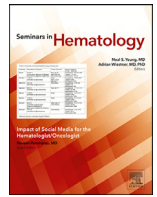




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Palliative care needs of patients with hematologic malignancies and family caregivers and challenges of palliative care provision in Asia: A review of evidence

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ABSTRACT

Patients with hematologic malignancies often experience fatigue, lack of vitality, and energy, and high psychological distress. High levels of unmet care needs of patients with hematologic malignancies in Asia were identified. This review provides an overview of current evidence on the experiences and palliative care needs of patients with hematologic malignancies and their families and the barriers and challenges of integrating palliative care into hematology care in Asia. Patients with hematologic malignancies who received palliative care could benefit from less aggressive end-of-life treatments. However, the uncertain and variable nature of the prognosis and illness trajectories of hematologic malignancies increase the difficulties of integrating palliative care into hematology care. Patients and their families are often referred to palliative care services late, which leaves a short window for palliative care teams to provide holistic needs assessment and person-centered care for those who need it. In addition, cultural differences in medical decision-making patterns and complex social norms and interactions among patients, families, and healthcare staff make it even more challenging to initiate palliative care conversations in Asia. Future research should focus on the development and evaluation of culturally appropriate palliative care for patients with hematologic malignancies and their family caregivers in Asia, given that the low rate of service intake and poor public awareness of the important role of palliative care in disease trajectories were reported. The socio-cultural context surrounding individuals should be taken into consideration to ensure the provision of person-centered care for this group of patients. Digital health could be one of the possible solutions forward to address local needs and challenges.

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Introduction

Hematologic malignancies are a heterogeneous group of cancers that comprise diverse subgroups of neoplasms. The 5th edition of the WHO classification of Hemato-lymphoid tumors provides a framework for the diagnosis of over 200 different malignancies [1,2] Worldwide, patients with hematologic malignancies, most of-

ten, undergo more aggressive treatments than patients with solid tumors from diagnosis to the end of life [3,4]. Diagnosis and treatment can affect patients with hematologic malignancies and their families physically, emotionally, logistically, and financially [5].

The medical technology and treatment can lead to patients facing symptom burdens and poor quality of life, especially those diagnosed with leukemia and multiple myeloma [6,7]. Thus, palliative care is necessary to improve the quality of life among people with haematological malignancies and can be integrated into an illness trajectory [8,9].

Evidence shows patients with hematological malignancies are more likely to be referred later to a palliative care team than patients with advanced solid tumors [10,11]. This may be related

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to the unpredictable hematologic malignancies disease course and prognosis which are more difficult to identify than in patients with a solid tumor [4,12]. Hematologists reported difficulties in initiating discussion with their patients about end-of-life wishes especially when patients' prognosis is uncertain at the time of recurrence [4,13,14]. Additionally, the physicians have misperceptions about the nature of the disease, resulting in late referral to palliative care consultation services [7,15,16]. After treatment, the patients' physical decline is stable and predictable until the abrupt symptoms occur in a short period before death [17]. These patients often die in the hospital [18] where patients and families may have a limited chance to meet palliative care specialists a few days before death because aggressive treatment such as chemotherapy is received which might have relatively good response to hematological cancer [4,19,20]. Recent studies recommended that palliative care should be initiated and integrated early into the care of patients with hematological malignancies and their families, especially goal of care and advance care planning conversations [20,21]. However, there are some challenges and barriers restricting the access to palliative care and end of life care among these group of patients [17,22].

The sociocultural context could shape Asian people's attitudes towards and practices of palliative care and therefore, enable the in-depth understanding of the needs and challenges related to palliative care for patients with hematologic malignancies [23]. In the context of Asia, cultural biases are identified as main barriers in the achievement of high-quality care at the end of life [24]. A literature review is needed to identify relevant evidence on the experience and palliative care needs of patients living with hematologic malignancies in Asia. This review would provide the health-care providers with an overview of the current situation in this area, which could inform the provision of palliative care for people with hematologic malignancies and future research.

Palliative care needs of patients with hematologic malignancies

Palliative care is a holistic care and multidisciplinary approach which aims to improve the quality of life of the patients, and their families and caregivers. It involves prevention, early identification, comprehensive assessment, and management of physical issues, including pain and other distressing symptoms, psychological distress, spiritual distress, and social needs [25]. Palliative care is considered as a basic human right and several international cancer organizations and societies have supported early integration of palliative care alongside cancer care [26]. However, evidence supporting this model have found primarily on solid tumors and from high income countries. The challenge for early applying palliative care to other health conditions and settings are related to the patient population, workforce shortages and lack of public policy in palliative care [27]. Knowledge needed to fully integrate palliative care and support patients and family needs since diagnosis to the end of life and across all settings (inpatient, outpatient, and home-based care), and clear communication between clinicians and patients/families are crucial to the provision of person-centred palliative care [27]. Public health strategies and sustainable policies should be integrated into health care plan as well as comprehensive training programmes for healthcare providers across all clinical settings and communities to ensure that patients can receive the right care, at the right place, and at the right time [26,27].

