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The Clinical Evaluation and Survival Rate of Pediatric Sarcoma in Dr. Sardjito General Hospital, Yogyakarta, Indonesia

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ABSTRACT

Background: Pediatric sarcoma is a heterogeneous group of tumors and accounts for approximately 10% of childhood solid tumors. The most common soft tissue sarcoma is rhabdomyosarcoma, and the most common bone sarcomas are osteosarcoma and Ewing's sarcoma. The prognosis for children with sarcoma depends on age, primary tumor site, tumor size, resectability, presence or absence of metastases, number of metastatic sites, presence or absence of regional lymph node involvement, histopathologic subtype, and in some cases, delivery of radiation therapy. This study aims to evaluate clinical signs, symptoms, and survival rates.

Methods: We carried out a retrospective analysis of clinical data from sarcoma patients in Dr. Sardjito General Hospital to provide a reference for the design of future pediatric sarcoma-specific studies. Data from patients with sarcoma entered in Dr. Sardjito General Hospital from 2012 until 2017 was collected. Patients who had confirmed pediatric sarcoma diagnosis were eligible for samples at study entry. Clinical manifestations were assessed, and overall survival was calculated with Kaplan-Meier.

Results: Among 400 patients coding with pediatric sarcoma, 154 were excluded because their medical records were broken and deleted, and 82 because the coding was not related to their diagnosis (non-pediatric sarcoma). Sixty patients were eligible for the analysis (28 men and 32 women, median age at diagnosis 13 years, range 0–18 years). Fifteen patients (25%) received chemotherapy, radiation, and surgery as a treatment, 16 patients (26.67%) received chemotherapy and surgery only, five patients (8.33%) received chemotherapy only, five patients (8.33%) received chemotherapy and radiation only, one patient (1.67%), and ten patients (16.67%) received surgery only. The most common primary tumor was located in the lower extremity (n = 29; 48.33%). At entry, metastases were mainly found in the lungs. The overall survival rate of pediatric sarcoma in Dr. Sardjito General Hospital was 19% or 88 months (95% CI median 48 months ± 4.658).

Conclusions: This study revealed a diverse range of clinical presentations and a concerningly low overall survival rate. These findings highlight the need for further research to improve treatment strategies and outcomes for pediatric sarcoma, particularly focusing on factors influencing survival and addressing the high rate of metastatic disease.

INTRODUCTION

Sarcomas are a rare case and heterogeneous group of malignant tumors of mesenchymal origin that comprise less than 1 percent of all adult malignancies and 10–12 percent of pediatric cancers [1]. The prevalence of cancer in the world has increased each year since 1980, but the exact data is not yet readily available. Data from WHO in 2018 showed 18.1 million new cancer cases, while 9.6 million deaths from cancer. Cancer incidence in children aged 1–14 years between 2001 to 2010 was 140.60 per one million people per year. In Southeast Asia, the record for the prevalence of pediatric cancer was 12,251 of 105,673,000 children from 2001 to 2010. The majority of children who had pediatric cancer in one study from Dr. Soetomo General Hospital between 2014 and 2015 were male (68,70%) [2]. Soft tissue sarcomas, although relatively rare, are

quite deadly. This could happen due to delayed diagnosis and advanced disease or metastasis at presentation [3].

Ewing's sarcoma is known that whites (Caucasians) are predominantly instead of other races. Therefore, the incidence rates in Asian and African populations are often considerably lower. Contrary to Ewing's sarcoma, other soft tissue sarcoma found blacks had the highest overall incidence rate, followed by Caucasians and American Indian/Asian Pacific. Further investigation of the prevalence and incidence of each region in Indonesia is needed to understand this sarcoma better [3].

Pediatric sarcomas can be divided into soft tissue sarcomas and osseous tumors. Soft tissue sarcoma is often found in the body's muscles, joints, fat, nerves, deep skin tissues, and blood vessels [1,5]. It can be further delineated into rhabdomyosarcoma and nonrhabdomyosarcoma. Rhabdomyosarcoma is the most common soft tissue sarcoma in children, constituting more than 50% of cases. The two main common types of pediatric rhabdomyosarcoma are the embryonal and alveolar subtypes, based on histological morphology. The embryonal subtype accounts for 70% of cases and is associated with younger age. Meanwhile, the alveolar subtype accounts for 15% of cases and is associated with older children [4]. Besides that, the most common bone sarcomas are osteosarcoma and Ewing sarcoma [1,5].

