic stem cell transplantation.

Scale (VAS; 37.5%), followed by Numeric Rating Scale (NRS; 25%). Most centers (81.3%) assess oral health status once daily. Patients with pain related to OM were managed with systemic pain medication (12/16; 75%), topical lidocaine (11/16; 68.8%), and/or magic mouthwash (11/16; 68.8%). Of the various pain control regimens, magic mouthwash was more likely to be prescribed by teams that included a dentist ( $p = 0.28$ ).

### Management of acute odontogenic complications

If a patient were to develop acute dental pain during HSCT, 11 centers (68.8%) were likely to request a consultation with other services (e.g., dental team in-house or infectious dis-

eases) to make a joint decision on a case-by-case basis (Table 4). Patients with dental needs during or early after HSCT were more likely to be referred to a dental service within the transplant center (56.3%) when the team included a dentist ( $p = 0.018$ ). Other centers indicated referrals to either a dental office of the patient's choice (25%) or an affiliated dental service (18.8%).

### Discussion

According to WHO, more than 50,000 HSCT procedures are carried out annually worldwide [14]. This special group of patients is typically at risk of myelosuppression as well as

**Table 4** Management of Oral Mucositis and Other Oral Complications.

Question	Response	Frequency (%)	
Please describe any measures routinely utilized for oral mucositis prevention:	Palifermin (Kepivance®)	4 (25.0)	
	Cryotherapy	3 (18.8)	
	Sodium bicarbonate and nystatin	1 (6.3)	
	Magic Mouthwash	1 (6.3)	
	None	7 (43.8)	
Which of the following are used for oral mucositis pain management? (you can choose more than one answer as applicable)	Lidocaine solution 2%	11 (68.8)	
	Magic mouth wash	11 (68.8)	
	Caphosol	2 (12.5)	
	Systemic pain medication and patches (opioid agents such as fentanyl transdermal patch, methadone, and patient-controlled analgesia)	12 (75.0)	
	Sucralfate	2 (12.5)	
	Cryotherapy	1 (6.3)	
	Menthol and phenol containing lozenges	1 (6.3)	
Which of the following are routinely used for oral mucositis assessment/measurement? (check all that apply)	World Health Organization (WHO) Oral Toxicity Scale with or without modifications	7 (43.8)	
	Oral Mucositis Assessment Scale (OMAS)	4 (25.0)	
	The European Organization for Research and Treatment of cancer/Radiation Therapy Oncology Group (EORTC/RTOG)	1 (6.3)	
	National Cancer Institute Common Toxicity criteria Scale (NCI)	3 (18.8)	
	Oral Mucositis Index (OMI)	1 (6.3)	
	Multinational Association of Supportive Care in Cancer (MASCC)	1 (6.3)	
	None	4 (25.1)	
	How frequently is oral mucositis assessed?	3 times daily	1 (6.3)
		2 times daily	1 (6.3)
1 time daily		13 (81.3)	
2–3 times weekly		1 (6.3)	
Which of the following pain scale is used to measure oral mucositis pain?	Visual analogue scale (VAS)	6 (37.5)	
	The Miller scale™ (an 11-point numeric scale)	1 (6.3)	
	The Whaley and Wong Faces Pain Rating Scale	2 (12.5)	
	Numeric Rating Scale (NRS)	4 (25.0)	
	Patient reported response (Yes/No)	1 (6.3)	
How do you manage a patient with acute dental pain during HSCT?	Manage with pain medication/antibiotics until a patient is discharged or otherwise fit for discharge	5 (31.3)	
	Consultation with other services (e.g., dental team in-house or infectious diseases) and make a joint decision on a case-by-case basis	11 (68.8)	
Where do you refer HSCT patients with dental needs during or early after HSCT (within the first 100 days)?	Dental service within your transplant center	9 (56.3)	
	Affiliated dental service	3 (18.8)	
	Patient can visit the dental practice of their choice	4 (25.0)	
Is antifungal therapy included as part of standard infectious disease prophylaxis for HSCT patients? If yes, please specify the agent, dose, and duration.	Yes	16 (100)	
	Voriconazole 200 mg (IV or orally twice a day)	1 (6.3)	
	Fluconazole 200 mg/d until engraftment (if concurrent with active fungal infection then a joint decision with infectious diseases team)	1 (6.3)	
	Fluconazole 400 mg orally once a day starting on Day 3	1 (6.3)	
	Voriconazole 200 mg twice a day for 3–6 months	1 (6.3)	

