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EPIDEMIOLOGICAL STUDY OF HEMATOLOGICAL CHANGES IN PRIMARY MALIGNANT BONE TUMOR IN ADULT AND PEDIATRIC AT BLOOD DISEASES CANCER OF THE SULAYMANIYAH PROVINCE OF IRAQI KURDISTAN

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Abstract

Primary Malignant Bone tumor in pediatrics are rare tumors that affect bones in children and adolescents, known (Sarcoma), common type sarcoma are osteosarcoma commonly affect appendicular skeleton (long bones) and Ewing sarcoma that effect axial skeleton(flat bone) .

Patients and methods : This study included 91 pediatric patient (0-18) years ages of both gender with primary malignant bone cancer ,registered and diagnosed in Hiwa Cancer Hospital\ Sulaymaniyah city, from the time period (2016-2019) to study the characteristics of patients: age, gender, symptoms and signs, clinical stages, primary site , and metastatic site of bone cancer.

Results: Male showed a significantly higher incidence than females, with a male-female ratio of 1.2:1 and rural population almost all parts of the country had highest incidence . Ewing sarcoma 1st most common type 53% with mean age 12.8 years, area involved 59% in appendicular skeleton and 40% in axial skeleton, 26% of patient had metastasis at diagnosis, mostly bone, lung and bone marrow , symptoms that might aid diagnosis ES included early local volume increase, neurological symptoms and the presence of fever. Osteosarcoma 2nd most common type 46% with a mean age of 15.7 years, were located 95% in appendicular skeleton and 4% in axial skeleton, 16% of patient had metastasis at diagnosis, mostly lung .

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Conclusion: In this study, Ewing sarcoma were the first most common type and osteosarcoma were second common type, with male predominance in both types. We haven't stage I in ES . Adolescent age group with OS not ES observed taller in comparison with other OS age group at time of diagnosis correlated to pubertal skeletal growth as a risk factor.

Keywords: Primary Malignant Bone Tumors, Osteosarcoma; Ewing's Sarcoma..

Introduction

Worldwide, primary malignant bone tumors are among the top causes of death and disability in children and teenagers. 1. The most common forms of sarcomas in children and adolescents are osteosarcomas (OS) and ewing sarcomas (ES), although there are more than twenty subtypes within this histologically diverse group. 2, 3 with systemic symptoms (fever, weight loss) and most typical complaints (pain, limping, limited movement of the afflicted extremity, fracture) 4, 5. Factors such as skeletal development, gender, age, genetics, and environment all contribute to the development of bone cancer in children. No. 6.

Osteosarcomas develop in the metaphyseal of rapidly growing bones such as the distal femur, proximal tibia, and proximal humerus during the first two decades of life; other types of Ewing sarcoma tumors include skin tumors of the chest wall, PNETs that affect the flat bones of the axial skeleton (especially the pelvis and costal arches), and PNETs that affect the long bones 7, 8, 9, and 10.

Imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), bone scans, positron emission tomography (PET) scans to assess the level of involvement in the skeleton, blood tests, and a biopsy are essential for a definitive histologic diagnosis; these procedures are best performed by a multidisciplinary team in a specialized center that includes pediatric medical oncology, radiation oncology, orthopedic surgery, and pathology. 11.

Although ALP is present in every tissue in the body, it is most abundant in the kidneys, liver, placenta, and bones. 12. It has been used to monitor initial bone lesions and is thought to have a role in the mineralization of freshly created bone. ALP, which is abundant in osteoblasts, is also a bone-forming marker. (13, 14).

The primary objective of this research was to evaluate the distribution and characteristics of primary malignant bone tumors (Osteosarcoma and Ewing's sarcoma) at Hiwa Cancer Hospital in Sulimania City.

Patients

Over the past nine years, from March 2010 to March 2019, data were gathered from the Pediatric Department of the Hiwa Cancer Center in Sulaymaniyah City. Permission to do so was granted by the Sulaimaniyah Director of Health and the Hiwa Hospital Manager.

Eligibility requirements: Patients from all across the nation, ranging in age from zero to eighteen, were included in the study group. They had recently been diagnosed with a malignant primary bone tumor, and the histological analysis determined their gender.

Patients must not meet the following criteria: they must not have a history of benign or secondary malignant bone tumors, extraosseous (soft tissue) ESFT, be above the age of 18, or have relapsed bone sarcoma.