The peak of incidence varies between these sarcoma types. They have bimodal age distribution, especially for embryonal rhabdomyosarcoma [6,7]. The first peak of osteosarcoma is in children and adolescents, and the second peak is in elderly patients related to Paget disease [7]. Most Ewing sarcoma cases occur in the second decade (85%). More than 60% of Rhabdomyosarcoma in children or equal to 3–5% of all malignancies in pediatrics happen in the first decade (younger than ten years) with a slight increase in incidence in late adolescents 20% [8]. The predominant gender that had been diagnosed with Rhabdomyosarcoma in children is males (1.3 males to 1 female) [9].

Anatomic location preference is also different between these tumors. The most common sites for rhabdomyosarcoma are the head and neck (36%), genitourinary tract (23%), and extremities (20%), while embryonal rhabdomyosarcoma only a few cases occur in the extremities compared with alveolar rhabdomyosarcoma [5]. About 10–20% of patients present with distant metastases, most commonly to the lungs, bone, bone marrow, or lymph nodes [1,5]. Alveolar Rhabdomyosarcoma can metastasize and appear as a rapidly growing and expansile mass in the extremities because of its more aggressive biological behavior [10]. Osteosarcoma is mainly located in the long bones. Only 4–13% of osteosarcoma in children occur in the pelvis. On the other hand, 33% of Ewing sarcoma happen in the lower extremities, 24% in the pelvis, and 12% in the thorax [1].

Clinical manifestation can be highly variable and depends on the location of the primary tumor and the presence or absence of metastases [1,5]. Rhabdomyosarcoma often presents with a visible or palpable mass due to compression or invasion of an adjacent structure.

Prognostic for Rhabdomyosarcoma can be seen based on their histological morphology. The embryonal subtype has a better prognosis. Meanwhile, the alveolar subtype tends to have a poorer prognosis [10].

This study aimed to review all cases of pediatric sarcoma, the prevalence of tumor types, and clinical presentations in patients at or younger than 18 years of age. Pediatric sarcomas have not yet been widely studied in Indonesia. Furthermore, it is hoped to help improve the knowledge about pediatric sarcoma and can be used for other research in the future, hopefully improving the therapeutic success and quality of life for children who have cancer.

METHODS

This research uses a retrospective cohort study of all patients who presented to the hematology-oncology pediatric department at the Dr. Sardjito General Hospital in Yogyakarta, Indonesia, and were diagnosed with pediatric sarcoma between January 2012 and December 2017. After approval from the Committee of Ethics of Universitas Gadjah Mada, patients were identified from the Medical Record Registry. Patients were included if they had the diagnosis of pediatric sarcoma at age 18 or younger. Patients must have available data on tumor type and location even if presented for a second or third opinion consultation or if they had been diagnosed and treated at a different institution. Patients were excluded if they had been diagnosed with pediatric sarcoma, but their medical records had been broken or missed.

Data on demographics, clinical presentation, tumor type, anatomic location, and metastatic status were collected from the medical records. Data was analyzed and presented using proportions and percentages for nominal variables and mean and standard deviation for continuous variables.

RESULTS

Patient characteristics

We identified 400 consecutive patients with pediatric sarcoma based on ICD-10 coding. While 154 patients were excluded from the analysis because their medical records were broken and deleted, 82 patients were excluded because the coding was unrelated to their diagnosis (non-pediatric sarcoma). Furthermore, only 60 patients met the inclusion criteria and formed the study cohort. There were 28 males (46.7 %) and 32 females (53.3 %). At presentation, the mean age was 11 ± 5.59

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years (range 0–19 years), and the median and mode age was 13 years old. The demographic characteristics and the type of tumor are presented in **Table 1.**

The most common type of soft tissue pediatric sarcoma was osteosarcoma (24 subjects (40%)) and rhabdomyosarcoma (21 subjects (35%)), while the rarest types were Leiomyoma, Hemangioma endothelioma, and chondrosarcoma (each one subject (1.7%). Other types of pediatric sarcoma that have been diagnosed at Dr. Sardjito General Hospital are Fibrosarcoma, Ewing sarcoma, Liposarcoma, and PNET.

