

# ORIGINAL ARTICLE

WILEY

## Palliative care service in patients with childhood cancer from a tertiary pediatric oncology center

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Received: 20 July, 2018

Accepted: 5 September, 2018

### ABSTRACT

**Importance:** Pediatric palliative care (PPC) has gained great attention in western countries, however data on Hong Kong children receiving PPC are limited. There are gaps in knowledge about the PPC needs in local children with cancer.

**Objective:** To assess the current situation of PPC service of Hong Kong children with cancer.

**Methods:** We performed a 10-year retrospective review in a tertiary pediatric oncology unit and studied the referral pattern, clinical characteristics and services provided.

**Results:** Totally 117 children were referred to PPC Team which constituted 65% deceased children within the study period. The commonest diagnoses were central nervous system tumour (32.5%), leukaemia (25.6%) and neuroblastoma (9.4%). Ninety-one percent of children were referred after the last relapse or stopping curative treatment. The median time of referral to death was 77 days [interquartile range (IQR): 35, 182]. The median number of hospital admission after referral was 2 (IQR: 1, 5), with a median of 27 days total hospital stay (IQR: 10, 60). The reasons for admission were palliative chemotherapy (16.1%), pain control (12.1%) and platelet transfusion (11.2%). For the death episode, the median duration of hospital stay was 15 days (IQR: 2, 46). Most patients received oxygen (82.0%), intravenous fluid (81.2%) and intravenous analgesic (52.1%). A total of 111 (94.9%) children died in hospital, 15 had been admitted into intensive care unit (ICU) but only 5 (4.5%) died in ICU.

**Interpretation:** Pain control and platelet transfusion were common reasons of readmission. Death in ICU and at home was uncommon in Hong Kong situation.

### KEYWORDS

Cancer, Children, Palliative care, Chinese

DOI: 10.1002/ped4.12094

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## INTRODUCTION

Palliative medicine (PM) has been expanding globally as the need of quality end-of-life care is increasingly recognized. Cicely Saunders established the St Christopher's Hospice in 1967 which is widely regarded as the founder of modern adult PM. In the late 1970s, there was growing attention on PM for children.<sup>1</sup> The first children's hospice, Helen House, was opened in the United Kingdom in 1982.<sup>2</sup> Due to the complex situation in pediatric palliative care (PPC), it remains a relatively underdeveloped discipline. The small number of children dying each year limits any one individual's exposure to PPC, making development and maintenance of expertise difficult. PPC encompasses care for children with life limiting conditions that not only include cancer but other chronic progressive illnesses such as genetic disorders, neuromuscular and metabolic conditions that are rare and with complicated illness trajectories. PPC also caters to the needs of diverse age groups of children, ranging from neonates to adolescents, whose physical, cognitive and psychological development vary greatly. Their limited ability to understand illness and the involvement of parents in care planning or decision making add to the challenges of palliative care specialists to provide family-centered care.

With the advance of medical care, the overall prevalence of children living with life-threatening or life-limiting conditions is increasing over the years. It is estimated that 1 in 1 000 children with life-threatening conditions require PPC. American Academy of Pediatrics and World Health Organization (WHO) have called attention to the needs of these terminally ill children and the formulation of guidelines for providing integral palliative care.<sup>3,4</sup> Many western countries have also published their experience in providing pediatric palliative care.<sup>5,6</sup> Existing Caucasian models, however, may not be fully implemented in Chinese population taking into account the cultural differences between the East and the West. This cultural factor bears implications on health seeking behaviour, perception of death as well as decisions on end-of-life care and place of death. With paucity of data on PPC in Chinese, we aim to study the clinical characteristics, timing and pattern of referral, type of palliative services provided for pediatric cancer patients in Hong Kong. It serves as a guide and platform for future planning of pediatric palliative care in Chinese patients.

## METHODS

The retrospective review was conducted at the Lady Pao Children's Cancer Center (CCC) of Prince of Wales Hospital, a tertiary referral center of pediatric oncology in Hong Kong that manages around 70 newly diagnosed Pediatric cancer patients each year. A master list of patients referred to the palliative care team at CCC from January 2000 was generated. Their medical charts and electronic

records on the public hospital computer data system were retrieved and reviewed to collect data on demographics, time of referral, utilization of hospital-based palliative care service and the death episode. Data on patients who died of cancer at CCC during the same period of time but were not referred to the palliative care team were also obtained from the computer data system to determine the referral rate and its trend. A descriptive analysis was performed on all data. The study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee (CRE Ref. No. 2013.109). The reporting guidelines of STROBE Statement was implemented in preparing the manuscript.