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The variables included patient age at diagnosis, gender, histology, residence, and tumor stage as determined by the Enneking system. An auto-analyzer (Architect/Plus USA) was used to quantify enzyme activity, and serum ALP levels were quantified in international units (IU). The fast bone turnover rate and high skeletal growth velocity in youngsters cause their serum ALP levels to be markedly raised. Hence, to accommodate for fluctuations in serum levels caused by age, serum ALP ranges of 60.0–300.0 IU/L for patients younger than 15 years and 38.0–115.5 IU/L for patients older than or equal to 15 years were deemed normal.

The Statistical Package for the Social Sciences (SPSS) tool, version 23, was utilized to input all patient data. Statistical descriptions are given as the mean plus or minus the standard error of the mean, while frequency counts are given as percentages.

To compare the two means, an independent sample t-test was employed. Results are displayed as tables and/or graphs in all statistical analyses with a p-value set at a level of significance probability of ($\leqslant 0.05$).

Results:

Based on the type of tumor, our study separated 91 patients into two groups: 49 patients (53.84%) with Ewing's sarcoma and 42 patients (46.15%) with osteosarcoma. There were 50 male cases (54.49%) and 41 female cases (45.05%), for a ratio of 1.2:1. Patients with osteosarcoma had an average age of 15.7 ± 2.8 years, while those with Ewing's sarcoma had an average age of 12.8 ± 3 years, according to a descriptive statistical study of patient ages. There was a statistically significant difference in ages between the two groups. According to the data in Table 1, there are 29 cases of ES (59.18%) in rural areas, compared to 20 cases in urban areas (40.81%). Similarly, there are 23 cases of OS (54.76%) in rural areas, compared to 19 cases in urban areas (45.23%).

Figure 1 shows that out of the 26–49 E.S. patients in our investigation, 53.1% had classic morphology and 47.0% were classified as PNET. No unusual subtypes were found.

Conventional (intramedullary high-grade) classical osteosarcoma accounts for 83.33% (35\42 instances) of all osteosarcomas. As shown in figure 2, the distribution of the various histologic subtypes of osteosarcoma in our sample was as follows: parosteal 7.14% (32/42 cases), telangiectatic 4.76% (2/42 instances), and a combined 2.38% (1/42 cases) of periosteal and small cell subtypes.

Stage I was not observed in any of the ES patients; however, 9.52 percent (4/42) of the OS cases were at this stage. Stage II was detected in 73.46 percent (36/49) of the ES cases and 73.8 percent (31/42) of the OS cases. As shown in table (2), the percentage of ES cases with metastatic illnesses at presentation is 26.53% (13/49), while 16.66% (7/42) are OS cases.

Discussion and Conclusion:

Consistent with a study conducted in Iraq ten years ago that found ES to be the most prevalent primary malignant bone tumor, accounting for 51.3% of cases, followed by OS at 48%, our analysis of 91 pediatric and adolescent patients separated into two groups based on the most common kind of bone tumor confirmed these findings. While 87 ES was listed as the most prevalent primary malignant bone tumor in several areas (16, 17), another study in southern Iraq (35.92%) indicated that osteosarcoma was the most common primary malignant bone tumor (18). There was a small male predominance in the whole bone sarcoma type, with 50/91 patients (54.4%) being male and 41/91 cases (45.0%) being female, for a ratio of 1.2:1. Consistent with

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study 19 in Kurdistan, where the gender breakdown was 42% for women and 55.1% for men, the current research's ES prevalence was 44.8% for females. According to the results of the study conducted in Turkey by Al-Jumaily et al. (20), the gender breakdown of OS participants was 54.7% male and 45.2% female. This finding is consistent with the study's results. 94 There may be a causative association between the ages of maximal skeletal growth and an increased vulnerability to bone cancer since OS is more common in boys than girls, according to Western statistics, particularly in adolescent patients. Our patients' ages varied from 0 to 18 years, with a median age of 15.7 ± 2.8 years for OS and 12.8 ± 3 years for ES bone tumors, according to the age distribution of 21. Distinct age groups showed statistically significant differences (P-value = 0.05), which is in line with other research. OS etiology may be influenced by the fast bone growth that occurs throughout puberty, as the greatest incidence of OS occurs during this time. However, the cause of Ewing sarcoma during this period is still unknown. 22.

According to previous research, the frequency of primary malignant tumors in rural areas was 52.1% higher than in urban areas, a difference that is consistent with other studies that have found that environmental, cultural, racial, and genetic factors all play a role in the variation in the prevalence of malignant tumors. 23. Ewing sarcoma is more common among black populations in the United States and Africa, and descriptive epidemiology supports early observations that relate risk to bone growth rate. 24.

