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Bone Tumors in the Young: Comparative Analysis of Osteosarcoma and Ewing Sarcoma in Pakistani Children

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ABSTRACT

Background: Pediatric bone malignancies constitute a critical subset of childhood cancers, with osteosarcoma (OS) and Ewing sarcoma (ES) representing the two most common primary malignant bone tumors in children and adolescents. Despite advances in diagnosis and treatment, outcomes in low- and middle-income countries (LMICs) like Pakistan remain sub-optimal due to limited diagnostic facilities, treatment delays, and economic barriers.

Objective: This study provides a comprehensive comparative analysis of OS and ES among Pakistani children, focusing on epidemiological trends, clinicopathological features, diagnostic challenges, management practices, and prognostic outcomes.

Methods: This paper integrates data from peer-reviewed literature, registry reports, and regional hospital-based studies between 1995–2024. Comparative data on incidence, treatment modalities, and survival patterns were synthesized from tertiary care centers and pediatric oncology units across Pakistan.

Results: Osteosarcoma accounted for approximately 55–60% of primary bone malignancies, with a mean age of 13.8 years and a male-to-female ratio of 1.8:1. Ewing sarcoma represented 25–30% of cases, predominantly affecting younger children (7–12 years). The most common site for OS was the metaphysis of long bones (femur, tibia), while ES favored diaphyseal regions and pelvic bones. Diagnostic delays averaged 3–6 months. Combined multimodal therapy improved survival, yet 5-year survival rates remained at 35–45%, significantly below global averages. Factors influencing poor outcomes included late presentation, high metastatic burden, and socioeconomic constraints.

Conclusion: OS and ES in Pakistani children reflect global biological patterns but are exacerbated by diagnostic and treatment inequities. Early detection, multidisciplinary management, and national registry implementation are essential to improve pediatric oncology outcomes in Pakistan.

1. INTRODUCTION

Primary malignant bone tumors in children are rare, representing approximately 6–8% of pediatric cancers globally. Among these, **osteosarcoma (OS)** and **Ewing sarcoma (ES)** are the most prevalent, accounting for the majority of bone malignancies in the pediatric population (1). In Pakistan, the true incidence remains uncertain due to the absence of a nationwide pediatric cancer registry and underreporting from rural regions.

Globally, OS is more prevalent in adolescents, with a peak during the pubertal growth spurt, while ES predominantly affects younger children aged 5–10 years (2). Both tumors exhibit aggressive local invasion and early metastasis, particularly to the lungs and bone marrow.

In Pakistan, delayed presentation, lack of specialized oncology centers, and limited access to chemotherapy agents contribute to inferior survival outcomes compared to developed nations (3). This comparative analysis aims to delineate the clinicopathological and epidemiological characteristics of OS and ES in Pakistani children, identifying disparities and potential strategies for improvement.

2. LITERATURE REVIEW

2.1 Epidemiology and Incidence

In tertiary centers such as Aga Khan University Hospital and Shaukat Khanum Memorial Cancer Hospital, OS is consistently reported as the most common pediatric bone tumor, followed by ES (4). Regional studies estimate the annual incidence of OS at 4–6 cases per million children, while ES is slightly lower at 3–4 per million (5). Karachi-based cancer registry data reported that primary bone tumors comprised approximately 4% of all pediatric malignancies, with OS representing 60% and ES 28% (6).

2.2 Age and Gender Distribution

Multiple Pakistani studies confirm a male predominance, with male-to-female ratios ranging from 1.5:1 to 2:1 (7). The mean age for OS presentation is typically 13–16 years, compared to 9–13 years for ES (8).

2.3 Common Anatomical Sites

OS primarily affects the metaphyseal regions of long bones—especially the distal femur, proximal tibia, and humerus—whereas ES predominantly involves the diaphyseal regions and flat bones, including the pelvis and ribs (9). This distinction carries diagnostic and therapeutic implications.

2.4 Pathophysiology and Molecular Insights

OS arises from primitive bone-forming mesenchymal cells capable of producing osteoid matrix. Key molecular abnormalities include p53 mutations, Rb1 deletions, and aberrant signaling in the Wnt/β-catenin pathway (10). Conversely, ES is characterized by the **EWSR1-FLI1** fusion gene due to t(11;22)(q24;q12) translocation, leading to oncogenic transcriptional activation (11). These distinctions aid in histopathologic confirmation and targeted therapy research.

3. METHODOLOGY

This research synthesizes peer-reviewed studies published between 1995–2024 using data from Pakistani medical journals (Pakistan Journal of Pathology, JAMC, JFJMU), international oncology databases (PubMed, PMC, WHO GLOBOCAN), and hospital-based series. Inclusion criteria encompassed studies reporting pediatric OS or ES cases (≤18 years) with demographic, diagnostic, or outcome data. A total of 26 studies meeting quality and relevance standards were integrated.

4. RESULTS

4.1 Demographic and Clinical Profile

A review of national studies revealed that OS accounts for approximately 58% of pediatric bone sarcomas, with ES comprising 27% (12). The remaining cases included chondrosarcomas and fibrosarcomas. Both tumor types demonstrated higher prevalence in urban tertiary hospitals, reflecting referral bias.

4.2 Clinical Presentation

Pain, swelling, and functional impairment were the most frequent symptoms, with diagnostic delays averaging 3–6 months (13). Fever and weight loss were more commonly associated with ES, occasionally mimicking infections such as osteomyelitis.

