Epidemiologic behavior of osteosarcoma in Mexican population from 2005 to 2014

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Abstract

Introduction: Osteosarcoma represents 15% of bone neoplasms. In Mexico, it accounts for 4.5% of all neoplasms and for 46.6 to74% of malignant bone tumors, with slight prevalence in teenage males; 50-80% affects the knee and the proximal humerus.

Objetive: To identify distribution, relative frequency and tendencies in osteosarcoma, and projections to a five-year time.

Materials and methods: Epidemiologic study of a patient database analyzing histological diagnosis of osteosarcoma between 2005 and 2014. We assessed the following data: age, sex, diagnosis, location, side and stage with descriptive statistics and dispersion. Results were subject to analysis using the Pearson's index and lineal regression by the method of least squares.

Results: We analyzed 4744 cases. The incidence of osteosarcoma was of 3.29%, and it accounted for 56.2% of all primary malignant bone tumors. Patients' age was 18.6 ± 16.8 years old, with greater incidence in the second decade of life (54.1%). Male to female ratio was 1.64:1. Osteosarcoma involved the knee in 55.8% of the cases, followed by the proximal humerus (7.1%). The prevalent histological variety was osteoblastic osteosarcoma (76.9%). Stage IIB was the commonest one (77.6%) followed by stage IIIB (13.8%). In a five-year time, we predict an increase in the incidence of osteosarcoma.

Conclusions: This is the greatest series in Latin America. We predict an increase in the incidence of osteosarcoma. It is necessary to identify risk factors to outline this particular behavior.

Key words: Osteosarcoma; epidemiology.

Level of evidence: IV

Comportamiento epidemiológico del osteosarcoma en la población mexicana entre 2005 y 2014

Resumen

Introducción: El osteosarcoma representa el 15% de las neoplasias óseas. En México, constituye el 4,5% de las neoplasias y el 46,6-74% de los tumores óseos malignos, con ligero predominio en los varones adolescentes y el 50-80% en rodilla y húmero proximal.

Objetivo: Identificar la distribución, la frecuencia relativa y la tendencia del osteosarcoma y su proyección a cinco años.

Materiales y Métodos: Estudio epidemiológico, de registro de pacientes con diagnóstico histológico de osteosarcoma entre 2005 y 2014. Se analizaron los siguientes datos: edad, sexo, diagnóstico, localización, lado y estadio con estadística descriptiva y dispersión.Los resultados se sometieron a análisis mediante el índice de Pearson y regresión lineal por método de mínimos cuadrados.

Conflict of interests: The authors have reported none.

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Resultados: Se analizaron 4744 casos. La incidencia de osteosarcoma fue del 3,29% y constituyó el 56,2% de los tumores óseos malignos primarios. La edad de los pacientes era 18.6 ± 16.8 años, con mayor incidencia en la segunda década de la vida (54,1%); la relación hombre:mujer era de 1,64:1. El 55,8% comprometía la rodilla, seguida del húmero proximal (7,1%). La variedad histológica predominante fue osteoblástica (76,9%). El estadio IIB fue más frecuente (77,6%), seguido del IIIB (13,8%). A los cinco años, se predice un aumento en la incidencia de osteosarcoma.
Conclusiones: Esta es la mayor serie de osteosarcoma en América Latina. Se predice un incremento en la incidencia de osteosarcoma. Es necesario identificar factores de riesgo para establecer este comportamiento particular.

Palabras clave: Osteosarcoma; epidemiología.
Nivel de Evidencia: IV

Introduction

There are 12 million people around the world who are diagnosed with cancer; 3% of them (360,000) are children. Cancer is the second cause of death in <20 year-old people around the world[1], and this is the reason why there is a need of improving early diagnosis and treatment.[2]

A 2012 review of pediatric cancer estimates a greater incidence in developing countries (147,000 cases per year),[2] Mexico among them, with an incidence of 145 cases/ million/ year (7000 cases per year); 60% of them dies.[1] Sarcoma represents 21% of all pediatric solid malignant neoplasms and <1% of all solid malignant neoplasms.[3] In the United Kingdom, malignant bone tumors account for 0.7% of all cancer diagnosis.[4]