Consistent with previous research, the most prevalent subtype was classical histology (53% of patients), followed by PNET (47.0%). No unusual subtypes were found. 25. The histological confirmation of osteosarcoma requires the presence of a malignant sarcomatous stroma linked to the formation of osteoid tumors, which are marked by a high level of genetic complexity. The conventional subtype of osteosarcoma, which accounts for 83.3% of cases, is consistent with previous research showing that high-grade OS is the most prevalent in children. Other less common subtypes include parosteal and telangiectatic, while the periosteal and small cell histologic subtypes are extremely rare, accounting for less than 5% of cases. These numbers align with previous research. 25, 26, 27.

Stages I through III of primary bone sarcoma were defined by the Enneking staging system, which considered tumor grade, cancer location on the bone, and metastasis. Using the Enneking staging system for bone sarcoma, we found that none of the ES patients were in stage I (all of the ES histological subtypes were high grade), but fewer than 10% of the OS cases were in stage I when diagnosed. With 73.4% of ES and 73.8% of OS patients in stage II at diagnosis, metastatic stage III is more likely in 26.5% of ES patients compared to 16.6% of OS patients. Similarities between our data and those of other studies (26, 28) are evident.

Additionally, ALP has been proposed as a tumor marker in osteosarcoma [5, 14]. Nevertheless, there has been no validation of the clinical significance of high ALP levels in certain conditions.

Recommendation:

To Ministry of health we recommended to provide people health education program for pediatric bone tumor to prevent disabilities, and bone scan for staging . In future research we suggest studies about the role of environmental pollution (smoking ,nuclear weapons) as a risk factor for pediatric primary malignant bone tumor .

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References:

1- Borges E J, Paymaster JC and BhansalI S K.Primary malignant tumours of the bone. Clinical study of 330 cases. Amer J Surg. 1997,113: 225-231.

2- Baena Ocampo LC, Ramirez-Perez E, Linares-Gonzalez LM, Delgado-Chavez R . Epidemiology of bone tumors in Mexico City: retrospective clinicopathologic study of 566 patients at a referral institution. Ann Diag Path.2009,13, 16-21.

3- Pizzo PA, Poplack DG. Principles and Practice of Pediatric Oncology. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.

4- Lanzkowsky P. Manual of pediatric hematology and oncology. 5th ed. Oxford: Elsevier; 2011.

5- Yaw KM. Pediatric bone tumors. Semin Surg Oncol. 1999;16:173-83.

6- Widhe B, Widhe T. Initial symptoms and clinical features in osteosarcoma and Ewing sarcoma. J Bone Joint Surg Am. 2000;82:667- 74.

7- Fletcher C, Krishnan Unni KK, Mertens F (2002). editors: WHO classification of tumours: pathology and genetics of tumours of soft tissue and bone. Lyon: IARC Press; 11: 298.

8- Potratz J , Dirksen U, Jürgens H, et al. Ewing Sarcoma: Clinical State-of-the-Art; Pediatric Hematology-Oncology. 2012, 29, 1: 1-11.

9-Gomez-Martinez R, Silva-Padilla N, Gutierrez-de la OM, Tavares-Macias G Osteosarcoma metastasises at diagnostsis: caracteristic clinica y pronostic. GAMO, 2012.11, 296-9.

10- Mirabello L, Troisi RJ, Savage SA. International osteosarcoma incidence patterns in children and adolescents, middle ages, and elderly persons. Int J Cancer, 2009. 125, 229-34.

11- Albritton K, Bleyer WA. The management of cancer in the older adolescent. Eur J Cancer. 2013;39(18):2584–99.

12- Moss, D. W. 1987. Diagnostic aspects of alkaline phosphatase and its isoenzymes. Clin. Biochem.20:225–230.

13- Watts, N. B. 1999. Clinical utility of biochemical markers of bone remodeling. Clin. Chem. 45:1359–1368.

14- Leung, K. S., K. P. Fung, A. H. Sher, C. K. Li, and K. M. Lee. 1993. Plasma bone-specific alkaline phosphatase as an indicator of osteoblastic activity. The Journal of bone and joint surgery. British 75:288–292.

15- Yang, L., and V. Grey. 2006. Pediatric reference intervals for bone markers. Clin. Biochem. 39:561–568.

16-Ahmed M, Ghani A, Mansoor A, Khan AH. Pattern of malignant bone tumour in northern areas of Pakistan. J Pak Med Assoc. 1994; 44(9): 203-205.

