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Evaluation of the Brazilian therapeutic and epidemiologic management of osteosarcoma in childhood and adolescence

Abstract

Objective: The aim of this study is to analyze the epidemiology of osteosarcoma in children and adolescents and its best therapeutic approach.

Data source: data was obtained from the Ministry of Health's databases (TABNET), made available by the Department of Informatics of the Unified Health System (DATASUS), available at the following website (http://www.data-sus.gov.br). As the database is in the public domain, it was not necessary to submit the project to the Research Ethics Committee.

Data synthesis: 51,901 cases of osteosarcoma were recorded in children and adolescents in Brazil, with a homogeneous distribution throughout the study period. The 15-19 age group accounted for the highest number of cases (41.2%) and also the highest mortality rate.

Conclusions: Osteosarcoma is a malignant and aggressive neoplasm which requires rapid diagnosis and treatment, based mainly on chemotherapy and limb salvage surgery (LSS) as adjuvant therapy.

Keywords: Osteosarcoma; Pediatrics; Osteogenic sarcoma.

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Introduction

Osteosarcoma (OSC) is a rare type of malignant bone neoplasm, with insidious onset and rapid progression, which mostly affects children, adolescents and the elderly.[1] It is an aggressive tumor that arises from remodeled primitive cells of mesenchymal origin, hence a sarcoma, which exhibits osteoblastic differentiation and produces malignant osteoid. Being a solid, irregular and hard tumor due to tumor spicules of calcified bone that radiate at right angles. OSC tends to affect regions around the knee in 60% of cases, 15% around the hip, 10% in the shoulder and 8% in the jaw.[2]

The high prevalence in men than women, with a ratio of 1.4:1 is a curious statistic, however, it represents less than 1% of all diagnosed cancer cases.[3,4] Its incidence peaks between the ages of 10 and 19, accounting for about 2% of children (1 to 14 years) and 3% of adolescents (15 to 19 years) with malignant neoplasia.[3,5] In older patients it occurs in an axial location, in contrast to young patients who arise in the metaphysis of long bones.[6,7] It is likely to be associated with rapid bone proliferation, which correlates with the growth spurt during puberty.[3]

Most tumors occur in the metaphyses of long bones and rarely in other locations such as the craniofacial, thoracic and pelvic regions.[8] However, some are located close to the central axis (spine, pelvis and thorax), representing a substantially higher risk of death than those of limbs/ extremities.[9] Axial location predicts worse prognosis because of the ease of infiltration of vital organs and consequently metastasization.[9,10] Although some cases of OSC are attributed to hereditary diseases, for example Fraumeni syndrome, Rothmund-Thompson syndrome and hereditary retinoblastoma, most appear to be sporadic, with no certain etiology.[11]

This proposed work has as objective the epidemiologic analysis of osteosarcoma in children and adolescents associated with its best therapeutic approach. Because it is an aggressive malignant neoplasm common in this age group, the initial diagnosis and treatment through clinical screening with studies based on randomized clinical trials, has great relevance.

Methods

The present scientific work is a qualitative and quantitative clinical investigation, retrospective, through an epidemiological study, whose data were obtained from the databases of the Brazilian Ministry of Health (TABNET), made available by the Department of Informatics of the Unified Health System (DATASUS), available at the electronic address (http://www.data-sus.gov.br). As this is a public domain database, it was not necessary to submit the project to the Research Ethics Committee.[12,13]

The research gathers health data and involves the category of neoplasic lesions in children with musculoskeletal involvement. The study sample were patients under the age of 1 to 19 years diagnosed with osteosarcoma in Brazil, during the years 2013 to 2022. Microsoft Excel 2019 was used to analyze and prepare the data and graphs. The search period in the databases used occurred from March 15, 2023 and June 15, 2023.

Inclusion criteria: During the search for articles in the databases searched, the following criteria were included: Works published in the last 10 years; studies that include diagnosis, treatment and prognosis of children and adolescents with ostessarcoma; articles whose reading of titles and abstracts related to the theme proposed by the study; articles in Portuguese, English and Spanish.