immunosuppression mediated by hematological disease, cancer therapy, or both [1]. This procedure frequently results in a series of oral complications with variable onset (during or after HSCT) and duration affecting up to 80% of HSCT patients [15]. One way to ensure optimum oral health status in patients undergoing HSCT is through the implementation of an oral care protocol as part of the HSCT process [1]. However, heterogeneity in oral care protocols may exist among different HSCT centers, and this could contribute to variability in outcomes.

The position paper from MASCC/ISSO has highlighted several aspects related to oral care for HSCT patients [1]. The primary, community dentist coordination with the oral medicine specialist and transplant team may have an important role in preparing the patient for transplant as well as management of short- and long-term oral complications. Pre-HSCT dental clearance and continuous follow-up after HSCT will decrease the risk of OM, infections, and dental caries. The position paper emphasized on the importance of multidisciplinary approach for this specific population of patients as a key for HSCT success.

It is increasingly recognized that a multiprofessional HSCT team is essential to improve transplant success and enhance patients' quality of life [16]. The presence of a dentist as part of the transplant team is crucial to establish and maintain the delivery of oral care protocols and manage acute oral complications as indicated. Moreover, the presence of a supporting dental service on-site facilitates patient management prior to, during, and after HSCT. Half of the centers in the current study reported having a dentist as part of the team, with half (4 centers) specifically staffed with Oral Medicine specialists. The size of the facility and the total number of transplant physicians may have an impact on the decision to include Oral Medicine specialists in the team: centers with one to four transplant consultants were less likely to have an Oral Medicine specialist as part of the team compared to centers with > 5 consultants, which accounted for 75% of the participating centers ( $p = 0.07$ ). Other potential roles for Oral Medicine specialists are diagnosis and management of oral mucosal and salivary gland diseases, which are common complications in this population of patients [1,17].

Most centers (14/16; 87.5%) have included dental clearance prior to HSCT in their routine protocol to reduce the risk of oral infections and complications. To complete the needed dental procedures prior to HSCT, a dental service affiliated or based within the transplant facility was available at all but one center (93.8%). This number is higher than the MASCC/ISSO report of 75% (55/74) of participating international members in a survey who stated that they referred patients for dental clearance, in which 25% (13/55) reported to have dental services delivered in-house [18]. The remaining 75% were likely to be referred to community-based dentists, an approach that has been reported to be effective with high levels of compliance [19]. Guidance from an Oral Medicine specialist to community-based dentists who are less familiar with HSCT patients may facilitate this process [17,19]. Although not investigated in this survey, potential barriers to completing pre-HSCT dental clearance include cost/lack of dental insurance, access to care, and time limitations [16].

As bleeding and infection risk must be considered in the context of HSCT patients, we attempted to better understand the transplant centers' views of dental procedures for this population of patients. Antibiotic prophylaxis was one measure reported by 50% of centers to prevent the risk of infection. This approach was more considered prior to invasive dental procedures (e.g., dental prophylaxis, deeper dental restorations close to the pulp and extractions) (7/16; 43.8%) and for patients with central venous catheters (6/16; 37.5%). As of today, no clinical documentation of catheter-related infection has been associated with dental procedures [20]. However, numerous recommendations in the literature endorse antibiotic prophylaxis administration, which continues to be a controversial topic. The risk of bleeding was also raised in this survey as the platelet count threshold set by participating centers (5 centers; 31.3%) was < 20 K/ $\mu$ L prior to dental prophylaxis and restorative dentistry and < 50,000 prior to dental extraction at 10 centers (62.5%). Even with the lack of clear guidelines, these thresholds are compared to what has been reported in the literature as an indication for platelet transfusion prior to invasive dental procedures ranging between 10 and 50 K/ $\mu$ L [21–23].

