

# Clinical and epidemiological characteristics of adolescent patients with osteosarcoma

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## ABSTRACT

Osteosarcoma (OS) is a malignant neoplasia that affects the bone tissue with no known cause. It most commonly affects the appendicular skeleton, mainly the femur and tibia bones, in children and adolescents. The surgery treatment consists of a resection of the tumor or amputation of the affected limb, associated with chemotherapy. The earlier it is diagnosed and treated, and the smaller it is, the better the prognosis will be. **Objective:** The main objective of this study was to present the clinical characteristics and epidemiology of adolescent patients from the Ceará Cancer Hospital (HCC) in the city of Fortaleza. Clinical and epidemiologic data about these patients, who ranged from the age of 10 to 19 years old, was investigated in order to fulfill our objectives with this study. **Method:** A retrospective cohort study was developed gathering information from patients' charts from the above-mentioned hospital from the period of January 2006 to December 2007. The data was collected through a semi-structured form that consisted of questions that appraised both the clinical and epidemiological characteristics of the patients, as well as the demographic data. After selecting 29 cases, only 26 were used for the analysis due to either incomplete information, abandonment of treatment, or hospital transference. **Results:** Our results show that Osteosarcoma was found to be more frequent in male patients (57.7%), in patients between 10 and 15 years old (73.1%), in afro-descendant patients (50%), and in patients that came from more rural areas (73.1%). This study also shows that 30.8% of the patients presented a family history of cancer. The symptom that these patients seemed to have in common was pain (24 patients), followed by an increase of local volume (20 patients), and previous trauma (8 patients). The femur bone was affected in 65.4% of the cases, with occurrence of metastasis (76.9%), almost always during the diagnosis and with the majority (15 patients) to the lungs. The treatment consisted of chemotherapy (96.2%) associated with the surgical resection (69.2%) and amputation (73.1%) or limb replacement. Other treatments such as Physical Therapy were prescribed in 42.3% of the cases, mostly during post-surgery (23.1%), and generally just to treat the complications. **Conclusion:** This study suggests that the common profile of a patient with Osteosarcoma is male, afro-descendant, coming from the more rural areas and presenting a family history of cancer. In conclusion, this study suggests the importance of knowledge about both clinical and epidemiological characteristics of Osteosarcoma patients, so that there is more regard from health professionals concerning multidisciplinary teamwork at the time of the diagnosis.

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## INTRODUCTION

Over time, Brazil is going through an epidemiological transition where one sees a reduction in mortality leading to an increased life expectancy and a consequent change in its epidemiological profile. Mortality, previously marked by infectious diseases, has come to now be marked by cardiovascular diseases, neoplasias, external causes, and other diseases considered chronic-degenerative.<sup>1-4</sup>

Adolescence is a transition phase between human childhood and adulthood where various transformations take place: physical, psychological, and social. The World Health Organization (WHO) currently classifies adolescence as the period between ages 10 and 19. The adolescent and youth population (10 - 24 years) represents 33.33% of the Brazilian population according to the census by the *Instituto Brasileiro de Geografia e Estatística* (IBGE) in the year 2007, and 29% of the population worldwide, according to the Ministry of Health in 2008.<sup>5</sup>

The most recent data released by the Brazilian Cancer Institute<sup>6</sup> estimates the occurrence in Brazil during the biennium of 2008/2009 to be around 8,890 cases of cancer per year among those under 18 years of age, making it the second leading cause of death in the country.

The survival rate of child cancer has improved thanks to the improvement of diagnostic methods, treatments, and multimodal therapy. However, the majority of children with cancer reside in developing countries and rural regions where access to proper treatment is limited and the general state of health is compromised by the prevalence of infectious diseases and by malnutrition.<sup>7</sup>

Osteosarcoma (OS) is a primary malignant tumor occurring in the osseous tissue and affecting children and adolescents mainly in the second decade of life-in other words, during the puberty phase. It accounts for 20% of the primary cancers and 5% of childhood tumors.<sup>8,9</sup>

The most common location is in the metaphysis of the long bones that are in the growth phase (such as the distal femur and proximal tibia) and their length varies from person to person. Prevalence is greater among the male gender, with a ratio of 1.5 to 2.1 : 1, occurring generally between the second and third decades of life.<sup>8-10</sup>

