

An Analysis of The Pattern and Frequency of Primary Malignant Bone Tumors in Nassyriah

Kareem Al-Zirkan¹

¹ M.B.Ch.B, F.I.C.M.S, College of Medicine, Al-Ayen University, Iraq. Email: kareem.kafy@alayen.edu.iq

KEYWORDS

Anatomical presentation

Bone tumors, Malignant tumors, Osteosarcoma, Prevalence,

ABSTRACT

Bone tumors are uncommon lesions and account for only 0.2% of all malignant tumors. Primary malignant bone tumors develop from bony tissue and are categorized according to their location of origin and the cell type that makes up the tumor. This research aims to report on the prevalence, geographic distribution, and comparison of malignant bone tumors in Nassyriha province. Malignant bone tumors were studied in 182 people (119 men and 63 females) between February 2021 and February 2023. Their ages varied widely (from 5 to 70), with the second decade being the most prevalent. The most common cancer was osteosarcoma, which accounted for 34.62 percent, followed by Ewing's sarcoma (24.73), chondrosarcoma (13.74), multiple myeloma (11.53), malignant giant cell tumors (8.14%), fibrosarcoma (2.74%), and 2 instances of chordoma (1.10%). None of the six instances (3.30%) could be definitively diagnosed. Primary malignant bone tumors are rising, with men being disproportionately impacted. Information gleaned from this study will be useful for both researchers and clinicians.

1. Introduction

Cancer is a major public health problem affecting millions worldwide, and its incidence continues to rise. Cancer remains a significant health issue despite significant advancements in oncology, with marked variations in incidence across geographical entities and time. One subset of cancer that has received much attention in recent years is primary malignant bone tumors. These tumors are relatively rare but can have a profound impact on the lives of those affected [1],[2],[3].

The study of primary malignant bone tumors dates back to the early 19th century when the English surgeon John Abernathy introduced the term "sarcoma" to describe these fleshy excrescences. In the United States, great strides were made in the mid-1900s in the field of bone pathology by Henry L. and his colleague Louis Lichtenstein. These advancements culminated in creating the Registry of bone sarcoma in 1921, a significant step towards better understanding and managing these tumors [4].

Despite being relatively uncommon, There are substantial differences in the prevalence, location, and age distribution of primary malignant bone tumors within countries. For instance, while these tumors constitute less than 1% of all cancers worldwide, they are more prevalent in south Iraq than in Europe. The exact causes of primary malignant bone tumors remain unknown, although some researchers hypothesize that they arise in centers of rapid skeletal growth. Other theories point to heredity factors, trauma, and exposure as possible causes[5],[6].

Primary malignant bone tumors may originate in osseous tissue (such as osteosarcoma, chondrosarcoma, and malignant giant cell tumor) or non-osseous tissue (such as Ewing's sarcoma, fibrosarcoma, and chordoma). Diagnosing and managing these tumors can be challenging, and there is a need for continued research and collaboration among clinicians and researchers to understand these tumors better and improve patient outcomes.

In 2021, Jain et al. [7] reviewed 97 cases of cancerous bone tumors. The most common ages for primary and metastatic bone tumors were between 11 and 20 years old and between 51 and 60 years old, respectively. Malignant bone tumors that started in the hip and spine were most common; the femur was the most prevalent location for subsequent bone tumors.

In 2022, Klangjorhor, Jeerawan, et al. [8] used information from 5 population-based cancer registries to look at the rates of bone sarcomas in Thailand between 2001 and 2015. Osteosarcoma, chondrosarcoma, and Ewing's sarcoma were the most common types of cancerous bone tumours.



Bone cancer is more likely to happen to men, and its rate changes with age in two ways. Patients with bone sarcoma in Thailand had 74% and 52% mortality rates after one year and five years, respectively. These rates were lower than those reported from other countries. Thailand needs better health education, care, and bone cancer treatments.

In 2022, Rani et al. [9] aimed to evaluate bone tumours' histopathological features and correlate them with demographic factors, clinical presentation, anatomical location, and radiological findings. 64 cases were studied, with 56.26% benign, 26.56% primary malignant, and 17.18% metastasis to bone. The most common benign tumor was Giant Cell Tumor, and the most common malignant tumor was osteosarcoma. These tumors pose a challenge to medical professionals due to their varied presentation, uncertain histogenesis, and response to treatment.