In the National Registry of Cancer in Children and Adolescents, bone tumors represent 8.2% and, in the Histological Registry of Malignant Neoplasms, osteosarcoma accounts for 5.36% of all cases.[1] In the Rivera-Luna et al.'s multi-center study, from 2007 to 2012, 3.9% (567 cases) of 14,178 patients with cancer was diagnosed with osteosarcoma, with a yearly incidence of 4.5 to 8.1 cases/ million in children < 18.[2]

At international level, there are reports of 5-6% of osteosarcoma among all pediatric malignant neoplasms[5] and 10% of all solid malignant tumors is reported as such; osteosarcoma represents the commonest primary bone cancer, with an incidence of 2 to 3/ million of inhabitants/ year, and it reaches 8-11/ million of inhabitants/ year among the 15-19 year-old ones.[6-9] In the United States, it is diagnosed in 400 <20 year-old patients per year and there are 900 cases every year.[10,11].

Among the pediatric inhabitants of the City of Mexico, osteosarcoma represents 4.5% of all neoplasms, 74% of malignant bone tumors;[12] it is ranked eighth among all the malignant neoplasms diagnosed in insured children at the Social Security Mexican Institute, and it represents the seventh cause of death by cancer.[5]

It is the second malignant bone neoplasm in frequency among children, adolescent and young adults,[13-20] and the commonest primary malignant bone tumor (it ranks seventh among pediatric malignant bone neoplasms); it accounts for 50 to 60% of all sarcomas.[21-22]

Osteosarcoma is expected to keep growing, because populations in the developing countries are younger and they become greater as time goes by.[2]

Materials and methods

Epidemiologic study carried out by the Histological Registry at the Orthopedics Hospital "Dr. Victorio de la Fuente Narváez", in which all the biopsies and the cases of osteosarcoma confirmed by histological assessment were identified.

The data collected are as follows: sex, age, histological variety, affected bone, geographic area, side and stage as stated by the Enneking's classification. There was registry of male and female patients of any age between 2005 and 2014, and no patient without confirmation of histological diagnosis was included.

Sampling techniques were adopted out of convenience and not because of probabilistic of consecutive cases.

We used descriptive statistics with central tendency measures: mean, median and mode for not-gathered data about quantitative variables, apart from dispersion measures: standard deviation. Descriptive statistics with measures of simple frequency: percentages for the qualitative variables. We performed calculation of incidence.

The calculation of lineal regression for the projection of data dispersion to a five-year time, and the proof of the incidental behavior of the osteosarcoma were carried out with the method of least squares and the Pearson's index, respectively.

Results

We found 4744 cases of bone and soft tissues tumor; 156 of them were osteosarcomas. Relative incidence was of 3.29%. Among primary bone tumors (2225 cases), osteosarcoma incidence was of 7.06% and, among bone malignant neoplasms (404 cases), it was of 38.6%. If we exclude hematologic neoplasms (plasmacytoma, multiple myeloma and lymphoma), osteosarcoma is associated with the greatest incidence (56.2%, n= 276), followed by chondrosarcoma, Ewin's sarcoma and other types of malignant mesenchymal neoplasms (Figure 1).