The main signs and symptoms are pain and a progressively increasing local volume, change in sensitivity, redness, the possibility

of limited movement, edema, infiltration of the soft tissues, signs of inflammation, and collateral circulation. Pathological fractures can be observed in 15% of cases.<sup>9-11</sup>

The diagnosis is done by clinical history and supplementary exams such as bone scintigraphy with radioisotopes, Computerized Tomography (CAT), and Magnetic Resonance Imaging (MRI), in addition to biopsies from lesioned-tissue samples. The previous study of the type of cancer via biopsy has allowed for a more precise diagnosis with fewer complications after oncological surgeries.<sup>12,13</sup>

Benign tumors are characterized by being well delimited, with regular and well-defined contours, and demarked by a surrounding area of sclerosis-this reflects slow growth and reactions of the bone. Malignant tumors have poorly delimited borders with irregular and poorly defined contours, which indicate a permeative and aggressive process that does not allow the hosting bone's response to the lesion. These lesions are routinely distinguished through a radiological exam and confirmed with a biopsy.<sup>14</sup>

There are reports of improved prognoses among patients with OS in recent decades, especially among those with localized illness. The main factor for this improvement is the association of chemotherapy with the surgery, in addition to advances in the orthopedic prostheses that contribute to the improvement in the quality of life of these patients.<sup>8</sup>

Despite having complications such as renal and hearing and side effects such as nausea, vomiting, dehydration, electrolytic disturbances, and depression, among other things, chemotherapy treatment is still the most recommended in serious cases. It is important to take care in choosing the drugs so that their toxic effects do not somatize; this helps reduce the patient's complications.<sup>15-17</sup>

When the cancer is not detected early, a more aggressive treatment is necessary and the chance of a cure is lower. Sequelae occur and can lead to the mechanical compression of vital structures and, also, when erroneous initial treatments are recommended, they compromise the prognosis and create a negative impact on the patient's quality of life. Then, there is an increased morbidity and/or a worsening of the general clinical presentation.<sup>5</sup>

OS affects the osseous tissues and adjacent soft tissues and is frequently observed in adolescents. It is not a common pathology, however, among the types of cancer that afflict adolescents, it is one of the most

common. After multiple myeloma, OS is the most commonly seen primary malignancy.<sup>18</sup>

Studies show that it is more predominant in the non-white races, at an age greater than ten years, with a history of previous trauma, greater involvement in the lower limbs and that the prognosis is better when the disease is localized and discovered in the initial phase of development.<sup>8,9</sup>

The survival rate of classical OS is 60% if there is no metastasis diagnosed, and 20% in cases where there is metastasis. In Brazil, 30% of those afflicted with OS already arrive at the hospital with metastasis detected in the diagnosis, reducing their expectations and quality of life.<sup>11</sup>

The earlier the pathology can be prevented and diagnosed, the more the patient will benefit from treatments and will have a lower risk of death. This is why it is important to know the clinical aspects and epidemiology of these patients.

Knowing the clinical aspects and epidemiology of these patients allows for a more directed planning and treatment, working toward prevention and reducing sequelae, treatment time, time of hospitalization, and the cost of health.

## OBJECTIVE

The general objective of this work was to learn the clinical characteristics and epidemiologies of adolescent patients with Osteosarcoma (OS) treated at the Ceará Cancer Hospital (*Hospital do Câncer do Ceará - HCC*) in the city of Fortaleza. To this end, the clinical data and epidemiology was investigated regarding adolescent OS patients (from 10 to 19 years old) and the most frequently used treatments for this population.

## METHOD

The present retrospective cohort study was carried out between December of 2009 and May of 2010 at the HCC, in the city of Fortaleza, which was chosen for its being the largest reference hospital in the treatment of cancer in northern and northeastern Brazil.

The present study investigated the medical records of a population composed of adolescent patients (aged between 10 and 19 years) afflicted with OS who underwent treatment at the HCC between January of 2006 and December of 2007.

The data was collected directly from the patients' medical records. The researcher

collected data for one month by going there once a week for an average of seven hours a day in the Medical and Statistical Archival Service (*Serviço de Arquivo Médico e Estatística - SAME*) of the HCC. The working instrument was a semi-structured sheet that contained questions regarding the patient's clinical characteristics and epidemiology, aside from identification data.