The ultimate purpose of this paper is to give a thorough review of primary malignant bone tumors to enable physicians and researchers better understand these tumors and improve patient outcomes.

2. Methodology

Over 2 years, from February 2021 to February 2023, in the Nassyriha area, 182 people with main invasive bone tumors were taken from the histopathology labs of private and public hospitals. This study contained comprising 63 females and 119 males. Each patient underwent a thorough clinical evaluation, including routine biochemical and haematological tests and plain radiography. Advanced imaging modalities such as bone, CT, and MRI were selectively employed.

Each patient's clinical traits, such as age, sex, clinical symptoms, imaging features, and the damaged bone's overall look, were carefully examined. Including private and governmental hospitals ensures a diverse patient population, and the comprehensive evaluation of clinical data allows for a more accurate analysis of the primary malignant bone tumors in the region.

Surgery remains the primary treatment option for tumors, with amputation or wide excision being the most commonly employed methods. The choice of surgical intervention depends on several factors, such as the tumor stage, grade, site, and metastases. The grade of the tumor, classified as low or high grade, plays a crucial role in determining the extent of surgical intervention required. Additionally, the tumour site, whether intracapsular, intra-compartmental, or extra-compartmental, and the presence of regional or distant metastases influence the decision for surgical management.

The incidence of amputation was evaluated in a cohort of patients diagnosed with osteosarcoma, Ewing's sarcoma, chondrosarcoma, multiple myeloma, malignant giant cell tumor, and fibrosarcoma. The results indicate that amputation as a treatment option varies depending on the type of cancer and underscores the need for individualized treatment plans for each patient.

All patients were referred to an oncology centre for post-surgical management to minimize the risk of recurrence and metastases. Chemotherapy was administered in 49.75% of cases, radiotherapy in 4.12%, and chemotherapy and radiotherapy in 46.13% of cases. Chemotherapy and radiotherapy is a standard approach to reduce the likelihood of cancer recurrence and improve overall patient outcomes. The follow-up period ranged between 6 and 24 months, which is a relatively short duration, and longer-term studies are necessary to evaluate the effectiveness of these treatment modalities in reducing the risk of recurrence and metastases in these types of cancers. Further studies may also identify potential adverse effects of these treatments, which could help optimize cancer management strategies.

3. Results and discussion

The distribution of age and sex among patients with primary malignant bone tumors is a topic of interest to medical professionals studying this disease. This study analysed 182 patients with primary malignant bone tumors to determine the age and sex distribution. Of these patients, 65.38% were male, and 34.62% were female, resulting in a male-to-female ratio of 1.88:1. The patients ranged from 5 to 70 years, with no patients under the age of 5 or over the age of 70.



The second decade of life, ranging from 10-19 years, was the most common age group affected, accounting for 64.84% of the cases. This finding is consistent with previous studies that have identified a bimodal age distribution for primary malignant bone tumors, with the first peak occurring in adolescence and young adulthood and a second peak occurring in later adulthood.

Table-1 shows the number of patients in each age category. Table-2 shows the gender distribution of patients. These tables help doctors and researchers analyze primary malignant bone tumor patients' demographics to create better therapies and preventative techniques.

Age of patients No. of patient 1 - 9 years 23 12.63% 10 - 19118 64..84 % 11 20 - 296.04% 30 - 397 3.85% 40 - 498 4.40% 10 50 - 595.49 % 3 60 - 691.65% 70 - 791.1%

Table 1. The Age Distribution

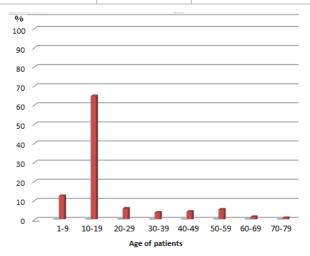


Figure 1: The patients' age dispersion

Table 2. The Sex Distribution

Gender	No. of patient	%
Male	119	65.38%
Female	63	34.62%
Total	182	



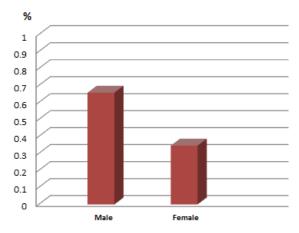


Figure 2: The patients' gender distribution

The clinical features observed in patients with the condition under investigation were analyzed in this study. Most patients (85.71%) reported experiencing pain as their primary complaint. Additionally, 72.52% of patients had a palpable swelling in the affected area. A smaller proportion of patients (13.73%) presented with signs of pathological or impending fracture, while ulceration was observed in only 4.94% of cases. Osteomyelitis was found to be a clinical feature in 2.74% of patients. These findings are summarized in Table 3, which presents the various clinical features observed in the patient cohort. It is important to note that further research is necessary to establish the correlation between these clinical features and the underlying condition.

