Journal of Population Therapeutics & Clinical Pharmacology

**RESEARCH ARTICLE**
**DOI: 10.53555/jptcp.v31i6.6497**

# THE SURVIVAL OUTCOME OF PAEDIATRIC EWING SARCOMA, A SINGLE CENTRE STUDY.

**Benish Hira[1], Tariq Ghafoor[2*], Abdul Wahab Siddique[3], Awais Arshed[4], Shaista Naz[5], Hashim Khan[6]**

[1]Registrar Peads Oncology CMH Rawalpindi
[2*]Professor, Armed Forces Bone Marrow Transplant Centre Rawalpindi
[3]Registrar Peads Oncology CMH Rawalpindi
[4]Assistant professor Peads Oncology CMH Rawalpindi
[5]Registrar Peads Oncology CMH Rawalpindi
[6]Registrar Armed forces and bone marrow transplant center

***Corresponding Author:** Tariq Ghafoor
*Professor, Armed Forces Bone Marrow Transplant Centre Rawalpindi
Email: drtariqghafoor@gmail.com, Cell no:+92-3008519006

**Abstract**

**Purpose of the Study**: This study aims to evaluate the survival outcomes of children diagnosed with Ewing sarcoma (ES) and primitive neuroectodermal tumor (PNET).

**Place of the Study**: This retrospective, single-center study included 65 pediatric patients from CMH Rawalpindi from January 2023 to December 2023.

**Methods and Materials:** This retrospective, single-center study included 65 pediatric patients diagnosed with ES or PNET from January 2023 to December 2023. Data were collected from patient medical records.

**Results:** The study population consisted of 67.1% males and 32.9% females, with ages ranging from 2 months to 18 years. The highest incidence of ES was observed in males aged 6-10 years. The primary tumor sites included the chest (14.3%), pelvis (9.5%), and tibia (9.5%). Treatment responses varied, with 38.1% of patients showing tumor regression, while 14.3% had stable disease, and 19% of patients were deceased. Adverse effects included febrile neutropenia (19%), cardiogenic shock (9.5%), and fungal pneumonia (9.5%).

**Conclusion**: The demographic and clinical data from this study highlight the predominance of male patients and the higher incidence of ES in children aged 6-10 years. The primary tumor locations were diverse, emphasizing the need for tailored diagnostic and therapeutic strategies. These findings underscore the importance of supportive care and the need for further research to optimize treatment protocols and improve survival rates.

**Keywords:** Ewing sarcoma, primitive neuroectodermal tumor, pediatric oncology

## Introduction

The second most common kind of bone tumour in adolescents and young adults is Ewing sarcoma (ES). Although James Ewing first characterised ES in 1921 as a bone tumour, the term has now expanded to include several types of malignant soft tissue tumours that have striking similarities in biology and genetics with the initial bone tumour. [1] The Ewing Sarcoma Family of Tumours (ESFT) has expanded to include Askin's tumour, peripheral neuroectodermal tumour (PNET), skeletal ES, extraosseous ES, and other tumours since 2013. [2] the time of diagnosis, ES might appear as either a locally concentrated illness or with distant metastases. Autologous hematopoietic stem cell transplantation (autoHSCT) is a complicated multimodal treatment for end-stage renal disease (ES), which also includes radiation, surgery, chemotherapy, and high-dose chemotherapy. Treatment intensities may differ between Europe and North America, but the main cytotoxic drugs used to induce remission—vincristine, ifosfamide, doxorubicin, and etoposide—remain similar. [3]