17 - Dorfman HD, Czernaik B, Bone cancers. Cancer 1995; 75(1): 203-210. Results of Iraqi Cancer Registry,1995-1997. Ministry of Health 1999; p. 82. nd location. Clin Orthop. 1999 (167):250-4

18 - L. Al-Nasrallah, A. Al-Ahmed, M. Moh.Saeed.The Pattern Of Osteosarcoma In Southern Part Of Iraq The Pattern Of Osteosarcoma In Southern Part Of Iraq. Bas J Surg,13, 2007 ; 13: 35-41.

19- Majeed S ; Muhammad H; Murad K.Treatment Outcomes of Pediatric Patients With Ewing Sarcoma in a War-Torn Nation: Single-Institute Experience From Iraq. American Society of Clinical Oncology. 2019, 5(3): 1-5.

20- AL- Jumaily MA, AL- Sabbagh NM. Primary malignant bone tumors in Mosul. Basrah Journal of Surgery 1998; 2: 129-132. 88- Sadighi S, Raafat J. Sarcoma in Iran. Asian Pac J Cancer Prev. 2003; 4(2): 95-98.

21- Larsson SE, Lorentzon R. The incidence of malignant primary bone tumors in relation to age, sex, and site: a study of osteogenic sarcoma, chondrosarcoma, and Ewing's sarcoma diagnosed in Sweden from 1993 to 2001. J Bone Joint Surg 2000;56B:534–540.
22- Albritton K, Bleyer WA. The management of cancer in the older adolescent. Eur J Cancer. 2013;39(18):2584–99.
23 - Kaatsch P ,Jeomal K, Stiller C, , et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1990s (the ACCISproject).an epidemiological study. Lancet 2004;364:2097–105.
24- Omololu AB, Ogunbiyi JO, Ogunlade SO, et al. Primary malignant bone tumour in a tropical African University Teaching Hospital. West Afr J Med. 2002; 21(4): 291-5.
25- Lahat G, Lazar A, Lev D: Sarcoma epidemiology and etiology: potential environmental and genetic factors. Surg Clin North Am 2018,
88(3):451–481.
26- Katchy KC, Ziad F, Alexander S, et al. Malignant bone tumors in Kuwait. A 10-year clinicopathological study. Int Orthop 2005; 29(6): 406-411.
27- Bahebeck J, Atangana R, Eyenga V, et al. Bone tumours in Cameroon: incidence, demography and histopathology. In Orthop .2013; 27(5): 315-317.
28- Bondar IV, Durnov LA, Lebedev V, et al. Metastatic lung tumors in children. Vopr Onkol. 2015;46:446-8.

Table (1): Demographic Distribution of Patient with Primary Bone Tumor.

Study groups		Ewing	Osteosarcoma	
Mean Age P-value		**12.8 ± 3**	**15.7 ± 2.8**	**P= 0.05**
Frequency %		**49**	**42**	**91**
		53.84%	**46.15%**	**100%**
Male Frequency %		**27**	**23**	**50**
		55.10%	**54.76%**	**54.94%**
Female Frequency %		**2**	**19**	**41**
		44.89%	**45.23%**	**45.05%**
Rural		**29 (59.18%)**	**23 (54.76%)**	**52 (57.14%)**
Urban		**20 (40.81%)**	**19 (45.23%)**	**39 (42.85%)**
ALP at diagnosis	**Normal**			
	Elevated			