Table 3. The Clinical Features (Presentation)

Presentation	No. of patient	%
Pain	156	85.71%
Palpable swelling	132	72.52%
Pathological or impending fracture	25	13.73%
Ulceration	9	4,94%
Clinical features of osteomyelitis	5	2.74%

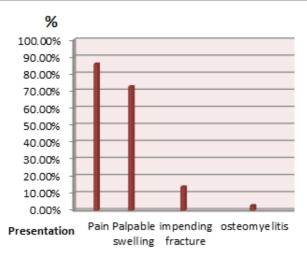


Figure 3: The clinical features

The primary malignant bone tumors exhibit varying anatomic distributions, with the femur being the



most frequently affected site, accounting for 59.34% of cases. The vertebrae follow the femur in terms of incidence of affection, with 17.58 % of cases reported. The tibia is the third most commonly affected site, with 14.29% of cases recorded. Other sites of the body are affected in 8.79% of cases. A detailed account of the anatomic distribution of primary malignant bone tumors can be found in Table-4. The data presented emphasizes the need for ongoing research to identify potential risk factors and improve early detection and treatment strategies.

 Anatomical site
 No. of patient
 %

 Femur
 108
 59.34%

 Vertebrae
 32
 17.58 %

 Tibia
 26
 14.29

 Others
 16
 8.79%

Table 4. The Anatomical Distribution

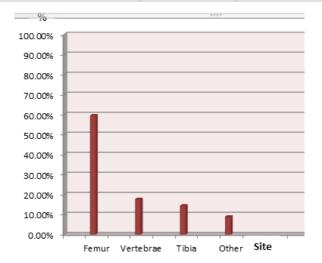


Figure 4: The anatomical distribution

The study investigated the histopathological findings of 182 patients with bone tumors. Osteosarcoma was identified in 63 patients, accounting for 34.62% of cases. Ewing's sarcoma was diagnosed in 45 patients, representing 24.73% of the cases, while chondrosarcoma was identified in 25 patients (13.74%). Multiple myeloma was found in 21 patients (11.53%), and malignant giant cell tumor was identified in 15 patients (8.24%). In addition, 5 patients (2.74%) had no clear diagnosis. Fibrosarcoma was detected in only 6 patients (3.30%), and chordoma in 2 patient (1.10%). These findings provide important information regarding the distribution of bone tumors and their prevalence in the studied population. The results of this study could be used as a foundation for future research to improve the diagnosis and treatment of bone tumors.

Anatomical site	No. of patient	%
Osteosarcoma	63	34.62%
Ewing's sarcoma	45	24.73%
Chondrosarcoma	25	13.74%
Multiple myeloma	21	11.53%
Malignant gaint cell	15	8.24 %
Fibrosarcoma	5	2.74%
Chordoma	2	1.10%
No clear-cut diagnosis	6	3.30%
Total	182	



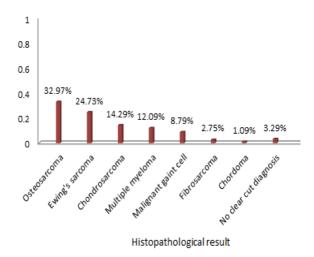


Figure 5: histopathological results

The study investigated the geographical distribution of bone tumors and their malignant transformation in Al Nassyriha province. The results revealed that the western part of the province, including Suq-Alshyuk, Nwashi, and Om ehnag, was the most commonly affected area, accounting for 60.39% of cases. The incidence of malignant transformation was observed in 6 cases of benign giant cell tumor, 3 cases of chondroma, and 2 cases of diaphyseal acalasia, representing 3.29%, 1.65%, and 1.1% of cases, respectively. The findings are summarized in Table-6, which displays the rates of malignant transformation among different types of bone tumors. These results highlight the need for further investigation into the factors contributing to the higher incidence of bone tumors and malignant transformation in this region.