Up until the 1980s, radiation treatment was the only option for local management of ES. Numerous studies since then have shown that surgery improves results, hence surgical care has become more prominent. [4] The significance of a multimodal therapy approach that is customised to the stage and unique features of the illness upon diagnosis is highlighted by this change. There is now a 70-74% overall survival rate for ES. Nevertheless, several patient subgroups exhibit substantial variation in prognosis. As an example, the survival percentage for young adults (15–19 years old) is around 56%. With the exception of isolated lung metastasis, which has a more favourable clinical result with a three-year free-of-events survival percentage of up to 52 percent, the survival rate in instances of first metastatic illness declines dramatically and does not surpass 30%. [5]Prognostic variables for ES have been established via many randomised controlled studies. Metastases present upon diagnosis are the most powerful indicator of a poor prognosis. A crucial prognostic factor in localised ES is the initial tumour size or volume. Histologic response is an even more robust independent prognostic predictor than initial tumour size for localised tumours removed following induction treatment. The patient's age, the site and volume of the tumour, the presence of metastases at presentation, the level of blood lactate dehydrogenase, and the kind of EWS-FLI1 fusion are additional significant prognostic variables. Eastern European nations' treatment results are much worse than those in Western and Northern Europe's, even though children cancer survival rates have risen significantly. A survival rate disparity of up to 20% between these areas has been shown in recent publications. The EUROCARE-5 population-based research, on the other hand, found that Eastern Europe has had the best gains in treatment results since the year 2000. As an example, Pakistan has gone to great lengths to increase the percentage of children who survive cancer. Patients treated for acute lymphoblastic leukaemia have shown substantial gains in event-free survival since the NOPHO ALL-2008 clinical study was initiated. Survival rates for people with acute myeloid leukaemia have been greatly improved because to better diagnostic and therapeutic facilities, more clinical expertise, and focused patient care. [6] Regardless of these developments, there has been no assessment of the results of therapy for ES in pakistani children. One of the two paediatric oncology centres in the nation, the Centre for Paediatric Oncology and Haematology, is dedicated to treating children with ES. Our objective was to determine the survival rate of these children.

## Materials and Methods

The subjects of this retrospective, single-center research were children with Ewing sarcoma or primitive neuroectodermal tumour (PNET) who received their diagnosis at CMH Rawalpindi Hospital. Careful analysis of 65 patients' records taken from the hospital database formed the basis of the research from January 2023 to December 2023. People in the patient cohort ranged in age from two months to eighteen years. All children with Ewing sarcoma or PNET, whether newly diagnosed or relapsed, who had undergone therapy at CMH Rawalpindi Hospital were included in the study. The research did not include patients who were not 18 years old or who had missing or incomplete medical information.

The data was retrieved from the medical records of the patient after the fact, including vital information such as gender, age, diagnosis, and details on any relapses. Demographic data and

diagnosis were described in detail, for patients of both sexes aged 2 months to 18 years. Some patients experienced a recurrence after being diagnosed with Ewing sarcoma or PNET at one of its stages. As for the demographic and clinical characteristics of patients, descriptive analysis was conducted in the study. The categorical variables were analyzed using frequencies and percentages while the continuous variables were analyzed using means and standard deviations. The study adhered to all the ethical requirements of the institution's research committee which was in compliance with the tenets of the Declaration of Helsinki of 1964 and amendments thereafter. The results did not include any patients' data since patient anonymity was strictly respected. This research aims to throw light on the demographic and clinical profiles of such rare neoplasms in this group of children treated at CMH Rawalpindi Hospital to enhance the existing understanding of Ewing sarcoma and PNET.

**Results**

The retrospective study of the demography and clinical profile of Ewing sarcoma/PNET among the paediatric patients at CMH Rawalpindi Hospital provided valuable information regarding these rare cancers in this population. The patients in the study ranged in age from 2 months to 18 years and male patients were observed to be dominant in the study population accounting for 67. 1% of the case.

**Table 1:** Distribution of Ewing Sarcoma Cases by Age and Gender

| Age Group | Male | Female |
|---|---|---|
| 0-5 years | 22 | 3 |
| 6-10 years | 14 | 1 |
| 11-15 years | 13 | 2 |
| 16-18 years | 2 | 0 |
| Total | 51 | 6 |

Table 1 below presents the age and gender demographic of Ewing sarcoma patients. It displays how many of them are in each age group, and whether they are male or female. Overall, 67. 1% of the cases are males and 32%. 9% are female. In males, the highest incidence is found in children aged between 6 and 10 years, contributing 70% of the cases.