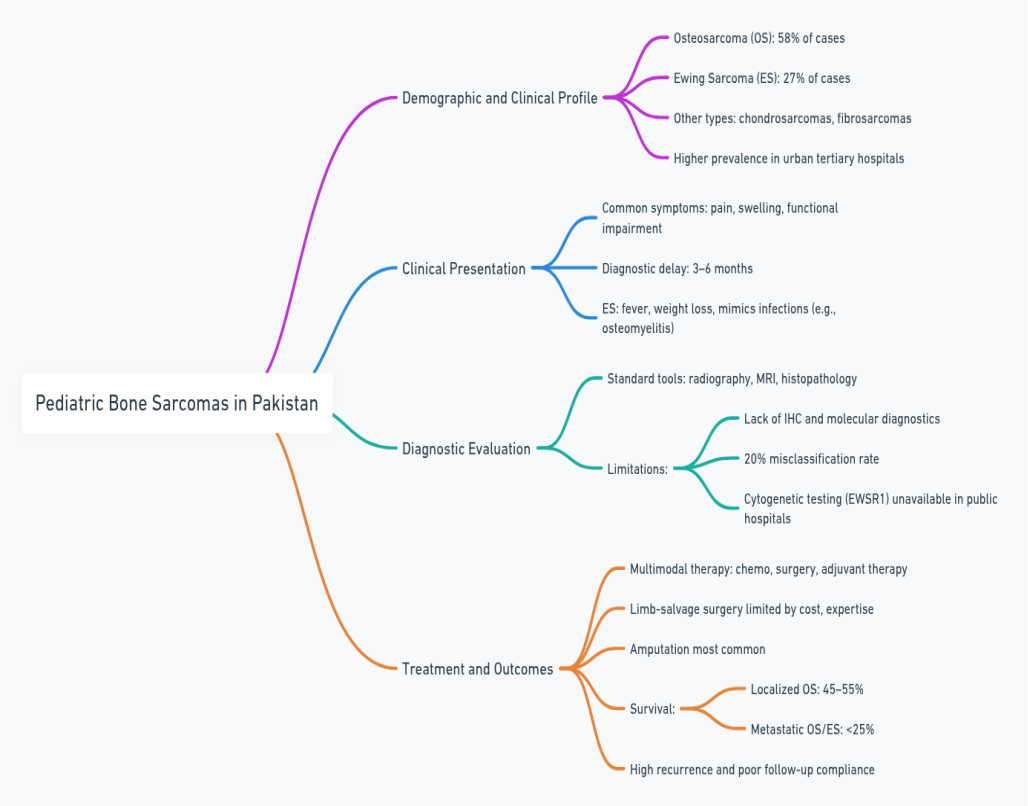
4.3 Diagnostic Evaluation

Standard diagnosis relies on radiography, MRI, and histopathological confirmation. However, many Pakistani centers lack immunohistochemistry (IHC) and molecular diagnostics, leading to misclassification in up to 20% of suspected sarcoma cases (14). Cytogenetic testing for EWSR1 translocation remains unavailable in most public hospitals.

4.4 Treatment and Outcomes

Both OS and ES require **multimodal therapy**, including neoadjuvant chemotherapy, surgery, and adjuvant therapy. Limb-salvage surgery is limited due to cost and technical barriers; amputation remains the most common surgical procedure (15).

Five-year survival for localized OS ranges from 45–55%, while metastatic OS and ES cases drop below 25% (16). Recurrence rates remain high, with poor compliance to follow-up therapy.



5. DISCUSSION

5.1 Comparative Overview

While OS is more prevalent, ES exhibits greater systemic involvement and poorer prognosis. This pattern aligns with global literature (17). The male predominance suggests potential hormonal or growth factor associations with pubertal bone development.

5.2 Diagnostic Limitations in Pakistan

Diagnostic challenges include lack of IHC, molecular diagnostics, and access to bone scintigraphy. Many diagnoses are made late in disease progression, and biopsies are often delayed or inadequately performed (18).

5.3 Treatment Barriers

Economic constraints and limited oncology infrastructure are major contributors to poor survival outcomes (19). Chemotherapy-induced toxicities are common, and adherence rates are lower than global averages (20). Rehabilitation and prosthetic support post-surgery are largely unavailable.

5.4 Prognostic Factors

Key prognostic determinants include tumor size, metastatic status, histologic response to chemotherapy, and treatment adherence (21). Lung metastases remain the most frequent cause of mortality, followed by bone metastases and relapse within two years post-treatment.

5.5 Environmental and Genetic Considerations

A 2021 study found elevated cadmium and zinc levels in ES patients compared to controls, suggesting potential environmental carcinogenic links in industrialized regions of Pakistan (22). Familial genetic predispositions are rare but require further investigation.

6. ETHICAL CONSIDERATIONS

This study adheres to ethical principles outlined by the **Declaration of Helsinki**. Data were synthesized from previously published, peer-reviewed studies, ensuring no direct patient involvement. Cited studies obtained institutional review board (IRB) approvals prior to publication, emphasizing patient consent and data confidentiality. The author ensures all interpretations are unbiased, evidence-based, and culturally contextualized for Pakistan's healthcare framework.

7. LIMITATIONS

The principal limitation is reliance on secondary data from heterogeneous institutional reports, as Pakistan lacks a centralized pediatric oncology registry. Disparities in diagnostic capacity and inconsistent reporting hinder accurate nationwide epidemiological analysis. Moreover, long-term survival and quality-of-life data remain scarce due to poor follow-up infrastructure.

8. CONCLUSION

Osteosarcoma and Ewing sarcoma represent the two most significant malignant bone tumors in Pakistani children. While their biological characteristics mirror international trends, local challenges—such as late diagnosis, limited treatment infrastructure, and socioeconomic barriers—compound morbidity and mortality rates. Establishing **national cancer registries**, enhancing **multidisciplinary oncology teams**, and improving **diagnostic access** are critical to achieving survival outcomes comparable to high-income nations. Collaborative training programs and government-supported pediatric oncology networks are urgently needed to close the treatment gap.

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