During HSCT, patients are typically at increased risk for OM with an international reported prevalence of OM ranging between 58% and 80% [24]. It presents clinically as breakdown and ulceration of the mucosal lining causing discomfort, pain, and/or dysphagia, and difficulty in speaking [17,24,25]. Palifermin (Kepivance®), a human keratinocyte growth factor, is one treatment option that has been developed for the prevention of OM and investigated extensively with mixed outcomes [26]. Cost, systemic route of administration, and lack of sufficient supporting evidence are the major factors that preclude the inclusion of palifermin as standard of care for HSCT patients [27–29]. In the current study, seven centers (43.8%) reported no specific measures implemented for OM prevention and 4 (25%) participating centers have implemented palifermin as part of their transplant protocol.

More than half of the centers in the current study ( $n = 9$ ; 56.3%) have implemented an oral care protocol with basic oral hygiene instructions, slightly higher than what has been reported previously [1,10,30]. Owing to increased risk of oral bleeding and/or infection, physicians/HSCT centers may refrain from allowing toothbrushing during the HSCT phase in the setting of severe thrombocytopenia (8/16; 50%) and severe neutropenia as reported by a single center (6.3%). However, six centers (37.5%) were more likely to allow such activity with no restrictions. Even with the MASCC/ISSO recent position paper advising for dental flossing for experienced HSCT patients with needed dexterity, four centers (25.2%) adopted limited use and it was completely restricted at nine centers (56.3%) [1].

Mouth rinses are frequently included as part of an oral hygiene regimen in HSCT patients for antimicrobial effects, lubrication and mechanical washing out of food debris [31,32]. Overall, sodium bicarbonate mouth rinse was the most frequently used among participating centers (11/16; 68%). The second most frequently used mouthwash was chlorhexidine gluconate, which despite not being effective in reducing the risk of OM, has well-established antimicrobial activities (10/16; 62.5%) [10].

Acute dental pain (e.g., dental abscess, fractured restoration), oral bleeding, and infections are potential

complications during HSCT, which pose a continuous challenge for the transplant team [1,33]. Once detected, clinical examination and further investigations are indicated, which could be performed by the transplant team or via consultation with other services in the facility to ensure a proper diagnosis. In this survey, 11 centers (68.8%) were more inclined to request a consultation from an in-house dental team or infectious disease services. This finding highlights the importance of having a dentist as part of the transplant team to ensure proper management and better access. Potential challenges for this approach include the cost and availability of dentists with knowledge and clinical experience to treat patients receiving HSCT [16].

The current study has several limitations. First, even with a response rate of 53.3%, the total starting number of participating centers is still small. Second, the oral care survey was completed by the transplant center director, which may not represent possible protocol variations between providers. In addition, dental-related questions may have not been answered accurately. Direct contact with individual transplant physicians may have provided different responses. Third, based on the nature of the study, no attempt was conducted to survey each HSCT center within the EMBMT group for more specific details on daily practice. Center-specific differences within each region or country may have existed. Lastly, there was potential for response bias, which may have inaccurately inflated certain reported oral care practices.

## Conclusions

Based on the current data, oral care prior to and during HSCT is implemented with a wide range of variability from one center to another, within and among countries in the EMBMT group. The inclusion of oral health specialists as part of the transplant team may help to facilitate the development and implementation of such protocols, and thereby minimize potential sequelae on the oral cavity. The lack of established universal protocols within EMBMT may compromise the level of oral health management delivered to this group of patients. Therefore, further efforts to disseminate, reinforce, and assess the current oral care guidelines under the umbrella of the EMBMT are warranted.

## Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available owing to privacy or ethical restrictions.

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We declare no funding was provided for this study.

## Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with

the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Informed consent

Informed consent was obtained from all individual participants included in the study.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- [1] Elad S, Raber-Durlacher JE, Brennan MT, Saunders DP, Mank AP, Zadik Y, et al. Basic oral care for hematology–oncology patients and hematopoietic stem cell transplantation recipients: a position paper from the joint task force of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) and the European Society for Blood and Marrow Transplantation (EBMT). *Support Care Cancer* 2015;23:223–36.
- [2] Boguslawska-Kapala A, Halaburda K, Rusyan E, Golabek H, Struzycka I. Oral health of adult patients undergoing hematopoietic cell transplantation Pre-transplant assessment and care. *Ann Hematol* 2017;96:1135–45.
- [3] Raber-Durlacher JE, Laheij AM, Epstein JB, Epstein M, Geertjigs GM, Wolffe GN, et al. Periodontal status and bacteremia with oral viridans streptococci and coagulase negative staphylococci in allogeneic hematopoietic stem cell transplantation recipients: a prospective observational study. *Support Care Cancer* 2013;21:1621–7.
- [4] Mawardi H, Glotzbecker B, Richardson P, Woo SB. Hematopoietic cell transplantation in patients with medication-related osteonecrosis of the jaws. *Biol Blood Marrow Transplant* 2016;22:344–8.
- [5] Graber CJ, de Almeida KN, Atkinson JC, Javaheri D, Fukuda CD, Gill VJ, et al. Dental health and viridans streptococcal bacteremia in allogeneic hematopoietic stem cell transplant recipients. *Bone Marrow Transplant* 2001;27:537–42.
- [6] Mikulska M, Del Bono V, Prinapori R, Boni L, Raiola AM, Gualandi F, et al. Risk factors for enterococcal bacteremia in allogeneic hematopoietic stem cell transplant recipients. *Transpl Infect Dis* 2010;12:505–12.
- [7] Gabriel DA, Shea T, Olajida O, Serody JS, Comeau T. The effect of oral mucositis on morbidity and mortality in bone marrow transplant. *Semin Oncol* 2003;30:76–83.
- [8] Elad S. The MASCC/ISOO mucositis guidelines 2019: the second set of articles and future directions. *Support Care Cancer* 2020;28:2445–7.
- [9] Elad S. The MASCC/ISOO Mucositis Guidelines 2019 Update: introduction to the first set of articles. *Support Care Cancer* 2019;27:3929–31.
- [10] Hong CHL, Gueiros LA, Fulton JS, Cheng KKF, Kandwal A, Galiti D, et al. Systematic review of basic oral care for the management of oral mucositis in cancer patients and clinical practice guidelines. *Support Care Cancer* 2019;27:3949–67.
- [11] EMBMT. Eastern Mediterranean Blood and Marrow Transplantation. [www.embmt.org](http://www.embmt.org).
- [12] World Health Organization. Quantifying environmental health impacts: country groupings available at: <http://www.who.int/>