The exclusion criteria: were articles that were not related to the research theme; works referring to children and adolescents with other neoplasms; studies on osteosarcoma analysis in the adult population; articles whose language differs from those mentioned above.

The articles used were selected from the SciELO, PubMed and LILACS databases, using the terms "osteosarcoma", "pediatrics" and "osteogenic sarcoma" from the Health Sciences Descriptors platform at <https://decs.bvsalud.org/>.

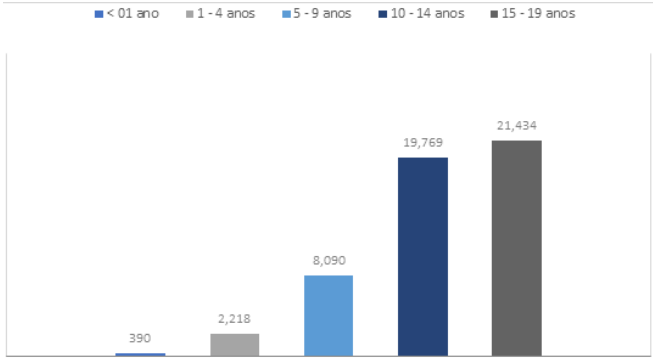
Results

Between 2013 and 2022, 51.901 cases of osteosarcoma were registered in children and adolescents in Brazil, with homogeneous distribution during the study period. The Southeast region accounted for 38.1% of Brazilian records, followed by the Northeast with 32.8%. Although the North region had the lowest number of cases when compared to the others (4.8%), it was the one with the highest mortality rate, 4.22 per 100,000 inhabitants (Table 1).[13]

Table 1 Mortality rate due to osteosarcoma in Brazil[13]

Region	Mortality rate
North	4.22 per 100 thousand inhabitants
Southeast	2,11 per 100 thousand inhabitants
Northeast	1,96 per 100 thousand inhabitants
Center - West	1,90 per 100 thousand inhabitants
South	1,25 per 100 thousand inhabitants

The age group of 15 - 19 years represented the highest number of cases (41.2%), while 10 - 14 years (38.0%), 5 - 9 years (15.5%), 1 - 4 years (4.2%) and under 1 year (0.7%) (Graph 1). In relation to the mortality rate, it was significantly higher in patients between 15 and 19 years (2.66 per 100 thousand inhabitants) followed by those under 01 year (2.05 per 100 thousand inhabitants). The highest prevalence was found in males (57.1%). Of the patients, 45.5% were brown.[13]



Graph 1 Prevalence of osteosarcoma cases by age group in Brazil during the years 2013 - 2022.[13]

During the period, 17.940 chemotherapies were performed for the treatment of osteosarcoma in the study population (Table 2). Corresponding to total hospital expenses of approximately 210 million reais. In relation to days of hospital stay, 681.091 were computed, with an overall average of 5.8 days. However, the North region had a higher average hospital stay than the others, 9.3 days.[13]

Table 2 Number of chemotherapies used for the treatment of osteosarcoma in children and adolescents during the period 2012 - 2023[13]

Region	No. of Chemotherapies
Southeast	8.3
Northeast	6.08
South	2.082
Center - West	1.146
North	332
	17.94

Discussion

Osteosarcoma is a neoplasm that mainly affects children and adolescents. The age group with the highest number of incidence was 15-19 years, also presenting the highest mortality rate, followed by children under 1 year of age. Chemotherapy was used as treatment in most cases of osteosarcoma in childhood and adolescence, totaling 17.940 procedures during the period.[13]

The Southeast region had the highest number of cases during the study period, while the North showed the lowest statistical data, although, when comparing the mortality rates of the different regions, a high rate was observed in this region when compared to the others. In addition, the average number of days of hospital stay per patient found was considerably higher in the North region. A scenario such as this reflects the need to search for possible causes of low investments in an area that presents long hospital stays without administration of effective treatment linked to high mortality rates.[13]