Table 6. The Malignant Transformation

Type of benign lesions	No. of patient	%
Benign giant cell tumor	6	3.29%
Chondroma	3	1.65%
Diaphyseal achalasia	2	1.1%
Total	11	6.04%

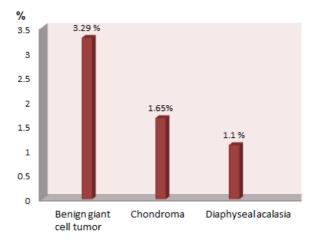


Figure 6: Lesion types

A study investigated the diagnostic procedures used in a group of patients. The results revealed that



most patients (82.42%) underwent open biopsy, while a smaller proportion (17.58%) had needle aspiration. The specific types of biopsy are presented in Table 7. It is important to note that biopsy is a common method for obtaining tissue samples for pathological analysis and is essential for accurate diagnosis and treatment planning.

Type of Biopsy % No. of patient Open incisional 150 82.42%

Table 7. The Types Of Biopsy

Needle aspiration 18 17.58% **Total** 182

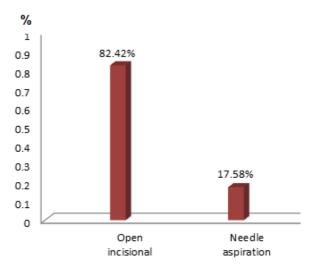


Figure 7: Types of biopsy

The table presented in Table-8 illustrates the various types of surgical interventions conducted. Out of all the procedures, a significant proportion of 156 (85.72%) resulted in amputations, while 16 (8.79%) patients underwent wide local excision. Additionally, 10 (5.49%) cases were considered inoperable, leading to the absence of surgical intervention.

Types of surgery No. of patient % Amputation 156 85.72% Wide local excision 16 8.79% **Inoperable** 10 5.49% **Total** 182

Table 8. Surgery Types

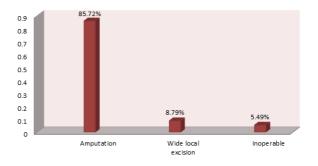


Figure 7: Type of surgery

The observation of local recurrences within amputation stumps is not uncommon, with a prevalence



rate of 3.96% in this study. Following such diagnosis, patients were subsequently referred to an oncology centre for treatment with chemotherapy, radiotherapy, or a combination of both modalities. Moreover, all amputees were directed to a prosthesis center for prosthesis fitting. The 2-year survival rate for this cohort was determined to be 37%. These findings underscore the importance of close post-operative monitoring and ongoing care for patients undergoing amputations.

Discussion

Although Osteosarcoma is a rare tumor it is an aggressive bone tumor that primarily affects the pediatric and young adult population. This neoplasm arises from mesenchymal cells that undergo malignant transformation, leading to osteoid or immature bone tissue formation. The incidence of osteosarcoma varies across different geographical regions, and in Iraq, the World Health Organization (WHO) has estimated the annual incidence to be approximately 3.4 cases per million population [10].

The current paper has revealed that osteosarcoma constitutes the predominant form of primary malignant bone tumors, with a proportion of 34.62%. The Iraqi cancer registry conducted between 2016 to 2020 [11] has reported a higher prevalence of osteosarcoma, accounting for 40.11% of all primary malignant bone tumors. It is important to note that these findings are not replicated from any prior studies and, therefore, novel in their contribution to understanding osteosarcoma epidemiology.

A study conducted in 2021[12] found that male predominance was more pronounced in Ewing sarcoma (EWS) than osteosarcoma, with a male-to-female ratio of 1.69 compared to 1.48. However, in the present study, male predominance was observed to be more prominent in osteosarcoma than EWS, with a male-to-female ratio of 1.88 compared to 1.40

Before the 1970s, osteosarcoma treatment primarily relied on surgical interventions, with limited success in improving patient outcomes. However, in 1972, a study from MD Anderson showed that chemotherapy could be used to treat osteosarcoma, with a 50% survival rate after two years. In 1981, a prospective study was started to see how two groups of osteosarcoma patients did. The first group had 27 people who didn't get any additional treatment. The second group had 32 people who got Adriamycin, high-dose methotrexate, or a mixture of bleomycin, Cytoxan, and actinomycin-D. This test stopped in 1984, when it was seen that people who got treatment did much better than those who didn't. 55% of those in the treatment group were still disease-free after two years, while only 20% of those in the other group were. Additionally, survival rates at two years significantly differed between the two groups, with 80% of patients in the treatment group versus 48% in the control group remaining alive [10].