Clinical manifestation of the tumor

Table 2 shows the clinical manifestations of the tumor. This research found that 48 patients (80%) had a tumor manifestation, of which the lower extremity is the primary location of the tumor (n = 29; 48.33%). Mostly, pediatric sarcoma had limited movement-related tumors (42 patients) and tumor pain (20 patients) in their general symptoms.

Table 1. Characteristics of the patients

Characteristics	N (%)
Age (years old)	
0–5	12 (21.4)
6–10	9 (16.1)
11–15	25 (44.7)
16–19	10 (17.9)
Gender	
Male	28 (46.7)
Female	32 (53.3)
Region	
Yogyakarta	20 (21.4)
Central Java	28 (16.1)
West Java	1 (44.7)
East Java	4 (17.9)
Sumatra	5 (16.1)
Kalimantan	1 (44.7)
Papua	1 (17.9)
Type of tumor	
Rhabdomyosarcoma	21 (35%)
Osteosarcoma	24 (40%)
Fibrosarcoma	5 (8.3%)
Ewing Sarcoma	3 (5%)
Liposarcoma	2 (3.3%)
PNET	2 (3.3%)
Leiomyoma	1 (1.7%)
Hemangioma endothelioma	1 (1.7%)
Chondrosarcoma	1 (1.7%)

The most common symptoms in this study were fever in 7 patients (11.5%), lymphadenopathy in 6 patients (9.8%), cough in 5 patients (8.2%), and weight loss without strict diet in 3 patients (4.9%).

Conjunctiva anemia was the most clinical manifestation of head and neck problems in this study. Besides that, three patients (4.9%) may have vision disturbance, and two patients (3.3%) had scurvy in their symptoms.

In our study, a small portion had manifestations in cardio and respiratory problems. Eight-point three percent (5 patients) had dyspnea from respiratory problems, and six-point six percent (4 patients) had chest pain. Cardiac manifestation had a minority in the population study, with only two patients (3.3%) and one patient (1.6%) having murmur and cardiomegaly, respectively. Three patients (4.9%) had abnormal urinary, which was the only genitourinary manifestation in this study.

Table 2. Clinical manifestations of the tumor based on its organ

Clinical Manifestation	N (%)
Tumor Characteristics	
Tumor	48 (80)
Limited movement-related tumor	42 (70)
Pain	20 (33.3)
Edema	15 (24.6)
Progression of size	12 (20)
Bleeding	4 (6.7)
General Problems	
Fever	7 (11.5)
Lymphadenopathy	6 (9.8)
Cough	5 (8.2)
Weight loss without a strict diet	3 (4.9)
Gastrointestinal Problems	
Abdominal pain	20 (33.3)
Nausea vomiting	1 (1.7)
Abnormal defecation	1 (1.7)
Head and Neck Problems	
Conjunctiva anemia	6 (9.8)
Vision disturbance	3 (4.9)
Scurvy	2 (3.3)
Cardiorespiratory Problems	
Dyspnea	5 (8.3)
Chest pain	4 (6.6)
Murmur	2 (3.3)
Cardiomegaly	1 (1.6)
Genitourinary Problems	
Abnormal urinary	3 (4.9)

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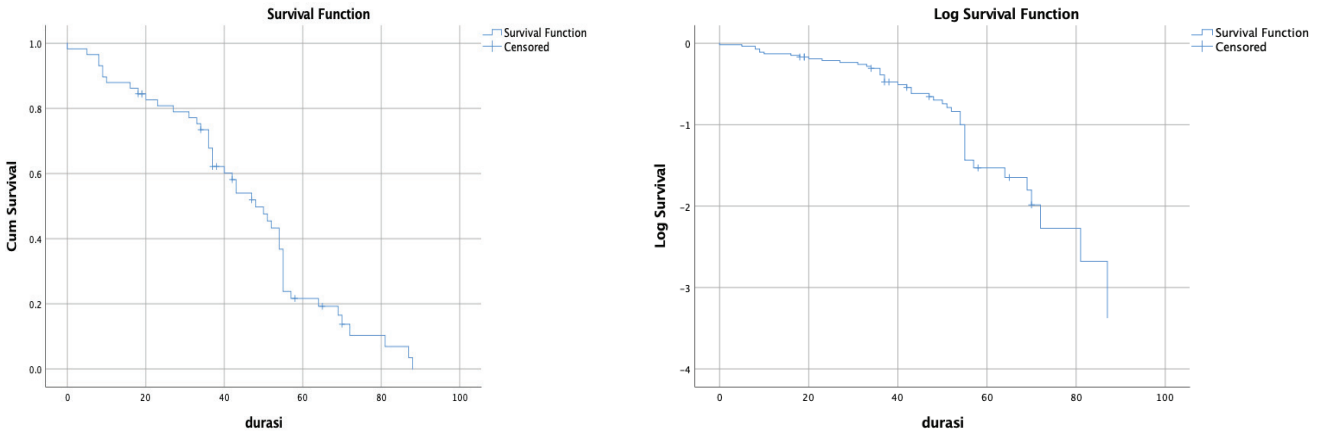