## RESULTS

During the 10 years study, 695 pediatric cancer patients were diagnosed and managed at CCC, and 180 patients died. A total of 117 pediatric cancer patients were referred to palliative care at CCC over a 10-year-period. The clinical characteristics of these children were summarized in Table 1. The three commonest diagnoses were central nervous system (CNS) tumour (32.5%), leukaemia (25.6%) and neuroblastoma (9.4%).

**TABLE 1** Clinical characteristics of 117 pediatric cancer patients referred to palliative care services

Characteristics	Description
Gender	M = 77 F = 40
Mean age at primary diagnosis	8.2 years (range 0–17.5 years)
Primary diagnosis	CNS tumour 38 (Brain stem glioma 7; GBM 7; Astrocytoma 5; Medulloblastoma 4; others 15) Leukaemia 30 (ALL 17; AML 9; CML 1; JMML 3) Neuroblastoma 11 Osteosarcoma 9 Rhabdomyosarcoma 7 Liver tumour 6 (Hepatoblastoma 3; Hepatoceular carcinoma 3) Lymphoma 4 (Burkitt's 1; B-cell 1; T-cell 2) Soft tissue sarcoma 3 (Desmoplastic small round cell tumor 1; Alveolar soft part sarcoma 1; High grade sarcoma 1) Germ Cell tumour 3 Ewing-PNET 3 Others 3
Anti-cancer treatment	Surgery 66; Chemotherapy 103; Radiotherapy 74

M, male; F, female; ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; CML, chronic myeloid leukaemia; CNS, central nervous system; GBM, glioblastoma multiforme; JMML, juvenile myelomonocytic leukaemia; PNET, peripheral primitive neuroectodermal tumor.

### Timing and pattern of referral

The median time of referral to palliative care after diagnosis for all children was 498 days [interquartile range (IQR): 189, 962]. For the three most common conditions

including CNS tumour, leukaemia and neuroblastoma, the median time of referral after diagnosis was 257 days (IQR: 40, 770); 748 days (IQR: 557, 1361) and 751 days (IQR: 394, 1137) respectively. Ninety-one percent of children ( $n = 107$ ) were referred after the last relapse or after stopping curative treatment. Only 9% ( $n = 10$ ) received palliative care early in the course of their illness. The median time of referral after last relapse or stopping curative treatment was 7 days (IQR: 2, 19), and the median time of referral to death was 77 days (IQR: 35, 182).

Overall 65% of oncology patients who died in our unit within this 10-year study period were referred to palliative care. The 5-year referral rate for all types of cancer increased from first 5-year period to second 5-year period except for those suffering from brain tumour and osteosarcoma. Especially of note is that the 5-year referral rate of patients with lymphoma, neuroblastoma and rhabdomyosarcoma increased respectively from 50%, 75% and 80% in first 5-year to 100% in second 5-year. The overall 5-year referral rate in the two period, however, remained static over the past 10 years (65.3% vs 64.6%).

### Hospital-based palliative care service and end-of-life symptoms

The median number of hospital admission for all patients after referral to palliative care was 2 (IQR: 1, 5), with a median total duration of hospital stay of 27 days (IQR: 10, 60). Forty-one percent of children were only admitted for the final death episode after palliative care referral. However 22% had five or more admissions (including the death episode). While 95% of hospitalization ( $n = 591$ ) were direct admissions arranged by oncologists or palliative nurse, 4.8% ( $n = 30$ ) were emergency admissions to CCC or other regional hospitals through the Emergency Department (ED). Patients with CNS tumour had more admissions via ED or admissions to acute care wards in other regional hospitals, accounting for one-third of all emergency admissions. The most common symptoms leading to emergency admission were dyspnoea, decreased general condition and abdominal pain (Table 2). Day admissions for ambulatory care included performing investigations, providing cancer-directed palliative treatment including chemotherapy, radiotherapy or minor surgery. In-patient admission was arranged for specific symptom control, supportive treatment with blood product transfusion, management of fever and other conditions (Table 3). Overall, palliative chemotherapy accounted for most of the day admissions (16.1%). For in-patient care, however, specific symptom control accounted for the majority (37.1%), which was followed by blood product transfusion (19.8%). The common symptoms leading to in-patient care were pain (12.1%), dyspnoea (4.0%), nausea and vomiting (4.0%), and fatigue (4.0%). Despite under palliative care, there were 5.6% ( $n = 41$ ) of admission episodes involved aggressive investigations

such as bone marrow examination, computed tomography (CT) scan and magnetic resonance imaging (MRI). Six patients (5.1%) received treatment with curative intent which accounted for 3.8% of all admissions.