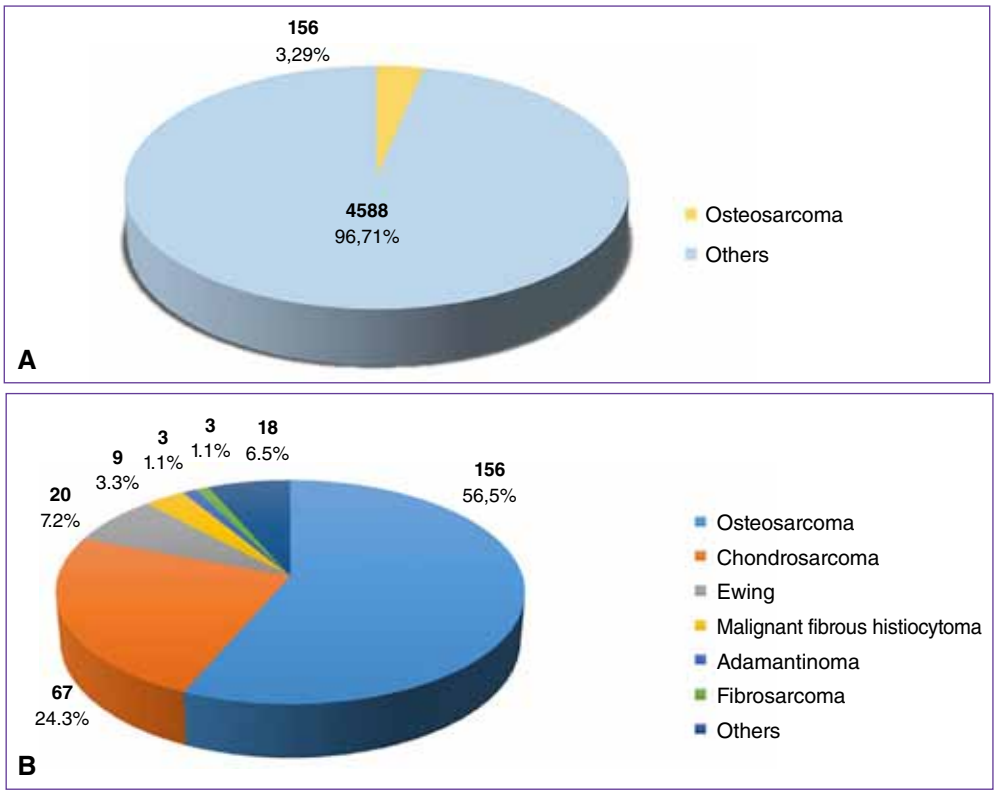

Figure 1. Review of 4744 cases of bone and soft tissues tumors.

Average age was 16 years old; median age, 18.62 ± 10.8 years old (ranging from 3 to 62) with a peak age of incidence in the second decade of life (54.19%). As regards sex, 95 cases (60.9%) occurred in males, and 61 cases, in females (39.1%), with a ratio males to females of 1.56:1 (Figure 2).

As regards bone affectation, 101 cases involved the femur (64.7%); 33, the tibia (21.2%); 11, the humerus (7.1%); five, the fibula (3.2%); one, the radius (0.6%) and one, the pelvis (0.6%); three cases involved the lumbar column (1.9%), and one, the cervical column (0.6%). Fifty-five dot eight percent occurred around the knee: in

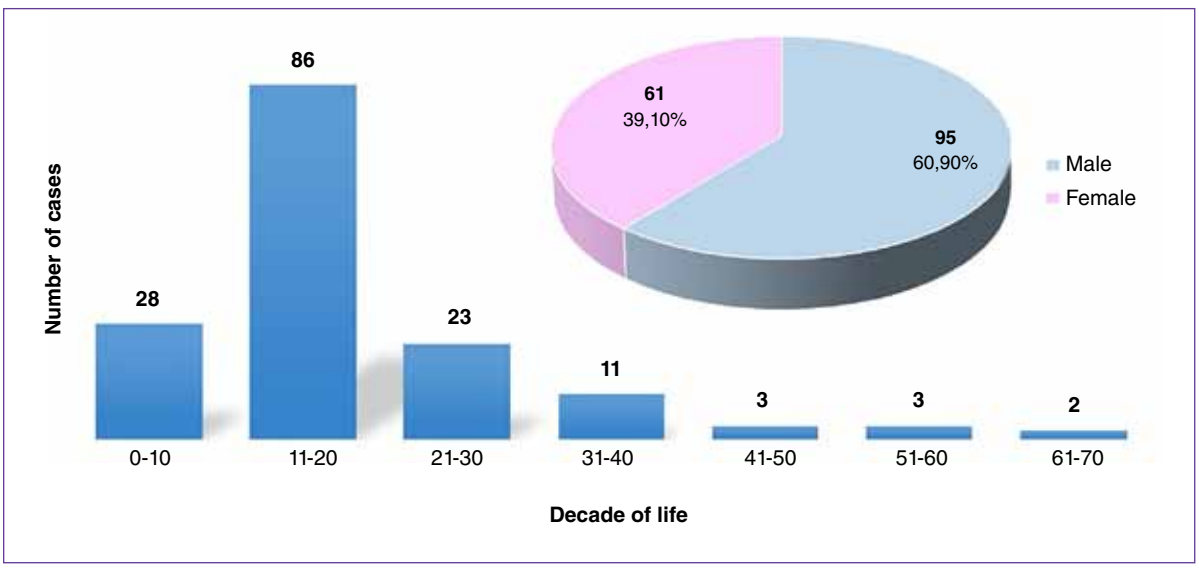

Figure 2. Distribution of osteosarcoma by sex and age: greater incidence in the second decade of life. More than 80% of all cases occur in the first three decades of life. Note the lack of the second pick age of incidence associated with the Paget's disease.

the distal femur (87 cases, 77%), in the proximal tibia (22 cases, 19.5%) and in the proximal fibula (4 cases, 3.5%). Proximal humerus ranked third among occurrence locations, with 11 cases (Table).