Figure 1. The overall survival rate of pediatric soft tissue sarcoma at Dr. Sardjito Hospital Yogyakarta

Table 3. Clinical manifestations of the tumor based on its organ

Types of Examination	N (%)
Chest Xray	50 (82)
CT-Scan	39 (63.9)
MRI	10 (16.4)
BMP	9 (14.8)
USG	19 (31.1)

BMP, bone marrow puncture; MRI, magnetic resonance imaging; USG, ultrasound sonography

Table 4. Treatments for pediatric soft tissue sarcoma

Kind of Treatments	N (%)
Chemotherapy and Surgery	16 (26.67)
Chemotherapy, Radiation, and Surgery	15 (25)
Surgery only	10 (16.67)
Chemotherapy only	5 (8.33)
Chemotherapy and Radiation	5 (8.33)
Radiation only	1 (1.67)
Other	8 (13.33)

Metastatic status

We identified that at the subjects in their beginning of diagnosis, seven subjects (11,67%) had already lung or skeletal metastatic. By the time of their survival, most of them had new metastatic status. The most common location of metastatic were lungs in 18 subjects (30%), skeletal metastatic in 7 subjects (11,67%), and three subjects had brain metastatic followed by hepatic, intestinal, and muscle metastatic (one subject of each (1,67%)).

Radiologic examination for pediatric sarcoma

Most subjects had a radiologic examination to help the physician diagnose the soft tissue pediatric sarcoma. **Table 3** shows 82% (50 patients) had Chest Xray, 63,9% (39 patients) had CT scan, 31.1% (19 patients) had USG, 16.4% (10 patients) had MRI, and BMP had 14.8% (9 patients).

Treatment for pediatric sarcoma

Our study had many kinds of treatments used by physicians for soft tissue sarcoma. We served the data on the treatment of pediatric sarcoma in the table below. Chemotherapy and surgery were most used for therapy in our subject (26.67% or 16 patients). The total of patients in this study who had surgery was 41; only 33 patients had surgery at Dr. Sardjito General Hospital, and the rest (8 patients) at another hospital.

Survival rate in pediatric sarcoma

The overall survival rate of pediatric sarcoma at Dr. Sardjito General Hospital between 2012 and 2017, shown in **Figure 1**, was 11 subjects (19%; with a survival rate of 88 months). The 95% CI median duration of survival rate was 48 months (± SD 4.658), with a range was 38.87–57.12 months).

DISCUSSION

The majority gender of children suffering from pediatric sarcoma in Dr. Sardjito General Hospital, 53.3%, are female. This data aligns with the research conducted in East Africa (Ethiopia) that the prevalence of pediatric sarcoma is that females are more likely to have it. In contrast, research from Dr. Soetomo Surabaya has stated that the most common gender is male. Also, the research in the USA shows that pediatric sarcoma incidence is lower in females than males. Meanwhile, the prevalence of pediatric cancer in Korea, Japan, and New Zealand is similar for males and females [2,11,12].

Osteosarcoma and Rhabdomyosarcoma are pediatric cancer types that are more common in Dr. Sardjito General Hospital. Clinical evidence shows that rhabdomyosarcoma is the most common soft tissue sarcoma in children (more than 50% of total pediatric sarcoma). Babatunde et al. [13] said in their research

that Rhabdomyosarcoma was the most common pediatric sarcoma. A systematic review found in 23 of 32 studies that pleomorphic sarcoma and liposarcoma were the most common histotypes reported in Asia-Pacific. However, the studies were only conducted in some countries (Australia, Hong Kong, Korea, Malaysia, Singapore, Taiwan, and Thailand). In the future, we need to conduct more research to reflect on the incidence of pediatric sarcoma, especially in Indonesia [14,15].