A strong male predominance and an early peak in the second decade of life characterize the incidence of primary malignant bone tumors. This is mainly attributed to the high frequency of osteosarcoma and Ewing's sarcoma, which account for approximately 59.15% of all cases.

Regarding the anatomical distribution of primary malignant bone tumors, the femur is the most frequently involved site, followed by the vertebrae and tibia. Pelvic involvement is less common, accounting for approximately 4.51% of cases, while humerus and rib involvement are rarer, with frequencies of 3.29% and 0.99%, respectively. These findings are consistent with those reported by Jarrallah [13], who investigated the pattern of osteosarcoma in the southern region of Iraq.

In a more recent study by Al-Hashimi et al. conducted in 2021 [14], it was observed that the pelvis is the most commonly involved site for Ewing's sarcoma, while the lower extremities are more frequently affected by osteosarcoma. In the case of chondrosarcoma, involvement of the vertebrae, humerus, and ribs is more common.

This study has identified that the tumour size is a significant prognostic factor, as evidenced by the 148 patients with tumors greater than 5 cm. The large size of these tumors may indicate delayed diagnosis, which explains the need for amputation in 156 cases and inoperability in 9 patients. This finding is consistent with previous studies that have also demonstrated the impact of tumor size on



patient prognosis [15],[16]..

Additionally, 10 patients in the current study had a positive family history of malignancy. As such, obtaining a thorough family history is an important component of patient evaluation. Similar observations were made in the Al-Jameel study[17], which also identified 10 patients with a family history of malignancy. These findings support the well-established fact of a genetic predisposition to certain types of cancer.

All patients in this study underwent a biopsy for a definitive diagnosis of malignant bone tumors. Among the patients, 32 underwent fine needle aspiration, while an open incisional biopsy was performed in 164. Most patients underwent open incisional biopsy due to the unavailability of more advanced techniques such as ultrasound-guided needle biopsy [18] and a lack of experienced pathologists in the province.

However, this study encountered difficulties in obtaining accurate biopsy results, which can be attributed to the challenges in interpreting tissue samples taken from bone tumors. In order to improve the accuracy of biopsy results, more sophisticated investigations may be necessary, and it is advisable to seek the opinion of multiple medical experts, including pathologists, orthopaedic surgeons, oncologists, and radiologists.

Surgical intervention, either through excision or amputation, may result in a potential cure for the patient. However, combining surgical treatment with chemotherapy, radiotherapy, or other modalities may further decrease the likelihood of recurrence and metastasis. In a particular study, 48.35% of patients were treated with chemotherapy, 3.85% with radiotherapy, and 47.80% received both treatments.

The delay in seeking medical attention and patients' reluctance to undergo surgical intervention in the initial stage resulted in many patients requiring amputation and inoperability in this study.

Sixteen patients underwent wide local excision, which produced satisfactory outcomes. To fill the defect, bone cement was utilized, though several other options are available for gap filling, as documented in the literature [19-25].

Local recurrence in the amputation stump was observed in 12 patients. The most crucial factor in decreasing the recurrence is to ensure that the resection margin is reasonable and includes a cuff of normal tissue.

The western region of Al Nassyriha province had the highest cancer incidence, with 110 cases (60.44%) reported in this area. This observation may suggest a possible association between malignancy and radiation exposure. Studies investigating the health consequences of depleted uranium (D.U) weapons used by US and British forces revealed an increasing incidence of cancer cases and a shift in the epidemiological pattern among military personnel in southern Iraq over time [26,33,34].

In our situation, complete coverage of bone cancer still poses some challenges due to the medical staff's lack of active cooperation in providing detailed medical information. Some of our patients sought medical advice in nearby cities and Baghdad, and neglection could be a result of poverty, lack of education, and the limitation of CT scan and MRI facilities.

4. Conclusion and future scope

The investigation findings reveal a noticeable increase in primary malignant bone neoplasms. This observation could have significant implications for public health, as the incidence of bone tumors has been increasing globally in recent years.