Regarding histological variety, in 120 cases (76.9%), the component was osteoblastic; in 8, telangiectasic (5.1%) and , in 28 cases (17.9%) , it was of other varieties: chondroblastic (6 cases, 3.8%), fibroblasatic (1 case, 0.6%), fibroblastic and chondroblastic (1 case, 0.6%), periosteal (1 case, 0.6%), parosteal (10 cases, 6.4%), of the small cells type (2 cases, 1.3%), of the malignant fibrous histiocytoma type (2 cases, 1.3%), of the low grade type (2 cases, 1.3%), and rich in giant cells (3 cases, 1.9%) (Figure 3).

As regards the stage neoplasms were diagnosed in, 118 cases (77.6%) were stage IIB; 21 (13.8%), stage IIIB; four (2.6%), stage IB and four (2.6%), stage IIA. Four cases (column) could not be classified using this system and, in 5 cases (3.3%) there was not enough information for tumor staging (Figure 4). Among the stage-IIB cases, 57.14% occurred in the distal femur; 13.45%, in the proximal tibia; 7.56%, in the proximal humerus; 6.72%, in the proximal femur, and 5.04%, in the distal tibia; the rest affected other locations. Among the stage-IIIB cases, 52.38% occurred in the distal femur; 9.52%, in the proximal femur; 9.52%, in the proximal fibula, and 9.52%, in the proximal tibia. The only case in the distal radius was staged as IIIB.

Table. Anatomic distribution of osteosarcoma.

Bone	Cases	%
Femur	*101*	*64.7*
Proximal (relative %)	9	8,9
Distal (relative %)	87	86.1
Diaphysis (relative %)	5	5.0
Tibia	*33*	*21.2*
Proximal (relative %)	22	66.7
Distal (relative %)	7	21
Diaphysis (relative %)	4	12.1
Humerus	*11*	*7.1*
Proximal (relative %)	11	100
Fibula	*5*	*3.2*
Proximal (relative %)	4	80.0
Distal (relative %)	1	20.0
Radius	*1*	*0.6*
Distal (relative %)	1	100
Pelvis	*1*	*0.6*
Ilion (relative %)	1	100
Column	*4*	*2.6*

More than 50% of the cases come up in the area of the knee, followed by the proximal humerus and other less frequent locations.