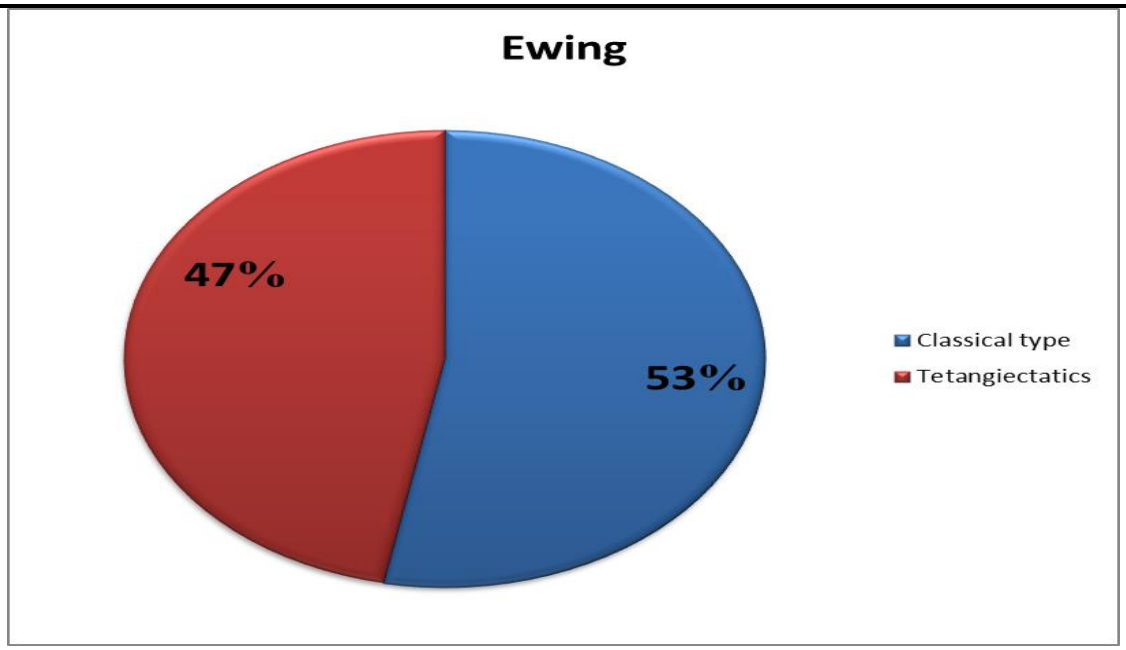

Figure (1): Histopathological Subtypes of Ewing sarcoma.

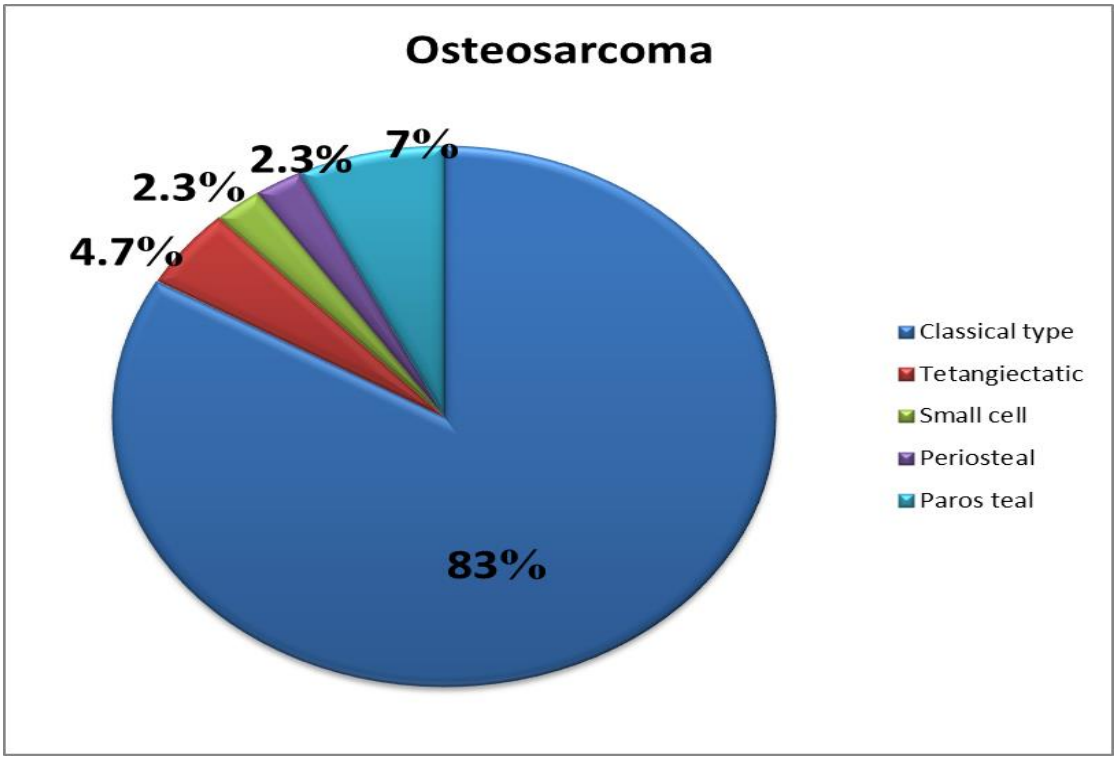

Figure (2) : Histopathological Subtypes of Osteosarcoma

Table (2): Staging of Tumors at Bone Sarcomas Diagnosis

Stages	ES (F, %)	OS (F, %)
Stage I A	/	**1 (2.38%)**
Stage I B	/	**3 (7.14%)**
Stage II A	**12 (24.48%)**	**16 (38.39%)**
Stage II B	**24 (48.97%)**	**15 (35.71%)**
Stage III	**13 (26.53%)**	**7 (16.66%)**
Total	**49**	**42**

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