- quantifying\_ehimpacts/global/ebdcountgroup/en/. Accessed Dec 18, 2020.
- [13] Krzanowski WJ, Kline P. Cross-validation for choosing the number of important components in principal component analysis. *Multivariate Behav Res* 1995;30:149–65.
- [14] World Health Organization. Haematopoietic stem cell transplantation HSCtx. Transplantation 2020. <https://doi.org/10.1177/1049909120971566>.
- [15] Epstein JB, Raber-Durlacher JE, Wilkins A, Chavarria MG, Myint H. Advances in hematologic stem cell transplant: an update for oral health care providers. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107:301–12.
- [16] Nuernberg MA, Nabhan SK, Bonfim CM, Funke VA, Torres-Pereira CC. Access to oral care before hematopoietic stem cell transplantation: understand to improve. *Support Care Cancer* 2016;24:3307–13.
- [17] Bos-den Braber J, Potting CM, Bronkhorst EM, Huysmans MC, Blijlevens NM. Oral complaints and dental care of haematopoietic stem cell transplant patients: a qualitative survey of patients and their dentists. *Support Care Cancer* 2015;23:13–9.
- [18] Barker GJ, Epstein JB, Williams KB, Gorsky M, Raber-Durlacher JE. Current practice and knowledge of oral care for cancer patients: a survey of supportive health care providers. *Support Care Cancer* 2005;13:32–41.
- [19] Waring E, Mawardi H, Woo SB, Treister N, Margalit DN, Frustino J, et al. Evaluation of a community-based dental screening program prior to radiotherapy for head and neck cancer: a single-center experience. *Support Care Cancer* 2019;27:3331–6.
- [20] Hong CH, Allred R, Napenas JJ, Brennan MT, Baddour LM, Lockhart PB. Antibiotic prophylaxis for dental procedures to prevent indwelling venous catheter-related infections. *Am J Med* 2010;123:1128–33.
- [21] Kaufman RM, Djulbegovic B, Gernsheimer T, Kleinman S, Tinmouth AT, Capocelli KE, et al. Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med* 2015;162:205–13.
- [22] Slichter SJ. Evidence-based platelet transfusion guidelines. *Hematology Am Soc Hematol Educ Program* 2007:172–8.
- [23] Karasneh J, Christoforou J, Walker JS, Manfredi M, Dave B, Diz Dios P, et al. World Workshop on Oral Medicine VII: platelet count and platelet transfusion for invasive dental procedures in thrombocytopenic patients: a systematic review. *Oral Dis* 2019;25:174–81.
- [24] Mercadante S, Aielli F, Adile C, Ferrera P, Valle A, Fusco F, et al. Prevalence of oral mucositis, dry mouth, and dysphagia in advanced cancer patients. *Support Care Cancer* 2015;23:3249–55.
- [25] Staudenmaier T, Cenzler I, Crispin A, Ostermann H, Berger K. Burden of oral mucositis in stem cell transplant patients-the patients' perspective. *Support Care Cancer* 2018;26:1577–84.
- [26] Langner S, Staber P, Schub N, Gramatzki M, Grothe W, Behre G, et al. Palifermin reduces incidence and severity of oral mucositis in allogeneic stem-cell transplant recipients. *Bone Marrow Transplant* 2008;42:275–9.
- [27] Schmidt V, Niederwieser D, Schenk T, Behre G, Klink A, Pfrepper C, et al. Efficacy and safety of keratinocyte growth factor (palifermin) for prevention of oral mucositis in TBI-based allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant* 2018;53:1188–92.
- [28] Mozaffari HR, Payandeh M, Ramezani M, Sadeghi M, Mahmoudiahmadabadi M, Sharifi R. Efficacy of palifermin on oral mucositis and acute GVHD after hematopoietic stem cell transplantation (HSCT) in hematology malignancy patients: a meta-analysis of trials. *Contemp Oncol (Pozn)* 2017;21:299–305.
- [29] Spielberger R, Stiff P, Bensinger W, Gentile T, Weisdorf D, Kewalramani T, et al. Palifermin for oral mucositis after intensive therapy for hematologic cancers. *N Engl J Med* 2004;351:2590–8.
- [30] Bystricka E, Ghelase R, Gorican IK, Mazur E, Vokurka S, East Forum ENG. Oral cavity care in patients after high-dose chemotherapy and stem cell transplantation: the East Forum EBMT Nurses Group standard of care. *Bone Marrow Transplant* 2012;47:149–50.
- [31] Rankin KV, Epstein J, Hubber MA, Peterson DE, Plemons JM, Redding SS, et al. Oral health in cancer therapy. *Today's FDA* 2009;21(37):9–45.
- [32] Axelsson P, Lindhe J. Efficacy of mouthrinses in inhibiting dental plaque and gingivitis in man. *J Clin Periodontol* 1987;14:205–12.
- [33] Guideline on dental management of pediatric patients receiving chemotherapy, hematopoietic cell transplantation, and/or radiation therapy. *Pediatr Dent* 2016;38:334–42.