Bone tumor in pediatric patients is a unique factor that puts children's health at risk.[14] Being a highly aggressive cancer, osteosarcoma can lead to metastasis to bone marrow, lung and other tissues in the early stage of the disease.[15,16] Tumors of the spine, chest and pelvis have a significantly higher risk of death than those of the limbs and skull.[9]

Osteosarcoma is initially identified on plain radiographs when the patient reports pain. The next step in diagnosis is contrast-enhanced MRI of the affected bone as well as adjacent bones. Histological diagnosis is based on findings in samples stained with hematoxylin and eosin, even though OSC has a wide morphological spectrum.[17] In addition to imaging the primary tumor, chest CT is essential for initial staging, as this tumor commonly metastasizes to the lung. A bone scan or PET-CT scan is usually recommended to assess for bone metastasis.[16]

Previous studies show that some prognostic factors: age, tumor location, type of surgery and local recurrence, affect the survival of patients.[17] Age is an independent risk factor for malignant bone tumors in children, with a lower survival rate for older children.[18]

Therapeutic management has changed over time; previously, before neoadjuvant chemotherapy, amputations and disarticulations were the dominant therapies, with a 5-year overall survival rate of only 20%.[19] In the current era, chemotherapy of OS consists of five drugs: high-dose methotrexate with leucovorin salvage, doxorubicin (adriamycin), cisplatin, ifosfamide and etoposide. With the use of effective neoadjuvant chemotherapy in the 1970s, limb salvage surgery (LSS) was highlighted as a potential therapy.[20] Usually, LSS has physiological and functional advantages over traditional amputation procedures when agreed with neoadjuvant or adjuvant chemotherapy.[21]

As for radiotherapy, its indication in children is controversial. Since it can cause a delay in bone or organ development, even if it has a therapeutic effect on tumors, it will affect the quality of life in the future.[22]

In response to treatment, when assessed radiologically, this tumor tends to increase in size, because of mineralization of the stromal tissue with tumor necrosis. Even if the tumor has few residual viable tumor cells after therapy, it will still occupy a considerable volume because of the matrix produced by the malignant cells, which do not disappear with cell death. Therefore, objective radiographic response is rare in OSC, even with complete tumor necrosis after neoadjuvant chemotherapy in newly diagnosed patients.[24] Despite this, increasing tumor size does not correlate with disease progression.[25]

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Conclusion

The incidence of the disease, according to the age group, was from 15 to 19 years, showing a higher mortality rate followed by children under 1 year, with a higher prevalence in males. Between the five regions of the country, the Southeast exposes the largest number of cases, while the North presents the lowest statistical data, however, in relation to mortality rates, this region has the highest rate and the highest average number of days of hospitalization. Since it is a malignant and aggressive neoplasm, and of great importance a rapid diagnosis and initiation of treatment, which is based mainly on chemotherapy and LSS, as adjuvant therapy. Regarding radiotherapy, its use is questionable because it affects the development of organs and osteoarticular apparatus.

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None.

Conflicts of interest

The Author declared that there is no conflict of interest.