Palliative care needs for patients with hematologic malignancies are similar or even higher than the solid tumor counterparts. However, symptoms such as pain, dyspnea, nausea, anorexia, tiredness, and drowsy burden were identified as high among hematologic malignancies patients who were reported to have worse end-of-life care experiences including more emergency room and intensive unit visits, longer hospital stays, and be-

ing more likely to receive aggressive care [28,29]. Experiencing hematologic malignancies was considered a stressful journey from the time of diagnosis until the last days of life [11]. Patients with hematologic malignancies frequently get aggressive disease-focused therapies till the end of their lives, which is accompanied by numerous visits to the emergency department (ED), intensive care unit (ICU) admission, and hospital deaths. The rapid decline of the patient's condition and uncertain prediction for the time of deterioration impact on a referral time to palliative care. Patients and their families are often referred to palliative care services late [11]. Maqsood et al. examine the characteristics and outcomes of patients with hematologic malignancies admitted to the ICU in 1 cancer center in Pakistan [30]. They found that the main cause of admission to the ICU was infection-related conditions. Most patients received aggressive treatments, such as invasive ventilation, vasopressor support, and other supportive care. Around 50% of patients died in ICU settings while one-fourth were either alive or dead at least 1 year after ICU admission. Similarly, in Hong Kong, half of the elderly patients with acute myeloid leukemia spent their last 30 days of life in hospitals. These elder patients died of infection-related conditions either in the acute ward and hematology units or the palliative unit [31].

Hematologic malignancies demonstrate more heterogeneity in disease trajectories. For example, certain types of hematologic malignancies are considered indolent and manageable with relatively low-intensity treatments, but others might be seen as aggressive and need intensive and high doses of toxic therapies such as chemotherapy or stem cell transplantation. Besides, patients with hematologic malignancies are often more responsive to chemotherapy than solid tumor patients with novel therapies available, therefore, standard prognosis and functional assessment developed with solid tumor populations do not work well for patients with hematologic malignancies. Blood transfusion is often beneficial to patients with hematologic malignancies for their symptom management (eg, anemia and thrombocytopenia) and redress burdens such as fatigue and dyspnea [32,33]. This can explain why hematologists often treat patients until their end of life as good outcomes could be potentially achieved.

A retrospective review by Cheng et al. on analysis of medical care in the last week of patients with hematologic malignancies in Hong Kong revealed that more than 85% of these patients received blood sampling and antibiotics, and more than half had blood transfusion [34]. Palliative care is therefore very challenging to be integrated into routine hematological care. The uncertain and variable nature of the prognosis and illness trajectories of hematologic malignancies increase the difficulties of palliative care integration with the primary hematology team. In Japan, Palliative Prognostic Index and prognostic model have been successfully validated to distinguish hematologic malignancies patients with different survival times [35], which could help to facilitate the timely palliative care referral for those patients.

Aggressive hematologic malignancies need inpatient and intensive treatment and symptom control, home palliative care is not possible for this group of patients as certain treatments cannot be performed at home (ie, blood transfusion, chemotherapy, and infection control). For those with indolent hematologic malignancies, they can receive outpatient clinics follow-ups and manage symptoms at home or care facilities. But their disease prognosis is uncertain [19], some might last for many years and be considered as "a war of attrition" [26]. Evidence showed that most patients with hematologic malignancies would need to receive inpatient palliative care services and die in the hospitals [36]. Different disease trajectories, disease-related symptoms, and risks of mortality among patients with hematologic malignancies would influence their quality of life and use of low-value and aggressive

care, which could be addressed by early palliative care integration. A population-based study analyzing Taiwan's Longitudinal Health Insurance Database reported patients with hematologic malignancies who had received palliative care could benefit from less aggressive end of life care in the final month of life. However, only 8.6% of Taiwanese patients with hematologic malignancies received palliative care [36].

Psychological support is also another area of unmet needs which requires attention [33]. Despite experiencing such a high level of distress, patients with hematologic malignancies tend to have less frequent use of palliative care services so as their family caregivers [22,26,33]. Hospitalized patients with hematologic malignancies received insufficient support from health care providers [37]. These findings were consistent with a systematic review in which high levels of unmet supportive care needs of patients with hematologic malignancies were identified in the information domain, followed by emotional, physical, practical, and family life/relational domains [38].

