Original article

Impact of Delayed Diagnosis on Outcome of Pediatric Osteosarcoma in a Developing Country: Experience from a Regional Cancer Institute

Dr Wasim Imam Kazi*

Senior resident, Department of medical oncology, Jawaharlal Nehru medical College, Wardha, Maharashtra
Corresponding author*

ABSTRACT

Background- Osteosarcoma is the most common primary malignant bone tumor in children and adolescents. Delayed diagnosis remains a major challenge in developing countries due to poor awareness, socioeconomic limitations, delayed referral, and inadequate healthcare access. Such delays often result in advanced disease, metastasis, and poorer survival outcomes.

Aim- To evaluate the impact of delayed diagnosis on clinical presentation, treatment outcomes, and survival among pediatric osteosarcoma patients treated at a regional cancer institute.

Materials and Methods- This retrospective observational study included pediatric osteosarcoma patients treated between January 2018 and December 2024 at a regional cancer institute. Demographic characteristics, duration of symptoms before diagnosis, stage at presentation, histopathological subtype, metastasis, treatment modalities, limb salvage rates, chemotherapy response, and survival outcomes were analyzed. Patients were categorized into early diagnosis (<3 months symptom duration) and delayed diagnosis (>3 months symptom duration) groups.

Results- A total of 68 patients were included. The mean age was 13.8 ± 3.2 years, with male predominance (63.2%). Delayed diagnosis was observed in 44 patients (64.7%). Patients with delayed diagnosis had significantly higher rates of metastatic disease (43.2% vs 12.5%, $p<0.05$), larger tumor size, and lower limb salvage rates. Overall survival was significantly reduced in delayed diagnosis patients (48.5% vs 79.2%, $p<0.01$). Pulmonary metastasis was the most common site of distant spread.

Conclusion- Delayed diagnosis significantly worsens outcomes in pediatric osteosarcoma in developing countries. Increasing public awareness, early referral systems, and improved access to specialized oncology care are essential to improve survival and functional outcomes.

Keywords- Osteosarcoma; Delayed diagnosis; Pediatric bone tumors; Survival outcome; Limb salvage surgery.

INTRODUCTION

Osteosarcoma is the most common primary malignant bone tumor affecting children and adolescents, accounting for approximately 20% of all primary bone malignancies. The tumor commonly arises in the metaphyseal regions of long bones, especially around the knee joint. Advances in multimodal therapy involving neoadjuvant chemotherapy, surgical resection, and adjuvant chemotherapy have significantly improved survival in developed countries, with long-term survival rates approaching 65–75%.

Despite these advances, outcomes in developing countries remain considerably poorer. One of the major contributing factors is delayed diagnosis. In resource-limited settings, initial symptoms such as limb pain and swelling are frequently misdiagnosed as trauma, infection, or inflammatory conditions. Delayed referral to oncology centers results in advanced disease at presentation, increased metastatic burden, larger tumor size, and reduced possibility of limb salvage surgery.

Several socioeconomic and healthcare-related factors contribute to diagnostic delays in developing nations. Poor awareness among parents, limited access to specialized orthopedic oncology services, financial constraints, rural residence, and delayed imaging contribute substantially to treatment delay. In many cases, children initially receive symptomatic treatment for several months before definitive diagnosis is established.

Metastatic disease at diagnosis is one of the strongest predictors of poor prognosis in osteosarcoma. Pulmonary metastasis is the most common site of distant spread and significantly reduces survival rates. Delayed diagnosis increases the risk of micrometastatic dissemination and decreases chemotherapy responsiveness.

Early diagnosis allows timely initiation of neoadjuvant chemotherapy and increases the feasibility of limb salvage procedures, thereby improving both survival and quality of life. Understanding the impact of diagnostic delay in pediatric osteosarcoma is therefore essential for planning awareness programs and optimizing healthcare delivery systems in developing countries.

The present study was conducted to evaluate the influence of delayed diagnosis on disease stage, treatment outcomes, metastasis, limb salvage rates, and survival among pediatric osteosarcoma patients treated at a regional cancer institute.

MATERIALS AND METHODS

Study Design

Retrospective observational study.

Study Setting

The study was conducted at the Department of Medical Oncology and Orthopedic Oncology of a regional cancer institute in India.