**TABLE 2** Symptoms for emergency admission to Children's Cancer Center or other regional hospitals ( $n = 30$ )

Symptoms	Number of cases, $n$ (%)
Dyspnoea	11 (36.7)
Decreased general condition	8 (26.7)
Abdominal pain	4 (13.3)
Loss of consciousness	3 (10.0)
Convulsion	3 (10.0)
Confusion	2 (6.7)
Nausea and vomiting	2 (6.7)
Cyanosis	1 (3.3)
Headache	1 (3.3)
Poor appetite	1 (3.3)

**TABLE 3** Reasons for direct admission to Children's Cancer Center ( $n = 730$ )

Reasons for direct admission	Number of cases, $n$ (%)
Day admissions for ambulatory care	172 (23.5)
Palliative chemotherapy	118 (16.1)
Palliative radiotherapy	11 (1.5)
Palliative surgery	2 (0.3)
Investigations	41 (5.6)
In-patient care	558 (76.5)
Specific symptom control	271 (37.1)
Pain	88 (12.1)
Others	183 (25.0)
Nausea and vomiting	29 (4.0)
Fatigue	29 (4.0)
Dyspnoea	29 (4.0)
Neurological deterioration	13 (1.8)
Poor appetite	8 (1.1)
Convulsion	6 (0.8)
Urinary retention	6 (0.8)
Abdominal distension	6 (0.8)
Blood product transfusion	145 (19.8)
Platelet	82 (11.2)
Packed cell	63 (8.6)
Fever	78 (10.7)
Others	64 (8.8)
Treatment with curative intent	28 (3.8)

The median number of scheduled out-patient clinic visit after referral to palliative care was 2 (IQR: 0, 9). Thirty percent of children had one or more unscheduled visits when they developed symptoms requiring medical attention. The median number of unscheduled clinic visit was 2 (IQR: 1, 32). The most common uncontrolled symptoms leading to unscheduled visits were bleeding tendency (29.5%), pain (21.5%), anaemic symptoms (14.3%), fever (10.0%) and nausea and vomiting (4.4%) (Table 4).

**TABLE 4** Symptoms leading to unscheduled out-patient clinic visits ( $n = 251$ )

Symptoms	Number of cases, $n$ (%)
Bleeding tendency	74 (29.5)
Pain	58 (21.5)
Anaemic symptom	36 (14.3)
Fever	26 (10.0)
Others	57 (24.3)
Nausea and vomiting	11 (4.4)
Neurological deterioration	5 (2.0)
Coryzal symptoms	5 (2.0)
Decreased general condition	4 (1.6)

### The death episode

All patients passed away during the study, and they were all either due to progressive disease or treatment-related complication. Eighty-nine percent of patients ( $n = 104$ ) died in the oncology ward; 4.3% ( $n = 5$ ) in intensive-care unit (ICU) and 0.9% ( $n = 1$ ) in ED. Four patients (3.4%) died at home. The median duration of the last hospital admission was 15 days (IQR: 2, 46). Fifteen patients (12.8%) had been admitted to ICU during the last episode but 10 could be discharged from ICU. The median duration of ICU stay was 4 days (IQR: 3, 9). Medical interventions provided in the last hospital admission were oxygen supplement (19.0%), intravenous fluid (18.9%), pain control (intravenous narcotics or patient-controlled analgesia) (12.1%), packed cell transfusion (8.5%), platelet transfusion (7.5%) and antibiotics (7.5%) (Table 5). Mechanical ventilation and inotropes were given in 8% ( $n = 8$ ) and 4.3% of patients ( $n = 5$ ) respectively.

## DISCUSSION

Neoplasm is the leading cause of childhood death and accounted for 30% of mortality in the age group 1–14 years in Hong Kong. The Children's Cancer Foundation pioneered palliative home care services for children with advanced cancer in late 1999. Three trained full-time nurses provide medical attention to patients in their homes while working in close liaison with pediatric

oncologists who provide hospital-based palliative care services. Palliative care nurses are also supported by a group of clinical psychologists, social workers and family counsellors in providing psychological support, respite care and bereavement.