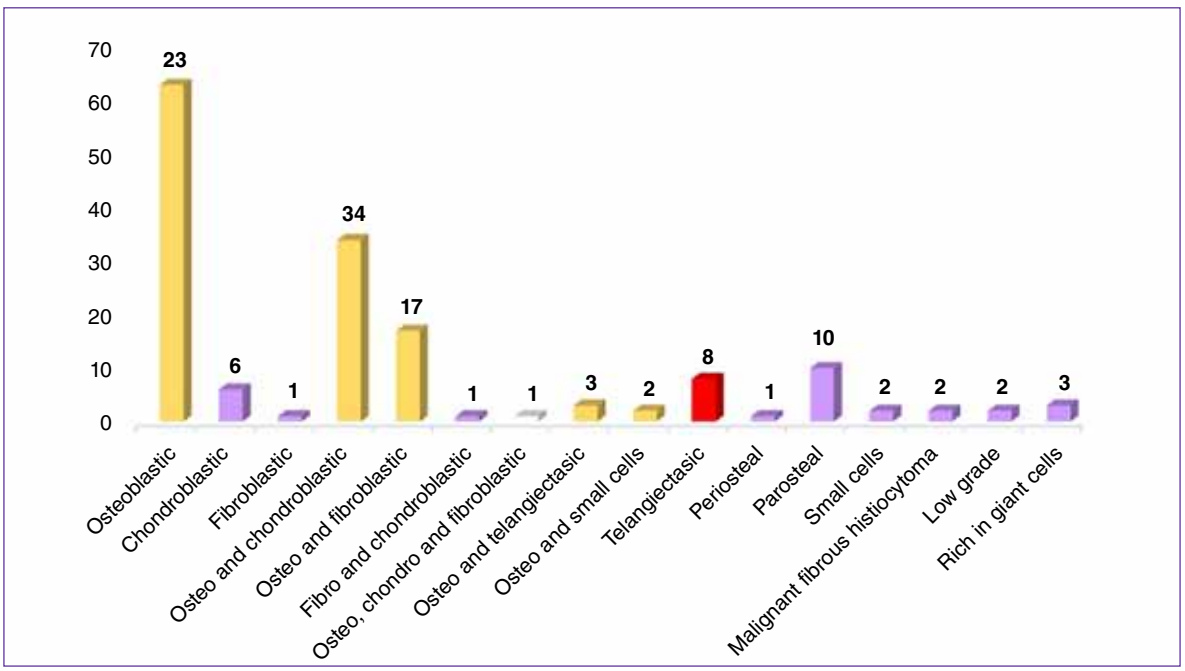

Figure 3. Osteosarcoma histological variety. Osteoblastic osteosarcoma was the commonest histological variety, followed by parosteal and chondroblastic osteosarcoma. Telangiectasic osteosarcoma occurred in 5.1% of the cases, what represents greater frequency than that previously reported.

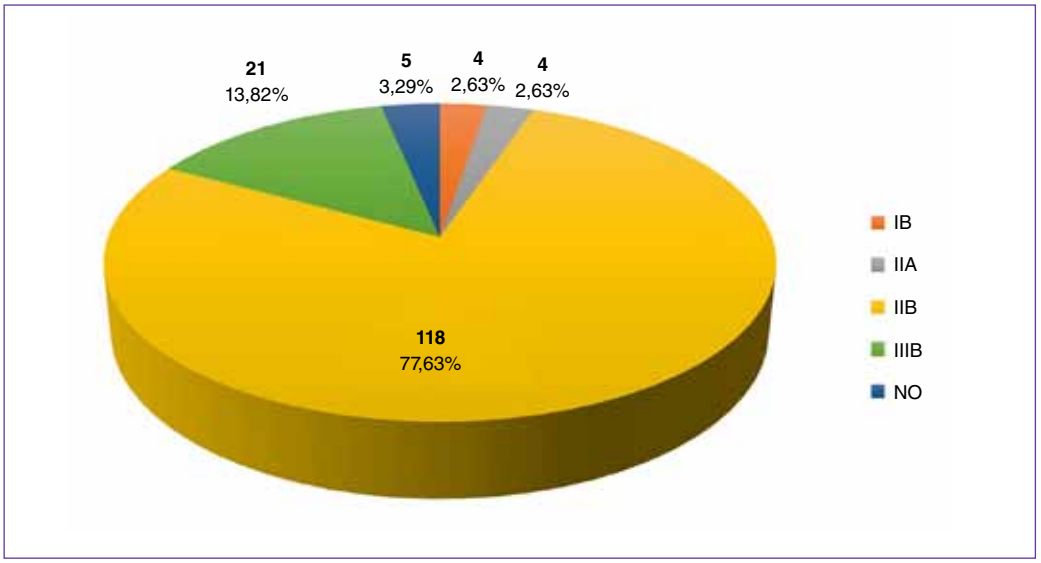

Figure 4. Osteosarcoma by staging at occurrence time (Enneking, 1986).

As the analysis of lineal regression suggests, the association was proved using the Pearson's index, it was positive with values of 0.00049. By means of this method, it is possible to predict a one-case-per-year increase in the incidence of osteosarcoma, with an up-to-4.29% relative incidence (Figure 5). Likewise, osteosarcoma incidence is expected to increase within some groups of histological varieties. Regarding anatomic location, incidence in the femur as a whole is expected to increase, in two cases, and in the proximal femur, in two cases in a five-year time and, unusually enough, occurrence in the distal femur and the femoral diaphysis is not expected to increase as compared to the latest year's registries. On the other hand, tibial incidence is expected to increase in three cases in a five-year time. Humeral incidence is expected to increase in one case in such time, and fibular incidence will show