There was a small number of patients with a diagnosis of Ewing's sarcoma. The incidence is also slighter in other countries such as the U.S., which is approximately three per million per year. Lower extremity is the primary location of the tumor (n = 29; 48.33%) [16].

The clinical manifestations of each patient may differ, one of them can be based on the location of the tumor and adjacent organs involved. The study found more than half of the patients had a tumor, who mostly fussed with limited movement related to the tumor and the rest might complained of pain, edema, progression of the size tumor, and bleeding on the tumor. Mackall, 2009 mentioned in their paper that extremity tumors could present with pain. The most common location of the tumor in the study was the lower extremity (n = 29; 48.33%). This result aligned with a systematic review that found extremities were a predominant site for sarcoma (50–96%) [15]. In addition, they might have had general problems, such as fever, lymphadenopathy, cough, and weight loss. They also could have had manifestations in certain organs related to the location of the tumor and the progressivity of the disease. Three patients had disturbance of their vision because of the space-occupied lesion. Other manifestations that may present in head and neck sarcoma are exophthalmos, diplopia, headache, congestion, nasal discharge, or cranial nerve palsies. Abnormal urinary (4.9%) was also found in this study in patients with genitourinary tumor sites. There was a study that accounts for approximately 20% of genitourinary Rhabdomyosarcoma cases suffered from urinary tract obstruction or constipation.

Eighty-two percent of the patients were being examined using an x-ray. Besides that, 63.9% of patients underwent computed tomography-scan (CT-scan). CT-scan and magnetic resonance imaging (MRI) are being used to help evaluate the diagnosis of pediatric sarcoma, mainly to figure out the primary location, and degree of disease, and map out their therapies. Furthermore, a CT-scan thorax and radionuclide bone scan are also required to check for metastases to the lungs and bone. Open or core biopsies may also be done [17].

Our study identified that less than a quarter of patients have metastatic status in their beginning diagnoses. Almost all of them had metastatic status by the time the treatment was begun. The other study found that nearly one-third of their patients have a baseline metastatic in the beginning followed by one-third of the metastatic after initial treatment [18].

The study had shown that mostly pediatric rhabdomyosarcoma is chemo-sensitive up to 85% at the beginning of the disease and radiotherapy takes part in the local control of the tumor. Complete surgical excision is the primary choice of soft tissue sarcomas treatment followed by adjuvant radiotherapy, chemotherapy, or both if indicated [19].

Pediatric sarcoma needs experienced multidisciplinary teams (radiologists, oncologists, surgeons, and radiation oncologists) to get the most appropriate therapies, such as surgery, chemotherapy, and radiation therapy. So, it is preferable to treat the patient at tertiary care centers [17]. The study has had many choices for the treatment of each patient. Around a quarter of the treatment had chemotherapy and surgery or chemotherapy, radiation, and surgery. The differences depend on the staging of the sarcoma.

The overall survival rate of pediatric sarcoma at Dr. Sardjito General Hospital between 2012 and 2017 was 19% or 88 months (95%CI median 48 months ± 4.658). Another paper said that patients with cancer including sarcoma had survival outcomes partly differ because of often present with advanced disease or seek another treatment elsewhere after inadequate resection. On the other hand, it also could be caused by cultural, economic, social, healthcare systems, and geographic differences among and within countries in the Asia-Pacific region [20,21]. Conclusion. The limited studies identified the most common pediatric sarcoma in Dr. Sardjito General Hospital, with their treatments and outcomes, many of these results require further validation on larger populations.

CONCLUSION

This retrospective study of pediatric sarcoma patients at Dr. Sardjito Hospital revealed a diverse range of clinical presentations and a concerningly low overall survival rate of 19%. The most common primary tumor site was the lower extremity, with lung metastasis being prevalent. These findings highlight the need for further research to improve treatment strategies and outcomes for pediatric sarcoma, particularly focusing on factors influencing survival and addressing the high rate of metastatic disease. This study provides valuable baseline data for future pediatric sarcoma research and emphasizes the importance of comprehensive data collection and analysis in this patient population.

DECLARATIONS

Competing interest

The authors declare no competing interest in this study.

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Ethics approval and consent to participate

The Ethics Committee of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada approved this study.