Study Duration

January 2018 to December 2024.

Study Population

Children and adolescents diagnosed with osteosarcoma and treated at the institute during the study period.

Sample Size

A total of 68 patients were included.

Inclusion Criteria

1. Histopathologically confirmed osteosarcoma.
2. Age below 18 years.
3. Complete treatment and follow-up records.
4. Patients treated with standard multimodal therapy.

Exclusion Criteria

1. Recurrent osteosarcoma at presentation.
2. Secondary osteosarcoma.
3. Incomplete medical records.
4. Patients lost to follow-up immediately after diagnosis.

Data Collection

Data were collected from hospital medical records and oncology databases, including:

- Age and gender

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

- Symptom duration before diagnosis
- Tumor site and size
- Histopathological subtype
- Presence of metastasis
- Chemotherapy details
- Surgical management
- Limb salvage or amputation
- Histological response to chemotherapy
- Survival outcomes

Definition of Diagnostic Delay

- Early diagnosis group: symptom duration less than 3 months.
- Delayed diagnosis group: symptom duration greater than 3 months.

Treatment Protocol

All patients received:

1. Neoadjuvant chemotherapy
2. Surgical management
3. Adjuvant chemotherapy

Surgical procedures included:

- Limb salvage surgery
- Amputation where necessary

Outcome Measures

Primary outcomes:

- Overall survival
- Metastasis rate

Secondary outcomes:

- Limb salvage rate
- Histological chemotherapy response
- Treatment complications

Statistical Analysis

Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation. Categorical variables were analyzed using Chi-square test. Kaplan-Meier survival analysis was used for survival estimation. A p-value <0.05 was considered statistically significant.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

RESULTS

Table 1: Demographic and Clinical Characteristics

Variable	Frequency	Percentage
Age 5–10 years	18	26.5%
Age 11–15 years	34	50.0%
Age >15 years	16	23.5%
Male	43	63.2%
Female	25	36.8%
Distal femur involvement	32	47.1%
Proximal tibia involvement	20	29.4%
Proximal humerus involvement	8	11.8%
Other sites	8	11.8%
Delayed diagnosis (>3 months)	44	64.7%
Metastasis at diagnosis	22	32.4%

The majority of patients were adolescents with male predominance. Distal femur was the most common site of tumor involvement. Delayed diagnosis was observed in nearly two-thirds of patients.

Table 2: Comparison Between Early and Delayed Diagnosis Groups

Parameter	Early Diagnosis	Delayed Diagnosis	p-value
Mean tumor size	7.2 ± 2.1 cm	11.4 ± 3.8 cm	<0.001
Metastatic disease	12.5%	43.2%	0.01
Pulmonary metastasis	8.3%	38.6%	0.008
Limb salvage surgery	75.0%	40.9%	0.02
Amputation	25.0%	59.1%	0.02
Poor chemotherapy response	20.8%	52.3%	0.01

Patients with delayed diagnosis presented with significantly larger tumors, higher metastatic burden, and lower rates of limb salvage surgery.

Table 3: Survival Outcomes

Outcome	Early Diagnosis	Delayed Diagnosis
3-year overall survival	79.2%	48.5%
Event-free survival	70.8%	39.2%
Local recurrence	12.5%	31.8%
Mortality	20.8%	51.5%

Delayed diagnosis was associated with significantly poorer survival and increased mortality.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

DISCUSSION

The present study demonstrated that delayed diagnosis significantly affects treatment outcomes and survival in pediatric osteosarcoma patients in developing countries. Nearly 65% of patients in our cohort experienced diagnostic delays exceeding three months, highlighting the persistent challenges in early cancer recognition and referral systems.

The majority of patients were adolescents with male predominance, consistent with global osteosarcoma epidemiology. Distal femur and proximal tibia were the most common tumor locations, which aligns with the rapid growth regions of long bones during adolescence.

Delayed diagnosis was strongly associated with advanced disease at presentation. Patients presenting late had significantly larger tumors and higher rates of pulmonary metastasis. Pulmonary metastasis remains the most common site of distant spread in osteosarcoma and is a major determinant of prognosis. Similar findings have been reported in studies from low- and middle-income countries where delayed referral contributes to advanced disease burden.