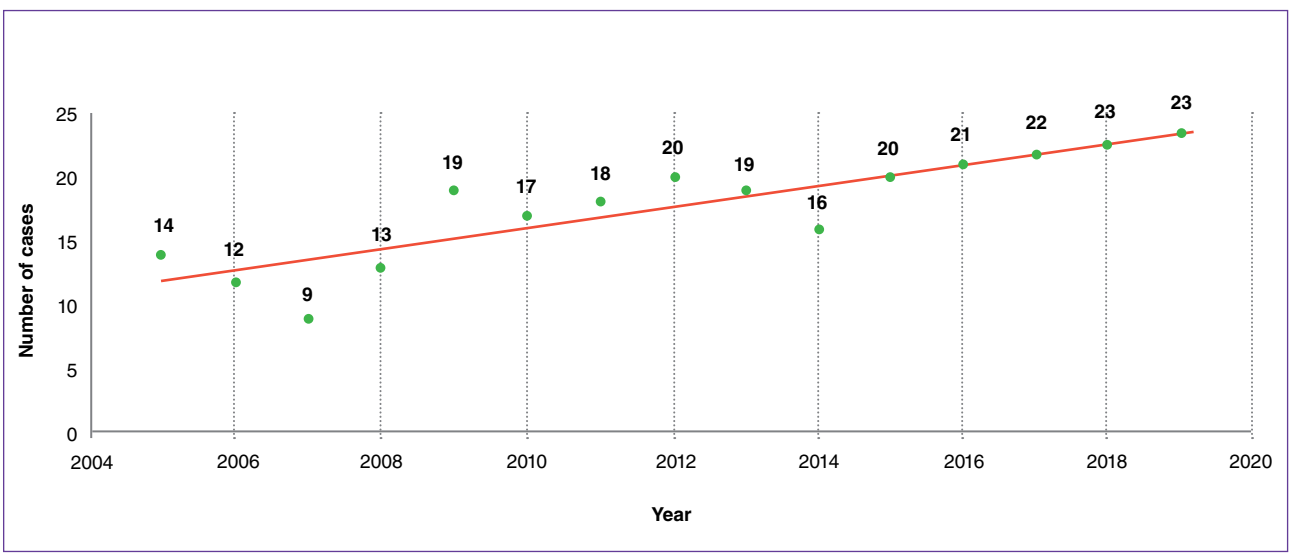

Figure 5. Yearly tendency in osteosarcoma.

no changes. Finally, regarding the stage the osteosarcoma is diagnosed in, stage IIB is expected to increase in five cases in a five-year time and stage IIIB is expected to increase in four cases in such time as compared to the latest year's registries, whereas within the other stages there are not expected changes (Figure 6).

Discussion

In our population, osteosarcoma represents 56.2% of all malignant bone tumors as stated by international literatura.[3,5] Its greatest frequency is during adolescence, from 11 to 20 years old (54.19%), with average age of occurrence of 16.[5-8] In the Mayo Clinic series, 1952 osteosarcomas were reviewed up to 2010 and only 61 of them had Paget's disease as precursor; and it accounts for 27.5% of all malignant bone tumors and 19.2% of all bone tumors. It is the commonest tumor, excluding myeloma.[21-23]

At the Orthopedics Hospital "Dr. Victorio de la Fuente Narváez", Social Security Mexican Institute, osteosarcoma diagnosis is, on average, 15 cases per year, and 13.8% is associated with metastasis when it is diagnosed, contrarily to the reported 15-20%, and there is not any commoner neoplasm.[9,10,13-15]

In the Histological Registry at the Orthopedics Hospital "Dr. Victorio de la Fuente Narváez", malignant bone neoplasms included 18.16% of the primary bone tumors in general; on the contrary, in the National Registry of Cancer in Children and Adolescents, malignant bone tumors occur in 8.2%,[1] and this is ascribed to the characteristics of the population admitted at our unit, because patients are specifically treated for conditions of the muscle-skeletal system.