References

1. Duong LM, Richardson LC. Descriptive epidemiology of malignant primary osteosarcoma using population–based registries, United States, 1999–2008. *J Registry Manag*. 2013;40(2):59–64.
2. Chen C, Xie L, Ren T, et al. Immunotherapy for osteosarcoma: Fundamental mechanism, rationale, and recente breakthroughs. *Cancer letters*. 2021;500:1–10.
3. Gao B, Wang MD, Li Y, et al. Risk stratification system and web–based nomogram constructed for predicting the overall survival of primary osteosarcoma patients after surgical resection. *Front Public Health*. 2022;10:949500.
4. Mirabello L, Troisi RJ, Savage SA. Osteosarcoma incidence and survival rates from 1973 to 2004: data from the surveillance, epidemiology, and end results program. *Cancer–Am Cancer Soc*. 2009;115(7): 1531–1543.
5. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. *CA Cancer J Clin*. 2022;72(1): 7–33.
6. Casali PG, Bielack S, Abecassis N, et al. Bone sarcomas: ESMO–Paed–Can–EURACAN Clinical practice guidelines for diagnosis, treatment and follow–up. *Ann Oncol*. 2018;29(Suppl 4): v79–v95.
7. Miller BJ, Cram P, Lynch CF, et al. Risk factors for metastatic disease at presentation with osteosarcoma: an analysis of the SEER database. *J Bone Joint Surg Am*. 2013;95(13):e89.
8. Mirabello L, Troisi RJ, Savage SA. Osteosarcoma incidence and survival rates from 1973 to 2004: Data from the Surveillance, Epidemiology, and End Results Program. *Cancer*. 2009;41;115(7):1531–1543.
9. Wang J, Zhanghuang C, Tan X, et al. A nomogram for predicting cancer–specific survival of osteosarcoma and Ewing's sarcoma in children: A SEER Database Analysis. *Front Public Health.* 2022.
10. Berner K, Bruland ØS. Prognostic impact of proximal versus distal localization in extremity long bone osteosarcomas. *Anticancer Res.* 2019; 39:2459–66.
11. Gianferante DM, Mirabello L, Savage SA. Germline and somatic genetics of osteosarcoma – connecting aetiology, biology and therapy. *Nat Rev Endocrinol.* 2017;13(8):480–491.
12. Pereira AS. Scientific research methodology. Santa Maria: UFSM, NTE; 2018.
13. Brasil. Ministry of health. Health information.
14. Uyeturk U, Helvaci K, Demirci A, et al. Clinical outcomes and prognostic factors of adult's Ewing sarcoma family of tumors: single center experience. *Contemp Oncol.* 2016; 20:141–146.
15. Teicher BA, Bagley RG, Rouleau C, et al. Characteristics of human Ewing/PNET sarcoma models. *Ann Saudi Med*. 2011;31:174–182.
16. Whelan JS, Davis LE. Osteosarcoma, chondrosarcoma, and chordoma. *J Clin Oncol*. 2018;10;36(2):188–193.
17. Kim MS, Lee SY, Lee TR, et al. Prognostic nomogram for predicting the 5–year probability of developing metastasis after neo–adjuvant chemotherapy and definitive surgery for AJCC stage II extremity osteosarcoma. *Ann Oncol*. 2009;20:955–960.
18. Arshi A, Shari J, Park DY, et al. Prognostic determinants and treatment outcomes analysis of osteosarcoma and Ewing sarcoma of the spine. *Spine J.* 2017;17:645–655.
19. Gaston CL, Nakamura T, Reddy K, et al. Is limb salvage surgery safe for bone sarcomas identified after a previous surgical procedure? *Bone Joint J.* 2014;96–B(5):665–672.
20. Carty CP, Dickinson IC, Watts MC, et al. Impairment and disability following limb salvage procedures for bone sarcoma. *Knee*. 2009;16(5):405–408.
21. Ferrari S, Palmerini E. Adjuvant and neoadjuvant combination chemotherapy for osteogenic sarcoma. *Curr Opin Oncol.* 2007;19(4):341–346.
22. PDQ pediatric treatment Editorial Board. Ewing sarcoma treatment (PDQ□R): patient version. In: PDQ cancer information summaries. Bethesda (MD): National Cancer Institute (US); 2020.
23. Baxter D. The foot and ankle in sport. St Louis: Mosby; 1995.
24. Joanne P Lagmay, Mark D Krailo, Ha Dang, et al. Outcome of patients with recurrent osteosarcoma enrolled in seven phase II trials through children's cancer group, pediatric oncology group, and children's oncology group: learning from the past to move forward. *J Clin Oncol.* 2016;1;34(25):3031–3038.
25. Schuetze SM, Baker LH, Benjamin RS, et al. Selection of response criteria for clinical trials of sarcoma treatment. *Oncologist*. 2008;13:32–40.