Challenges of integrating palliative care into hematological care in Asia

In Asian countries, most are family centric so during a disease and its treatments, family caregivers are crucial to the patient care and considered to be personal resources of the patients [39]. They help patients to cope with cancer, manage and monitor symptoms, and provide psycho-spiritual support to their loved ones who have cancer. A previous study found that good family support can reduce anxiety of death in Chinese patients with cancer [40]. However, caregiving demands of patients with hematologic malignancies created pressures on family caregivers who need support from healthcare providers. Spiritual distress, caregiving constraints, and caregiver burden as well as economic constraints have been reported in some Asian countries [41–43]. The studies which had been done in Asia found that psycho-spiritual distress among family members or bereaved families stemmed from decisional conflicts. Conflicts in decision-making on issues related to treatments and care during the course of disease [41] and places of death [44] lead to regret experience among bereaved families. Furthermore, caregivers of adolescents, and young adults with cancer had moderate to serve anxiety and depression [45]. Several studies in Asia have reported the unmet needs of caregivers of patients with cancer. The most common unmet needs were related to information about cancer and the process of its treatment and care, psycho-emotional support, and financial/economic concerns [42,45–49].

Asian families often protect their loved ones from knowing about the bad news of life-limited illness [50]. Complex social norms and interaction among patients, families, and healthcare staff make it more challenging to initiate palliative care conversations, resulting in often late/no referral for these patients and their families before death in Asia [51]. Hematologic malignancy specialists often express discomfort discussing death or hospice referral as well as indicating the patient's failure regarding treatment goal [15]. The study in Singapore found that Asian physicians in ICU tend to be more aggressive in their treatment compared with their Western counterparts [52]. Physicians are reluctant to discuss life-sustaining treatments and end-of-life care because there is no strong culture of making advance directive in Asia, and death and dying is perceived as a taboo subject in many Asian cultures. Meanwhile, patients and family members also avoid speaking openly about death [50], which might impact on initiating discussions about patients' prognoses among patients, families, and physicians. Moreover, this situation might prevent healthcare and others to know about patients' preferences [53]. Consequently,

the neglect of the patients' wishes, together with traditional Asian values may lead to futile treatment even at the end of life.

As a family-oriented culture, decisions regarding end-of-life care plans usually transfer to senior family members and/or medical doctors, as trustful persons [54,55]. The cultural value of death conversation as bad luck remains in several countries in Asia [56]. End-of-life discussion is rarely initiated as family members and healthcare providers feel reluctant to talk about death. Family caregivers had inadequate end-of-life discussions with the patients [56]. Therefore, decision making regarding end-of-life care is perceived as burdensome for family members [57]. It is also interesting to note that financial burden has been highlighted as unmet needs among patients with cancer, particularly hematologic malignancies in Asian countries [41,43,47]. Financial problems intensified psychological problems among caregivers of patients with hematologic malignancies [41].

The recent studies have confirmed that the biggest obstacle was the healthcare professional inadequate capabilities, which was partly the result of poor palliative care training [58,59]. The study about palliative care in South-East Asia reported that the difficulties in improving palliative care, regardless of the region's degree of development, include the problem of popular conceptions of death and dying, which have complicated the discipline's development [60]. Therefore, relevant education and training programmes are still needed to promote palliative care among healthcare professionals in Asia.

What are the proposed solutions?

Given the great challenges in palliative care provision among people diagnosed with hematologic malignancies in Asia, solutions and opportunities are suggested to mitigate the obstacles for better quality care.

Culturally appropriate and tailored care model

Given the different pathology, illness trajectories, and care needs between solid tumor and hematologic malignancies, care plan different from oncological approaches should be revisited [28,33]. More empirical evidence on culturally appropriate care for the Asian population is needed as the low rate of service intake and poor public awareness of the important role of palliative care in the hematologic malignancies disease trajectories were reported [36]. Meanwhile, the diverse demographic characteristics of Asian ethnicities, healthcare systems, local jurisdictions, and social norms would shape palliative care for hematologic malignancies very differently in terms of the infrastructures of care provision, the timing for care initiation, intervention components and procedures, manpower and logistics, and evaluation. Successful implementation relies on appropriate cultural adaptation based on local perceptions and acceptance of palliative care [17].

Early integration of palliative care into routine care

Early integration of palliative care into routine care for patients with hematologic malignancies upon hospital admission or diagnosis of the advanced staging of hematologic malignancies is urgently needed [22,26]. The primary hematology team and palliative care team should collaborate for better symptom management and psychosocial support. Advance care planning is encouraged for this group of patients and families to improve goal-concordant care even though evidence reported rare occurrences in clinical practice [61].