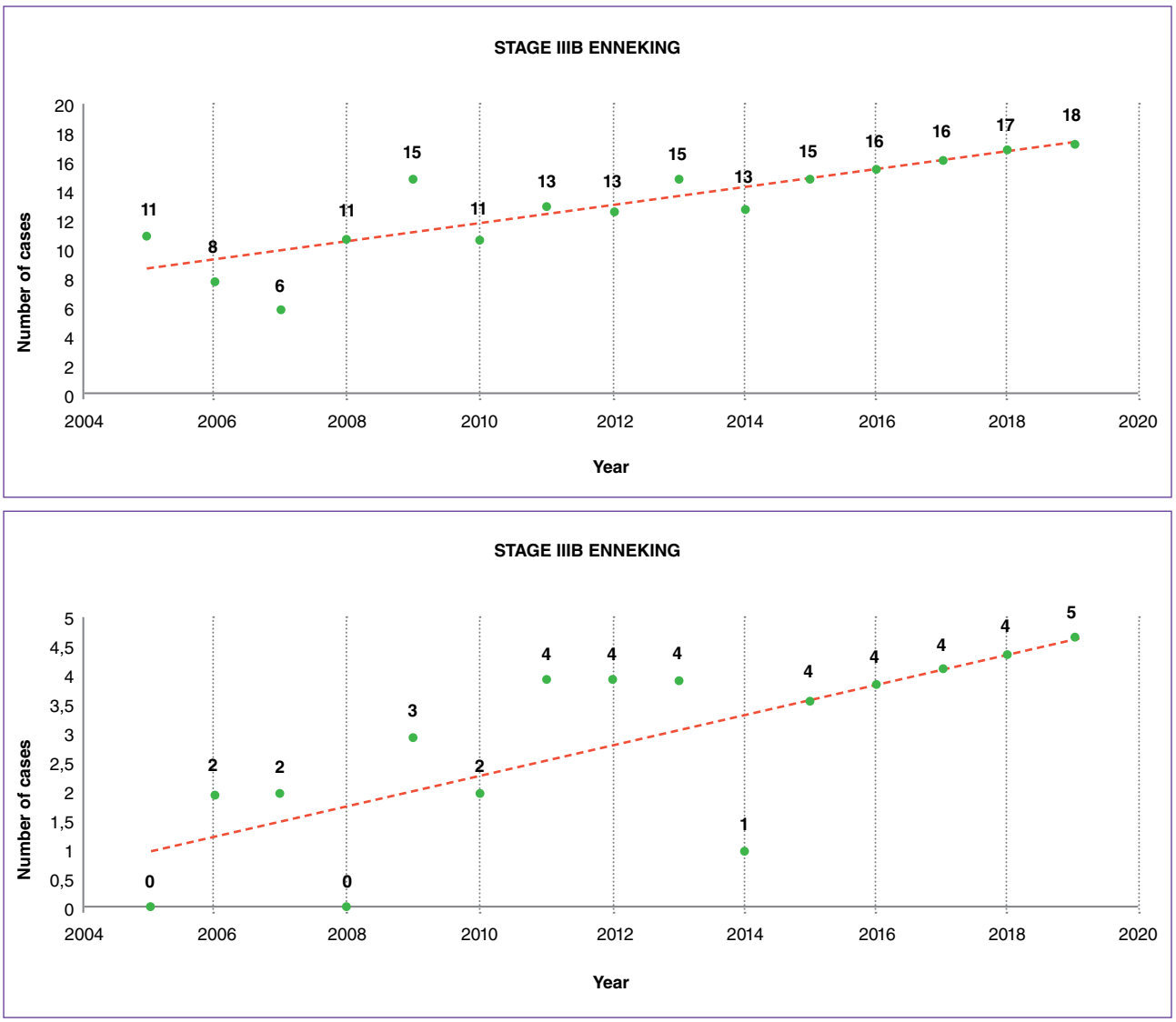

Figure 6. Proportional increase in cases of osteosarcoma in stages IIB and IIIB; increases in stages IB, IIA and others are not expected.

In the Histological Registry of Malignant Neoplasms, osteosarcoma represents 5.36% of all cases[1] and, in this study, 38.86% of malignant bone tumors in general.