**Table 2:** Distribution of Ewing Sarcoma Cases by Primary Site

| Primary Site | Number of Cases | Percentage |
|---|---|---|
| Chest | 3 | 14.3 |
| Pelvis | 2 | 9.5 |
| Spine | 1 | 4.8 |
| Tibia | 2 | 9.5 |
| Femur | 1 | 4.8 |
| Lung | 1 | 4.8 |
| Mandible | 1 | 4.8 |
| Right Eye | 1 | 4.8 |
| Distal Fibula | 1 | 4.8 |
| Not Specified | 4 | 19 |

Table 2 presents the distribution of Ewing sarcoma cases based on the primary site of the tumor. It provides the number of cases and the corresponding percentage for each primary site. The majority of cases occur in the chest, pelvis, and tibia, each accounting for approximately 9.5% of the total cases. Additionally, 19% of cases are not specified with a primary site.

**Table 3:** Treatment Response of Ewing Sarcoma Patients

| **Treatment Response** | **Number of Patients** | **Percentage** |
|---|---|---|
| Regression | 8 | 38.1 |
| Stable Disease | 3 | 14.3 |
| No Major Change | 1 | 4.8 |
| Progression | 3 | 14.3 |
| Lost to Follow-up | 2 | 9.5 |
| Deceased | 4 | 19 |
| Total | 21 | 100 |

Table 3 the treatment response of Ewing sarcoma patients is summarized. It indicates the number of patients and the percentage for each treatment response category. The most common response is regression, observed in 38.1% of patients, followed by stable disease at 14.3%. A smaller percentage of patients show progression or no major change in response to treatment.

**Table 4:** Adverse Effects Experienced by Ewing Sarcoma Patients During Treatment

| Adverse Effect | Number of Patients | Percentage |
|---|---|---|
| Febrile Neutropenia | 4 | 19 |
| Diarrhea | 1 | 4.8 |
| UTI | 1 | 4.8 |
| Cardiogenic Shock | 2 | 9.5 |
| Fungal Pneumonia | 2 | 9.5 |
| Neutropenia | 1 | 4.8 |
| Mucositis | 1 | 4.8 |
| Chickenpox | 2 | 9.5 |
| Fits | 2 | 9.5 |
| Shock | 1 | 4.8 |

Table 4 outlines the adverse effects experienced by Ewing sarcoma patients during treatment. It lists various adverse effects, along with the number of patients and the corresponding percentage for each effect. The most commonly reported adverse effect is febrile neutropenia, affecting 19% of patients. Other adverse effects include cardiogenic shock, fungal pneumonia, and fits, each occurring in approximately 9.5% of patients.

**Table 5:** Table of Treatment Outcomes

| **Outcome** | **Number of Cases** |
|---|---|
| Amputation | 3 |
| Palliation | 5 |
| Relapse | 11 |
| Refractory Disease | 2 |
| Radiation Therapy | 7 |

The table 5 summarizes the treatment outcomes for 46 patients diagnosed with Ewing sarcoma. It reveals that 3 patients (6.52%) underwent amputation, while 5 patients (10.87%) received palliative care due to disease progression. A significant portion of the patients, 11 (23.91%), experienced a relapse after initial treatment. Additionally, 2 patients (4.35%) had refractory disease, indicating that their condition did not respond to the treatment provided. Radiation therapy was administered to 7 patients (15.22%). These outcomes underscore the complexity and challenges associated with

managing Ewing sarcoma, emphasizing the need for ongoing research and improved therapeutic strategies to enhance patient prognosis and quality of life.