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REFERENCES

1. Astekar M, Metgud R, Sharma P, Ramesh G. Oral Alveolar Rhabdomyosarcoma: A Case Report with Immunohistochemical Analysis. Clin Pract. 2012;2(1):e17.
2. Badr MA, Al-Tonbary YA, Mansour AK, Hassan TH, Beshir MR, Darwish A, El-Ashry RA. Epidemiological Characteristics and Survival Studies of Rhabdomyosarcoma in East Egypt: A Five-Year Multicenter Study. ISRN Oncol. 2012:1–8.
3. Burningham Z, Hashibe M, Spector L, Schiffman JD. The Epidemiology of Sarcoma. Clin Sarcoma Res. 2012 Oct;2(1).
4. Doyle LA. Sarcoma classification: An update based on the 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone. Cancer. 2014;120(12):1763–1774.
5. Esiashvili N, Goodman M, Marcus RB. Changes in incidence and survival of Ewing sarcoma patients over the past 3 decades: Surveillance Epidemiology and End Results data. Journal of Pediatric Hematology/Oncology. 2008;30(6):425–430.
6. Fithriyah I, Konginan A, Maramis M, Mahajudin M, Muhdi N, Margono H, Warsiki E, Basoeki L, Yitnamurti S. The Epidemiology of Pediatric Cancer In The Palliative Care Unit At Dr. Soetomo General Hospital, Surabaya. Jurnal Berkala Epidemiologi. 2020 Jan;8(1):65.
7. Freling NJM, Merks JHM, Saeed P, Balm AJM, Bras J, Pieters BR, Adam JA, van Rijn RR. Imaging findings in craniofacial childhood rhabdomyosarcoma. Pediatr Radiol. 2010;40(11):1723–1738.
8. Jo VY, Fletcher CD. WHO classification of soft tissue tumours: an update based on the 2013 (4th) edition. Pathology. 2014;46(2):95–104.
9. Kelly B, Lundon D, Rowaiye B, Daly P, Walsh K. Embryonal rhabdomyosarcoma of the testis. Canadian Urological Association Journal. 2011;5(1):E7–E10.
10. Loeb, DM, Thornton K, Shokek O. Pediatric soft tissue sarcomas. Surgical Clinics of North America. 2008;88(3):615–vii.
11. Martin-Giacalone BA, Weinstein PA, Plon SE, Lupo PJ. (2021, May 9). Pediatric Rhabdomyosarcoma: Epidemiology and Genetic Susceptibility. J Clin Med. 2021 May;10(9):2028.
12. Merchant MS, Mackall CL. Current Approach to Pediatric Soft Tissue Sarcomas. The Oncologist. 2009;14(11):1139–1153.
13. Babatunde TO, Akang EEU, Ogun GO, Brown BJ. Pattern of childhood cancer in University College Hospital, Ibadan during 1991–2010 and comparison with the previous three decades. Paediatr Int Child Health. 2015;35(2):144–150.
14. Ngan, R. Soft-tissue sarcomas in the Asia-Pacific region: A systematic review. Asian Pac J Cancer Prev. 2013;14(11):6821–6832.
15. Ngan R, Wang E, Porter D, Desai J, Prayogo N, Devi B, et al. Soft-tissue Sarcomas in the Asia-Pacific Region: A Systematic Review. Asian Pac J Cancer Prev. 2013;14(11):6821–32.
16. Ognjanovic S, Linabery AM, Charbonneau B, Ross JA. Trends in childhood rhabdomyosarcoma incidence and survival in the United States, 1975-2005. Cancer. 2009;115(18):4218–4226.
17. Ottaviani G, Jaffe N. The Epidemiology of Osteosarcoma. Cancer Treat Res. 2009:3–13.
18. Pushpam D, Garg V, Ganguly S, Biswas B. Management of Refractory Pediatric Sarcoma: Current Challenges and Future Prospects. Onco Targets Ther. 2020;13:5093–5112.
19. Sankaranarayanan R. Cancer survival in Africa, Asia, the Caribbean and Central America. Introduction. IARC Sci Publ. 2011;162:1–5.
20. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics. CA Cancer J Clin. 2014 Jan;64(2):83–103.
21. Wong CK, Lam YL, So YC, Ngan KC, Wong KY. Management of extremity soft tissue sarcoma after unplanned incomplete resection: experience of a regional musculoskeletal tumour centre. Hong Kong Med J. 2004;10(2):117–122.