**TABLE 5** Interventions initiated in last hospital admission ( $n = 503$ )

Interventions	Number of cases, $n$ (%)
Oxygen supplement	96 (19.0)
Intravenous fluid	95 (18.9)
Pain control (IV narcotics or PCA)	61 (12.1)
Packed cell transfusion	43 (8.5)
Platelet transfusion	35 (7.0)
Antibiotics	35 (7.0)
Others	94 (18.7)
Nasogastric tube feeding	23 (4.6)
Pain control (transdermal)	21 (4.2)
Anticonvulsant	20 (4.0)
Steroid	15 (3.0)
Pleural/peritoneal drainage	11 (2.2)
Palliative chemotherapy	10 (2.0)
Mechanical ventilation	8 (1.6)
Inotropes	5 (1.0)
Electrolyte control	5 (1.0)
Foley's catheter	4 (0.8)
Total parenteral nutrition	2 (0.4)
Palliative radiotherapy	2 (0.4)
Pain control (oral analgesics)	2 (0.4)
CT scan	1 (0.2)
Defibrillation	1 (0.2)
Palliative surgery	1 (0.2)
Palliative intrathecal chemotherapy	1 (0.2)

IV, intravenous; PCA, patient-controlled analgesia; CT, computed tomography.

The palliative care referral rate of pediatric oncology patients in this study was 65%, which is comparable with the adult palliative coverage of 67.4% in Hong Kong in 2005.<sup>7</sup> Studies from other countries revealed that 88% of pediatric oncology patients in Eastern Canada received palliative care consult prior to death,<sup>8</sup> while 37.6% of children who died from cancer in Yorkshire in the United Kingdom were referred to palliative care service.<sup>9</sup> Although the overall referral rate in our cohort remained static over the 10 years, there was a rising trend of referral in 9 out of 11 categories of cancer, indicating a heightened awareness of the positive role of palliative care in enhancing quality of life in children with terminal illness. Similar to other countries, referral in our unit, however, occurred late in the course of disease in a majority of patients. The median time of referral was 498 days after diagnosis and



77 days to death. Also, 91% of patients were referred only after the last relapse or after curative treatment was stopped. Palliative care has long been equated with end-of-life care. In a survey of pediatricians from the United States, more than 40% would only refer once cure was no longer the goal.<sup>10</sup> In general, physicians are also more ready to incorporate palliative care into the discussion of treatment goals when the timing of death is predictable. Nonetheless, existing evidence suggests that pediatric palliative care should be integrated early into the course of illness while treatment of curative intent is attempted. WHO and American Academy of Pediatrics recommend palliative care to be introduced to all children with cancer at the time of diagnosis, especially in malignancies with a low likelihood of cure, such that an active approach could be taken to improve symptom control, to facilitate parental adjustment and to involve them in making advance care planning for end-of-life decisions.<sup>11</sup> In line with this new paradigm, education and training in palliative care must reinforce the concept of early introduction of palliative care. Other barriers to referral such as cultural denial of death in children, request of life-prolonging treatment and negative perception of palliative care must be overcome by efficient communication with parents in order to allow timely referral. There should be more public education on life journey and quality of life in patients with life-threatening and life-limiting conditions. The acceptance of referral by patients and parents to palliative care should be enhanced.

Avoiding repeated hospital admission is one of the outcome measure of palliative care.<sup>5</sup> In our cohort repeated admissions after referral (including the death episode) and emergency admissions were common. The majority, on the other hand, only required limited utilization of health care services. With the availability of palliative nurse as a coordinator organizing home care and closely liaising with referring oncologists, it is our goal to minimize unnecessary hospital admission and clinic visits. Bleeding is the top symptom bringing patients back for unscheduled out-patient clinic visits, this was related to high prevalence of leukemia patients receiving palliative care service. In Germany where 70% of children's cancer departments provide palliative home care service, 26% of the children requiring blood or platelet transfusions received them at home.<sup>12</sup> Despite foreseeable legal and organizational difficulties, home transfusion service is a potential area for future development in pediatric palliative care in Hong Kong. A significant proportion of cancer children could benefit from reduced travelling and hospital visits if they could receive pre-emptive blood product transfusion at home.

In our study, uncontrolled pain was also among the top reasons for direct admission and unscheduled clinic visits apart from other common symptoms such as dyspnoea, fatigue and vomiting. Pain has been consistently reported

as the most common symptom suffered by children at the end of life.<sup>13-15</sup> According to a survey of parents whose children died of cancer, more than 50% of children suffered "a great deal" from pain in their last month of life but the attempt to treat this symptom was successful in less than 30%.<sup>16</sup> Given that pain medication is readily available, this success rate is unexpectedly low. In order to control pain adequately, accurate pain assessment is foremost important. Physicians' knowledge and skills on pain assessment and management should be enhanced and common misbeliefs such as fear of respiratory depression, hastening death and tolerance to opioids should be corrected. Other obstacles to effective pain management such as parental fear of addiction, and patients' dislike of side effects must be rectified in order to optimize pain control and reduce unnecessary hospital admission.