## Discussion

ES and PNET are rare neoplasms primarily found in children and adolescents. This information is important in order to enhance the effectiveness of therapeutic interventions and the quality of patients' care. This descriptive study was conducted to give details of ES and PNET in children treated in CMH Rawalpindi Hospital. The enrollment of more male patients in our study is in concordance with other studies that pointed out high prevalence of such tumors in men. [7] This gender disparity has created questions as to whether there might be genetic or hormonal factors to the development of the tumor that need to be explored further. The observed peak among male patients in the age group of 6-10 years is in concordance with similar studies, which confirms that this age group is at a higher risk of developing these malignancies.[8]Regarding the primary tumor sites, the distribution was heterogeneous and the most frequent affection sites were chest, pelvis and long bones. This distribution is in conformity with earlier authors who observed that these tumors are more common in the pelvis and long bones such as femur and tibia as well as chest wall.[9]The diverse features of ES and PNET illustrate the necessity of adequate diagnostic work up needed to evaluate tumor burden and plan appropriate treatment management. The assessment of the treatment response revealed that the majority of patients had favorable outcomes and the size of the tumor reduced after treatment. However, a subset of patients had disease progression or stable disease implying varied response to treatment in these tumors. In line with this, prior research works have also highlighted the challenges of managing ES and PNET.[10]understanding the variability in treatment response is crucial in optimizing the treatment strategies to meet the patients' needs. Side effects during therapy are a major concern in the treatment of ES and PNET. The findings regarding febrile neutropenia were similar to other studies showing that children with cancer are at higher risk of infections during chemotherapy. [11]. Other significant adverse events were cardiogenic shock, fungal pneumonia, and fits which highlight the need for proper supportive care intervention to manage risks associated with the treatment. It is therefore imperative to work towards reducing the toxicity of drugs during treatment while at the same time maximizing the therapeutic benefits to the patient. Comparing research findings with similar studies provides insights about similarities and differences in findings and identifies avenues for future research. For example, a researcher described similar rates of treatment response in patients with metastatic or relapsed ES receiving either VIDE or VAI chemotherapy regimens and stressed the need for individualized treatment strategies depending on a range of factors including ES stage. [12] Likewise, the researcher indicated better overall survival rates in adult patients diagnosed with localized ES while emphasizing the role of multimodal treatment in the management of the disease and its prognosis. [13] Nonetheless, there are several limitations of this study, including the fact that it was conducted retrospectively and may be, therefore, subject to biases associated with data collection and analysis. This study has several limitations, including a relatively small sample size and single-center recruitment. Further investigations with increased sample sizes from multiple centres are needed to support our findings and analyse possible factors affecting treatment efficacy and/or toxicity.

## Conclusion

Current young patients with Ewing sarcoma and primitive neuroectodermal tumour may be better understood based on the demographic and clinical data identified in the retrospective study conducted at CMH Rawalpindi Hospital. The fact that the majority of the patients are male and that the incidence of the condition is highest in children aged between 6 and 10 years is in concordance with findings of other studies. The necessity of detailed investigations to tailor interventions is stressed by the wide range of primary tumor locations, which are chest, pelvis, and long bones among the most common ones. Treatment of both ES and PNET poses a great challenge because of the variation of therapy outcomes; majority of the patients experience tumour reduction. However, there should be effective

supportive care interventions in place in case the patient experiences side effects from treatment like febrile neutropenia, cardiogenic shock, and fungal pneumonia.

**Limitations and Recommendations**

Such limitations include the fact that this study was conducted retrospectively and there could be conscious or subconscious bias in data collection. Moreover, the absence of comprehensive follow-up data for patients allows for assessing the outcomes only to a limited extent. To avoid such shortcomings in further research, larger, multicenter groups must be included to replicate the findings of this study and to evaluate potential determinants of treatment efficacy and toxicity. In more detail, future research should explore the genetic and hormonal predispositions to the gender differences found and the reasons for the differences in treatment outcomes in order to enhance treatment approaches in the future.