Contrarily to the results of the retrospective study carried out at the Rehabilitation National Institute, in which malignant bone tumors were found to account for 28.4% of all cases and the osteosarcoma to be the commonest malignant bone tumor (46.6%), followed by chondrosarcoma,[10] in this study primary malignant bone tumors were found to represent 12.4% and, the osteosarcoma, 56.88%, coinciding with literature.[2,9,24]

As regards age, 69.8% of osteosarcoma occurred in the two first decades of life in this study, whereas bibliography reports it to occur between 15 and 25 years of age in up to 75% of the cases. Occurrence median in our study was 18.5 years old, 2.5 later than what is reported in other studies.[4,21-23,25,26] A second peak age of incidence at the end of adulthood has been reported, but it was not found in this study. Osteosarcoma is hardly frequent in <6 year-old children and >60year-old adults; however, we found two patients in each of these groups. [16-19,21-23,25] In osteosarcoma, the male to female ratio is approximately from 1.4:1 to 1.5:1, with slight prevalence of males,[4-6,12] a tendency that showed slightly stronger in our study (1.56:1).[21-23]

Osteosarcoma occurs mainly in the justaepiphyseal areas of long bones fast growth in 80-90% of cases.[12] It has been reported that 50-80% of all osteosarcomas comes up in the area of the knee and the proximal humerus as a whole; in this study, however, 62.9% of them was detected in such areas and the remaining 37.1% in other locations, as shown in the Table. [20,21-23,27] According to the American national cancer database, osteosarcoma occurs in the distal femoral and proximal tibial metaphyses (knee) in 57.6% of all cases, and in the proximal humerus in 11.7%.[17-19] Jaffe et al., however, report the femur (42%, with 75% in the distal femur), the tibia (19%, with 80% in the proximal tibia) and the humerus (10%, with 90% in the proximal humerus) as the commonest occurrence locations. Other likely locations are the skull or the jaw (8%), and the pelvis (8%)[28] and, in this study, the fibula (3.2%), the distal radius (0.6%), the pelvis (0.6%) and the column (2.6%).

In 80% of the cases, initial occurrence is circumscribed,[9,29-31] something which coincides with our study.

The osteoblastic variety prevails in more than 85% of the cases;[5] between 1981 and 2002, Eyre et al. reported 209 osteoblastic osteosarcomas, 14 chondroblastic osteosarcomas, six fibroblastic osteosarcomas, five telangiectasic osteosarcomas and two small cells osteosarcomas;[4] among the conventional osteosarcomas reported by the Mayo Clinic, 56% are osteoblastic osteosarcomas, 20% are chondroblastic osteosarcomas and 24% are fibroblastic osteosarcomas and, among general osteosarcomas, 3.4% are of the telangiectasic type.[21-23] On the contrary, in our study, we found more histological variability in osteosarcoma, what coincides with the World Health Organization's reports.[32]

As regards the stage osteosarcoma is diagnosed in, it was stage IIB in 118 cases (77.6%), IIIB in 21 cases (13.8%), IB in four cases (2.6%), and IIA in four cases (2.6%). It was not possible to classify the lesion in four cases (column) with this system and, in five cases (3.3%) there was not enough information for tumor staging.

Since 2010, in Mexico, cancer ranks second among the main causes of death in children between 4 and 15 years of age, and it represents a national health issue. In most Latin American countries, early cancer diagnosis fails, there are no clinic essays about treatment protocols, and we lack in appropriate health systems. Nowadays, pediatric cancer should be a global health priority.[2]

Conclusions

In this study, we found yearly incidence rates of osteosarcoma similar to those reported in the specialized literature and, due to the characteristics of the population admitted, it is the commonest one, being even commoner than multiple myeloma and plasmacytoma. The male to female ratio and the occurrence age coincide with those reported; in the population assessed, however, we do not find the second pick age of incidence associated with the Paget's disease. We confirm that the prevailing location of anatomic occurrence is around the knee, followed by the proximal humerus, the ankle, the column, the distal radius and the pelvis.

From the histological point of view, the osteoblastic component was the commonest, followed by the parosteal one, the telangiectasic one, the chondroblastic one and other less frequent varieties. As stated by the Enneking's staging, state IIB was the commonest, followed by stages IIIB, IB and IA.

The analysis of lineal regression predicts rising tendencies in the incidence of osteosarcoma and, within the cases, in that of all the histological varieties, in the femur, the tibia and the proximal humerus. Regarding staging, incidences of stages IIB and IIIB are expected to increase, with no changes in the other ones in a five-year time.

It is necessary to carry out studies to identify risk factors and, this way, prove the differences in osteosarcoma behavior within the assessed population.

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