In our cohort 20 patients had undergone invasive investigations and imaging studies, including bone marrow examination, CT scan and MRI despite curative treatment was already aborted. According to WHO, palliative care includes "those investigations needed to better understand and manage distressing clinical complication". As in our cohort, performing CT scan and MRI in children with CNS tumours who developed neurological deterioration might help parents understand the disease progression and anticipate death process. However, futile investigations, especially invasive procedures, should always be avoided. After all, physicians should strive to alleviate children from iatrogenic-induced pain and distress.

Yet another goal of palliative care is to facilitate patients to live and die in their place of choice. A general preference of end-of-life care in the community over a hospital setting was identified among European countries. A survey of parents who have lost a child to cancer in Germany revealed that a majority of parents would have preferred home to be the place of death even though only 48% of them died at home.<sup>16</sup> In the United Kingdom, children who were referred to palliative care upon discharge from pediatric ICU were also more likely to die at home or in hospice compared to non-palliative discharges.<sup>17</sup> Yet from our data, only a minority of pediatric cancer patients under palliative care (3.4%) in Hong Kong chose end-of-life care and death at home. This finding is echoed by a local study on adult palliative care where only six patients died at home from the period of 1999 to 2003 among a total of 1300 patients under care.<sup>18</sup> Adult studies in Japan and Taiwan also revealed that dying at home is not popular among oriental patients.<sup>19,20</sup> The places of death vary with local culture, and there are multiple factors that might limit dying at home in our locality. The crowded living environment, social taboo of death, and perceived threat to real estate value in case death occurs at home all play a role. Interestingly, a study on palliative care discharge from pediatric ICU in the United Kingdom showed that South Asian children referred to palliative

care were also more likely to receive care in a hospital than in a community setting.<sup>21</sup> This suggests that cultural factor prevails despite a change in environment. While dying at home might not be the preference of all patients and especially not in our locality, it is important that coordinated support from the palliative care team and the community is available to offer home death as an option to families if they so wish. There are currently also logistic hurdles for dying at home, including certifying death at home by registered doctors, applying special permit for transferring dead body by special licensed vehicle to funeral houses. The government should help to clear the above hurdles to facilitate the option of dying at home.

Lastly, 12.8% of our patients were admitted to ICU during the death episode and 4.3% finally died there. A high percentage of these patients who died in ICU were actually not cared by their parent medical team; they were admitted to other nearby local hospitals due to rapid deterioration of clinical condition. Unfortunately a majority of them were given unnecessary mechanical ventilation and inotropes. As the end of life approaches, overburdened life sustaining treatment is futile. Yet most often such treatment was initiated because the doctors from other hospitals were not familiar with the patient's condition and the palliative intent of care was not well communicated. It is the goal of palliative care to introduce advanced care planning so that parents and children are psychologically prepared for the last journey and have a chance to express their wish for end-of-life treatments. It is crucial that end-of-life decisions are clearly documented so that invasive intervention could be withheld in case of emergency admission. In adult patients, advanced directives may be signed for the purpose but this is not possible in children. In Hong Kong, a Do-Not-Attempt Cardio-Pulmonary Resuscitation for out-of-hospital patients is developed, and this will facilitate the documentation of advanced care plan in pediatric patients. Documentation in the Alert section of the electronic Clinical Management System in the Hong Kong Hospital Authority System will help medical staff of other hospital promptly knowing the palliative care intent being accepted by primary care team and the family. Unnecessary resuscitation or ICU admission may be avoided.

This is a descriptive study that aims to illuminate on the current situation of pediatric palliative care for cancer children in Hong Kong. Symptoms at the end of life described in this study were abstracted from the chief complaints of patients on admission or upon visiting outpatient clinics. They did not reflect the full spectrum of symptoms suffered by cancer children at end of life. This is a single center study, the results may not be generalized to all pediatric oncology patients in Hong Kong nor do they represent the pattern of palliative care referral and service delivery across the territory. The clinical data of dying oncology children who did not receive palliative

care were not complete, thus comparison between the groups receiving or not receiving palliative care cannot be performed.

In Hong Kong, majority of children with advanced cancer received palliative care, albeit late in the course of their illness. Among children of Eastern origin, dying at home might not be the preferred choice as in the West. This study serves as a platform for future planning of palliative care in Hong Kong. The importance of developing a culturally sensitive model so that cancer children and their families could be facilitated to live to their full potential while accepting death as a normal process.

## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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**How to cite this article:** Ho KKH, Cheng FWT, Lin MKY, et al. Palliative care service in patients with childhood cancer from a tertiary pediatric oncology center. *Pediatr Invest.* 2018;2:209-215. <https://doi.org/10.1002/ped4.12094>