The data was tabulated by statistical software (*Microsoft Excel*® 2007 and *Statistical Package for Social Sciences* (SPSS)) and then expressed in graphics and tables and discussed in parallel with the reference literature.

## RESULTS

Twenty-nine sheets were filled in with data collected from the patient's medical records, but only 26 were used due to either incomplete information, abandonment of treatment, or hospital transference.

The analysis referring to the year 2006 contained a total of 14 records, while from 2007 there were 12. The average age of the patients in the study was 14.64 years, with a standard deviation of  $\pm 2.2$ , and the most common age was 15. The present study showed that 57.7% of the patients were male, 50% were afro-descendant, 30.8% were white, and 19.2% mixed. From the records analyzed, 84.6% of the patients lived with their parents, who came with them for treatments, 3.8% with other family members (siblings, uncles, or grandparents), and 11.5% gave insufficient data.

When analyzing for any family history of cancer, 11 records had no information due to incomplete medical evaluation, 8 (30.8%) showed a family history of cancer, and 7 (26.9%) reported or knew of no such family history.

The records contained data on the chief complaint of the patients at the time they were admitted during medical evaluation. Pain was identified as the main complaint given by the records (24 patients), followed by increased local volume (20, and previous trauma (08). Most of the analyzed records (20) presented data regarding metastasis; of those 20 (76.9%), a majority (15) had metastasized to the lungs.

In the present study, 73.1% of the records reported amputation surgery and 69.2% reported tumor resection; however, many times the resection was followed by amputation. It is believed that this high percentage of amputations was due to a late

diagnosis, which many times was already in the process of metastasizing.

Physiotherapy was identified as part of the treatment, however, few patients (11) received such treatment while hospitalized. It is known that not seeking physiotherapy contributes to sequelae, as well as other premature complications.

Among the 26 records, 42.3% registered physiotherapy as part of the hospital treatment, 23.1% began post-surgery, 11.5% after receiving the prosthesis, and 7.7% as of admission.

From among the 26 records analyzed, 5 deaths by OS and/or complications were identified, 20 had complications with no mortality, and one gave insufficient data. Among the complications given in the medical records, the most common were: nausea, vomiting, diarrhea, fever, headaches, pain, constipation, loss of appetite, fatigue, and coughing.

Correlating the data from the locations of the tumors with the locations of the metastasis, one sees that, regardless of where the tumor was, the majority of cases presented metastasis to the lungs, followed by metastasis to the same bone (recurrence).

Reviewing the data and correlating the information, it was observed that with a family history of cancer there was a high incidence of metastasis, that a majority of those with side effects also showed metastasis, and that delaying for less time between diagnosis and treatment did not influence the occurrence of metastasis, because many times metastasis was already detected in the diagnosis.

Patients who resided in rural areas presented more side effects and more occurrences of mortality. It is believed that due to the lack of resources and early diagnosis their situation becomes more difficult far from the capital.

The time delay between medical diagnosis and hospital admission did not influence the incidence of amputation, since even the patients who were admitted in less time suffered the same limb amputation due to late diagnosis.

There was a statistical relationship between family history and metastasis, generating a Friedman Test score of 0.046.

Physiotherapy had a  $p = 0.5$  in the Binomial Test; in other words, it was not statistically significant. However, it is important data, for it shows us that health professionals must stay up to date as to the recommendations and benefits of the physiotherapy that must be done on all the patients in the present study.

## DISCUSSION

Rech et al.<sup>8</sup> found that, of the medical records of 50 patients diagnosed with OS between January of 1992 and December of 2001 at the *Hospital das Clínicas* in Porto Alegre, 68% of them were male. Castro et al.<sup>14</sup> made a retrospective study on the clinical and laboratorial characteristics of OS at the Pediatrics Department Oncology Service of the *Santa Casa de Misericórdia*, a hospital in São Paulo, reporting the predominance of the male gender (36%) and of non-white race (39%) which corroborates the findings of the present study that showed that 57.7% of the patients were male, 50% were afro-descendant, 30.8% were white, and 19.2% were mixed.