Redressing the misconception for early palliative care referral

The concept adjustment would facilitate service referral at the early disease stage as well as reduce the fear of patients associating hematologic malignancies with death and end-of-life care issues [62]. Continuous evidence-based education for both the public (goal of hematologic malignancies and service provision) and healthcare providers (hematology-specific knowledge for palliative care team and palliative care-specific knowledge for hematology team) is warranted [15].

Role of complementary and alternative medicine in mainstream palliative care provision

Although the use of complementary and alternative medicine (ie, massage, acupuncture, acupressure, tai chi, and herbal medicine) is evident for significant alleviation in cancer patients' symptoms (eg, pain, nausea and vomiting, fatigue, anxiety, and breathlessness) [63], the integration of complementary and alternative medicine into palliative care for hematology cancer patients is not a common practice (only 2/61 included studies in Keene et al.'s systematic review in 2019; one study is from Italy, another is from Malaysia) [64]. This has been speculated to be a result of cultural attitude to endorse and access to the conventional and complementary and alternative medicine therapies. For example, in Malaysia, majority of Malaysian hematological cancer patients reported complementary and alternative medicine was effective, however, 60% of them confessed not informing their physicians regarding its usage [65]. In contrast, Traditional Chinese Medicine is covered by National Health Insurance in Taiwan improving its uptake and acceptance in the society [66]. Other concerns for complementary and alternative medicine would be the uncertainty and risk of drug-drug interaction between herbal medicine/Chinese medicine and hematological treatment (ie, chemotherapy). Additionally, physical measures (ie, massage, acupuncture, or acupressure) might cause harm to patients with low blood cell count, for example thrombocytopenia or neutropenia after chemotherapy. Therefore, complementary and alternative medicine is rarely deployed in routine hematology palliative care provision. Cautiously integrating complementary and alternative medicine into palliative care provision is warranted as high-quality evidence is lacking to inform practice. In addition, it is important that the physicians play an active role in seeking information from patients and monitoring possible drug-herbal-physical measure interactions.

Digital health innovations for continuous care provision

The development of palliative care among Asian countries varies, for example some do not equip palliative care specialists for advanced symptom management, and others even have not yet developed palliative care programmes nationwide with limited access to pain control medication [67,68]. The provision of digital health (eg, video and telephone call conversations, mobile applications, smart watch, and remote monitoring devices) depends on the local regulation and healthcare system. Such services could support primary caregivers not only in addressing patients' physical needs, but also alleviating caregivers' psychosocial distress (eg, anxiety, depression, uncertainty) which were reported to be significant burdens [69]. By doing so, home care-based patients (ie, people with indolent hematologic malignancies and bone marrow transplantation) could reduce suffering from the frequent transition from home to the hospital, while patients with aggressive hematologic malignancies could receive timely care by a multidisciplinary team when they were hospitalized.

Financial support and resource allocation

Although novel remedies and medications are available reflecting the rapid development of hematologic malignancies treatments, the expenditure of such treatments is pricey. Financial concerns and appropriate needs-based resource allocation for patients and their family caregivers is vital and should be taken into account when tailoring care plan for this population.

High quality evidence to inform future practice and training

High quality studies to inform clinical practice and training is lacking in Asia. For example, in Zeng et al.'s systematic review in 2018, only 17 studies incorporating complementary and alternative medicine in the palliative or hospice care settings were identified. Of these, none was conducted in Asia [63]. Another systematic review on assessing the use of complementary and alternative medicine for end-of-life patient symptom management corroborates that very few high quality studies were included [70]. Evidence based on Asian cultural and contextual characteristics for hematology patients is required, along with more investment in research and training in this area for both the public and healthcare professionals.

Conclusions

Common challenges have been identified to integrate palliative care into hematology practice in Asia. Exploring and evaluating the culturally appropriate care models such as the use of digital health and complementary and alternative medicine to manage complex physical and psychological symptoms and address unmet needs of patients with hematological malignancies and families has a long way to go. The socio-cultural context surrounding individuals influences the formation of care preferences, communication patterns, interpretation of different meanings of suffering, and decision-making processes about care, therefore, should be taken into consideration to ensure the provision of person-centered care for this group of patients. Improving palliative care for patients with hematological malignancies and their families with cultural perspectives need to be further investigated.

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.

CRedit authorship contribution statement

Yupawadee Kantabanlang: Conceptualization, Methodology, Writing – original draft. **Cheng-Pei Lin:** Writing – original draft. **Kittikorn Nilmanat:** Writing – original draft. **Ping Guo:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

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