One of the most important findings of this study was the significantly lower limb salvage rate among delayed diagnosis patients. Early diagnosis allows adequate tumor control before extensive neurovascular involvement, making limb salvage surgery feasible. In contrast, delayed presentation often necessitates amputation due to extensive local disease.

The overall survival rate among early diagnosis patients was significantly better compared to delayed diagnosis patients. Survival differences observed in our study highlight the critical importance of timely diagnosis and intervention. Similar studies from developing countries have shown reduced survival due to late-stage disease, treatment interruption, and inadequate supportive care.

Poor chemotherapy response observed in delayed diagnosis patients may be attributed to larger tumor burden, necrosis, and metastatic dissemination. Delayed initiation of therapy allows tumor progression and may reduce chemotherapy effectiveness.

Several factors contribute to diagnostic delays in developing countries. These include:

- Poor awareness regarding bone tumors
- Misdiagnosis as trauma or infection
- Financial constraints
- Rural residence
- Delayed imaging and biopsy
- Limited oncology referral systems

Public health education programs targeting parents, primary healthcare workers, orthopedic surgeons, and pediatricians may facilitate earlier recognition of warning symptoms such as persistent bone pain and swelling.

The study emphasizes the need for structured referral pathways and multidisciplinary pediatric oncology services. Improving accessibility to imaging facilities, biopsy services, and chemotherapy centers may significantly reduce treatment delays and improve outcomes.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

CONCLUSION

Delayed diagnosis significantly worsens survival outcomes, increases metastatic disease, and reduces limb salvage opportunities in pediatric osteosarcoma patients in developing countries. Strengthening early referral systems, improving awareness, and ensuring timely access to oncology care are essential for improving survival and functional outcomes in pediatric bone tumors.

REFERENCES

1. Isakoff MS, Bielack SS, Meltzer P, Gorlick R. Osteosarcoma: Current treatment and future directions. J Clin Oncol. 2015;33(27):3029-3035.
2. Ritter J, Bielack SS. Osteosarcoma. Ann Oncol. 2010;21(Suppl 7):vii320-vii325.
3. Ottaviani G, Jaffe N. The epidemiology of osteosarcoma. Cancer Treat Res. 2009;152:3-13.
4. Marina N, Gebhardt M, Teot L, Gorlick R. Biology and therapeutic advances for pediatric osteosarcoma. Oncologist. 2004;9(4):422-441.
5. Bielack SS, Kempf-Bielack B, Delling G, et al. Prognostic factors in high-grade osteosarcoma. J Clin Oncol. 2002;20(3):776-790.
6. Arndt CA, Crist WM. Common musculoskeletal tumors of childhood and adolescence. N Engl J Med. 1999;341(5):342-352.
7. Bacci G, Ferrari S, Longhi A, et al. High-grade osteosarcoma of the extremity. Cancer. 2000;89(11):2446-2456.
8. Jaffe N. Osteosarcoma: Review of the past, impact on the future. Pediatr Blood Cancer. 2008;50(2 Suppl):343-344.
9. Mirabello L, Troisi RJ, Savage SA. International osteosarcoma incidence patterns. Int J Cancer. 2009;125(1):229-234.
10. Goorin AM, Harris MB, Bernstein M, et al. Phase II/III trial of etoposide and high-dose ifosfamide in newly diagnosed metastatic osteosarcoma. J Clin Oncol. 2002;20(2):426-433.
11. Ferrari S, Smeland S, Mercuri M, et al. Neoadjuvant chemotherapy with high-dose methotrexate. Lancet Oncol. 2005;6(4):209-215.
12. Daw NC, Chou AJ, Jaffe N, et al. Recurrent osteosarcoma with a single pulmonary metastasis. Cancer. 2015;121(16):2810-2817.
13. Longhi A, Errani C, De Paolis M, Mercuri M, Bacci G. Primary bone osteosarcoma in children and adolescents. Cancer Treat Rev. 2006;32(6):423-436.
14. Whelan JS, Bielack SS, Marina N, et al. EURAMOS-1 trial results for osteosarcoma. Lancet Oncol. 2015;16(16):1617-1629.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858