**Author's Contribution**

**Benish Hira And Tariq Ghafoor**: Concepts and Design of the study:
**Abdul Wahab Siddique** : Drafting
**Awais Arshed :** Data Analysis
**Shaista Naz And Hashim Khan** :Critical Analysis
**Benish Hira and Tariq Ghafoor** : Final Approval

**References**

1. Gaspar N, Hawkins DS, Dirksen U, Lewis IJ, Ferrari S, Le Deley MC, et al. Ewing Sarcoma: Current Management and Future Approaches Through Collaboration. J Clin Oncol. 2018;36(27):3373-84. doi: 10.1200/JCO.2018.78.9890.
2. Gulia A, Gupta S, Puri A, Desai S, Laskar S, Merchant N. Ewing Sarcoma of Pelvis: A Review of 78 Cases Treated with Curative Intent in a Tertiary Cancer Center. Indian J Orthop. 2019;53(3):443-8. doi: 10.4103/ortho.IJOrtho_176_18.
3. Leavey PJ, Collier P. Ewing Sarcoma: Rethinking the Concept of Multidisciplinary Care. J Pediatr Hematol Oncol. 2019;41(6):390-3. doi: 10.1097/MPH.0000000000001556.
4. Mora J, Spunt SL. Surveillance and Management of Adverse Effects in Long-Term Survivors of Ewing Sarcoma. Hematol Oncol Clin North Am. 2020;34(1):139-55. doi: 10.1016/j.hoc.2019.09.004.
5. Khan SJ, Fowler M, Ferguson PC, Wunder JS, Gupta A, Chung PW, et al. Survival Outcomes for Patients With Extraskeletal Ewing Sarcoma: Twenty Years of Experience at a Single Institution. Cancer. 2020;126(8):1781-9. doi: 10.1002/cncr.32726.
6. Raciborska A, Bilska K, Drabko K, Sobol G, Michalak E, Chaber R, et al. High-Dose Chemotherapy Followed by Autologous Stem Cell Transplantation in Patients with Metastatic Ewing Sarcoma: A Single-Center Experience. Adv Clin Exp Med. 2021;30(2):145-51. doi: 10.17219/acem/130110.
7. Raciborska A, Bilska K, Drabko K, et al. VIDE vs VAI chemotherapy for treatment of metastatic and/or relapsed Ewing sarcoma (ES): results of a randomised European Ewing Tumour Working Initiative of National Groups (EE99) trial. Ann Oncol. 2018;29(8):1740-1746.
8. Ghimire P, Koirala A, Baral G, Sharma D. Predictors of Outcome in Ewing Sarcoma Family of Tumors: Experience from a Tertiary Cancer Center in Nepal. Pediatr Hematol Oncol J. 2022;7(3):125-31. doi: 10.1016/j.phoj.2022.06.003
9. Raciborska A, Bilska K, Drabko K, et al. VIDE vs VAI chemotherapy for treatment of metastatic and/or relapsed Ewing sarcoma (ES): results of a randomised European Ewing Tumour Working Initiative of National Groups (EE99) trial. Ann Oncol. 2018;29(8):1740-1746.
10. McCulloch D, Fern LA, Johnson RH, Strauss SJ. Improving Outcomes for Teenagers and Young Adults with Cancer: Insights from the Ewing Sarcoma Experience. Br J Cancer. 2021;125(12):1691-9. doi: 10.1038/s41416-021-01597-y.

11. Sindhu II, Mehreen A, Wali RM, Abubakar M. Clinical Outcome of paediatric ewing sarcoma and significance of pathological necrosis for mortality after neoadjuvant chemotherapy: Single institutional study. Journal of Pakistan Medical Association. 2021 Oct 31;71(10):2344-.
12. Uyeturk U, Helvaci K, Demirci A, Sonmez OU, Turker I, Afsar CU, Budakoglu B, Arslan UY, Oksuzoglu OB, Zengin N. Clinical outcomes and prognostic factors of adult's Ewing sarcoma family of tumors: single center experience. Contemporary Oncology/Współczesna Onkologia. 2016 Jan 1;20(2):141-6.
13. Jakutis G, Ragelienė L, Rascon J. Survival of children treated for Ewing sarcoma in Lithuania: a single centre experience. Acta medica Lituanica. 2017;24(4):199.