The second decade of life exhibited the highest frequency of bone tumor incidence, which aligns with previous reports on primary bone tumors. This pattern could be related to the rapid growth and bone development during this period.



The study indicates a male predominance in the incidence of primary malignant bone tumors. This observation is consistent with previous research, which suggests that males are more prone to bone tumors than females due to various factors, including differences in hormonal profiles, genetic predisposition, and lifestyle factors.

The rising incidence of bone tumors highlights the need for improved surveillance and prevention measures to address this public health concern. Early detection and intervention can improve treatment outcomes and reduce the morbidity and mortality associated with bone tumors.

Further research is needed to explore the underlying causes of the observed increase in bone tumor incidence and to identify potential risk factors. A better understanding of the etiology and pathogenesis of bone tumors could lead to the development of more effective prevention and treatment strategies.

Reference

- [1] Markel, Justin E. Monitoring the Systemic Immune System to Understand and Improve the Efficacy of Immunotherapy for Metastatic Osteosarcoma. West Virginia University, 2022.
- [2] Chim, Letitia Kai-Ling. Tissue-Engineered Microenvironments to Model Mechanical Cues and Tumor-Associated Macrophages in Osteosarcoma. Diss. Rice University, 2022.
- [3] Zhong, Wei, et al. "Prognostic analysis of telangiectatic osteosarcoma of the extremities." *Frontiers in oncology* 12 (2023): 7400.
- [4] Czerniak, Bogdan. Dorfman and Czerniak's Bone Tumors E-Book. Elsevier Health Sciences, 2015.
- [5] Noori, Firas Abdullah, and Amjed Hassan Saheb. "A giant cerebral hydatid cyst required urgent operation: case report." *University of Thi-Qar Journal Of Medicine* 17.1 (2019): 183-193.
- [6] Al-Mosawi, Aamir Jalal. "Iraq healthcare system: An update." *Lupine Online Journal of Medical Sciences (ISSN: 2641-1725)* 4.3 (2020): 404-411.
- [7] Jain, Aakash, and Mohit Dhingra. "Epidemiology of Malignant Bone Tumors in a Tertiary Care Hospital of the Himalayan Region of India: a Review of 97 Cases." *SN Comprehensive Clinical Medicine* 3.11 (2021): 2312-2318.
- [8] Klangjorhor, Jeerawan, et al. "An analysis of the incidence and survival rates of bone sarcoma patients in thailand: reports from population-based cancer registries 2001–2015." *Cancer Epidemiology* 76 (2022): 102056.
- [9] Rani, Rekha, Ishani Gupta, and Jyotsna Suri. "Histopathological Study of Bone Tumours-4 Years Study in A Tertiary Care Centre." *JK Science: Journal of Medical Education & Research* 24.4 (2022): 243-248.
- [10] Misaghi, Amirhossein, et al. "Osteosarcoma: a comprehensive review." Sicot-j 4 (2018).
- [11] Hwang, Sinchun, Meera Hameed, and Mark Kransdorf. "The 2020 World Health Organization classification of bone tumors: What radiologists should know." *Skeletal Radiology* 52.3 (2023): 329-348.
- [12] Bordbar, Mohammadreza, et al. "The Outcome of Children With Malignant Bone Tumors: A Single-Center Experience." *Global Pediatric Health* 8 (2021): 2333794X211042238.
- [13] JARRALLAH, LAMIA. "THE PATTERN OF OSTEOSARCOMA IN SOUTHERN PART OF IRAQ." *Basrah Journal of Surgery* 13.2 (2007): 35-41.
- [14] JARRALLAH, LAMIA. "THE PATTERN OF OSTEOSARCOMA IN SOUTHERN PART OF IRAQ." *Basrah Journal of Surgery* 13.2 (2007): 35-41.
- [15] AL-Shahrabalee, Suha Q., and Hussein A. Jaber. "The Impacts of Calcium Ions Substitution in Hydroxyapatite with Neodymium and Zinc on Biological Properties and Osteosarcoma Cells." *Engineering and Technology Journal* 40.12 (2022): 1-9.
- [16] Owadh, Hasanain K. Hasan, et al. "The autophagy inhibitor hydroxychloroquine enhances sensitivity of osteosarcoma cell line mg-63 to doxorubicin treatment." *Systematic Reviews in Pharmacy* 11.5 (2020): 63-69.