According to Tsai et al.,<sup>19</sup> there is a predominance of the male gender in patients with OS, for in his research with 23 patients treated at the Pediatric Oncology Institute (*Instituto de Oncologia Pediátrica*) of the Federal University of São Paulo between June of 1999 and June of 2006, there were 18 male patients and 5 female, thus agreeing with the present study that demonstrated the predominance of the male gender in OS patients.

From the records analyzed, 84.6% of the patients lived with their parents, who came with them for treatments, 3.8% with other family members (siblings, uncles, or grandparents), and 11.5% gave insufficient data. In the same way that this study showed that the mother and father were the most likely to accompany the treatment of the patients, Stolaghi et al.<sup>10</sup> showed in their study that the main caregiver of the OS patient was the mother in 32% of the cases and siblings in 20%.

Pain was seen as the main complaint cited in the records (24 patients), followed by increased local volume (20), and previous trauma (08). According to the study by Rech et al.,<sup>8</sup> 78% of the patients presented pain in the diagnosis, 50% an increased volume, 46% had a history of trauma, 42% had pathological fractures, and 62% were observed having difficulty walking.

Some studies<sup>8,20,21</sup> showed that OS develops with a certain predominance in the femur, followed by the proximal tibia and humerus, which corroborates with the findings of this research, which detected femoral OS in 65.4% of the cases, followed by the tibia in 26.9% and the humerus in 7.7%.

In the study referred to, it was shown that 76.9% of the patients' diagnoses already

presented metastasis, and in the majority of those cases it occurred in the lungs. Another study<sup>8</sup> also found pulmonary metastases in the diagnoses.

According to the study by Rech, et al.,<sup>8</sup> 52% of the patients were submitted to amputation and 34% to more conservative limb surgery. In the present study, 73.1% of the records reported amputation and 69.2% did a resection of the tumor, although many times the resection was followed by amputation. It is believed that this high percentage of amputations was due to a late diagnosis, which many times were already in the process of metastasizing.

Physiotherapy was identified as part of the treatment, however, few patients (11) received such treatment while hospitalized. In the study by Tasi et al.<sup>10</sup> it was observed that the 23 patients treated received physiotherapy after the definitive diagnosis for a minimum of six months post-surgery in contrast to the present study. It is known that not seeking physiotherapy contributes to sequelae, as well as other premature complications.

In the study by Penna et al.<sup>21</sup> on osteosarcoma of the knee, they showed that 21.4% of the cases ended in death by OS and/or its complications, the same as in this study, which observed 5 deaths.

Stolaghi et al.<sup>10</sup> showed the occurrence of side effects during OS treatments by the report from a family member who said: *"The difficulty was from the side effects of the chemotherapy; he got very sick, became very thin, vomited, didn't eat right, his mouth became all full of sores, lost his hair, couldn't smell anything, coughed, passed out, became depressed-I thought he was going to die."* This concurs with the findings on side effects from the present research.

## CONCLUSION

The epidemiological characteristics in the studied adolescent OS patients showed that there is a slight favoring of the male gender, an average age of 14.64 years, with African ancestry, who generally reside in the interior, and who tend to have a family history of cancer.

This study also shows us the clinical characteristics these patients have in common such as pain, increased local volume, and

the development of a tumor correlated with previous trauma. The femur was the area of the highest incidence of OS, with the diagnosis almost always showing metastasis, and almost always to the lungs.

The data identified in this study leads us to reflect on the reality of the treatment of OS patients, where it clearly shows that they seldom received the benefit of an early diagnosis. It is good to point out that the treatment for this pathology must be multidisciplinary, that is, several professionals must act to find the best for that sick person. However, it was observed that the intervention strategies focused on the reality of functional rehabilitation were not duly begun with the diagnosis, but only requested following complications resulting from the most used forms of treatment, which were chemotherapy associated with surgical resection and amputation or replacement of endoprosthesis.

This study concludes that it is important and necessary to know the clinical characteristics and epidemiology of the OS patient, thereby facilitating an early diagnosis, and thus preventing complications such as amputations and aggressive treatments. This is the way to improve the patient's chances of survival by redirecting the attention of health professionals towards the importance of including a multidisciplinary team in the diagnosis.

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