An Analysis Of The Pattern And Frequency Of Primary Malignant Bone Tumors In Nassyriah. SEEJPH 2024 Posted: 24-07-2024

- [17] Al-Jameel, Waseem H., et al. "Immunohistochemical expression of proliferation markers in canine osteosarcoma." *Iraqi Journal of Veterinary Sciences* 36.4 (2022): 1097-1102.
- [18] Yoon, Min A., et al. "Risk factors for diagnostic failure of ultrasound-guided core needle biopsy of soft-tissue tumors based on World Health Organization classification category and biologic potential." *American Journal of Roentgenology* 214.2 (2020): 413-421.
- [19] Tabib, William, and Hanna Haddad. "Management of second metacarpal chronic osteomyelitis by induced membrane technique." *Case Reports in Plastic Surgery and Hand Surgery* 5.1 (2018): 49-53.
- [20] Medellin, M. R., et al. "Mechanisms of failure and survival of total femoral endoprosthetic replacements." *The Bone & Joint Journal* 101.5 (2019): 522-528.
- [21] Schajowicz, Fritz. Tumors and tumorlike lesions of bone and joints. Springer Science & Business Media, 2012.
- [22] Bus, M. P. A., et al. "Is there still a role for osteoarticular allograft reconstruction in musculoskeletal tumour surgery? A long-term follow-up study of 38 patients and systematic review of the literature." *The bone & joint journal* 99.4 (2017): 522-530.
- [23] Ran, Yonghong, et al. "A review of biological effects and treatments of inhaled depleted uranium aerosol." *Journal of Environmental Radioactivity* 222 (2020): 106357.
- [24] Al-Sadoon, I. I., Al-Nuaimy, H. Y., & Al-Diwan, J. K. "Cancer incidence among military personnel exposed to depleted uranium in Iraq": A meta-analysis. Environmental research, (2021): 198, 111235.
- [25] Margiana, Ria, et al. "Functions and therapeutic interventions of non-coding RNAs associated with TLR signaling pathway in atherosclerosis." *Cellular Signalling* 100 (2022): 110471.
- [26] Arif, Anam, et al. "The functions and molecular mechanisms of Tribbles homolog 3 (TRIB3) implicated in the pathophysiology of cancer." *International Immunopharmacology* 114 (2023): 109581.
- [27] Lafta, Holya A., et al. "Tumor-Associated Macrophages (TAMs) in Cancer Resistance; Modula-tion by Natural Products." *Current topics in medicinal chemistry* (2023).
- [28] Lei, Zimeng, et al. "Detection of abemaciclib, an anti-breast cancer agent, using a new electrochemical DNA biosensor." *Frontiers in Chemistry* 10 (2022): 980162.
- [29] Hjazi, Ahmed, et al. "Unraveling the Impact of 27-Hydroxycholesterol in Autoimmune Diseases: Exploring Promising Therapeutic Approaches." *Pathology-Research and Practice* (2023): 154737.
- [30] Gupta, Jitendra, et al. "Double-edged sword role of miRNA-633 and miRNA-181 in human cancers." *Pathology-Research and Practice* (2023): 154701.
- [31] Hjazi, Ahmed, et al. "The pathological role of CXC chemokine receptor type 4 (CXCR4) in colorectal cancer (CRC) progression; special focus on molecular mechanisms and possible therapeutics." *Pathology-Research and Practice* (2023): 154616.
- [32] Sane, Shahryar, et al. "Investigating the effect of pregabalin on postoperative pain in non-emergency craniotomy." *Clinical Neurology and Neurosurgery* 226 (2023): 107599.
- [33] Alwan, Nathera Hussin, et al. "The Effectiveness of Semantic Therapy on Death Anxiety, Pain Catastrophizing, Chronic Pain Acceptance, and Pain Intensity in Patients with Breast Cancer." *International Journal of Body, Mind & Culture* (2345-5802) 9 (2022).
- [34] Gupta, J., Suliman, M., Ali, R., Margiana, R., Hjazi, A., Alsaab, H. O., ... & Ahmed, M. Double-edged sword role of miRNA-633 and miRNA-181 in human cancers. *Pathology-Research and Practice*,(2023): 154701.