Open Access

Original Article

Clinical Spectrum and Treatment Outcomes of Pediatric Hodgkin Lymphoma: A Retrospective Study from a Resource-Limited Setting

Nazia Rafique, Muhammad Hassan Laique, Nuzhat Yasmeen, Sughra Zulfiqar*, Ruqayya Manzoor, Hijab Shaheen

Department of Pediatric Oncology, Pakistan Institute of Medical Sciences, Islamabad Pakistan, *Department of Pediatric, Watim Medical College Rawalpindi Paksitan

ABSTRACT

Objective: To evaluate the epidemiological, clinicopathological features, and treatment outcomes of Pediatric Hodgkin Lymphoma (HL) in low- and middle-income countries (LMICs) over 15 years.

Study Design: Retrospective Analytical Study

Place and Duration of Study: Pediatric Hematology and Oncology Center, Pakistan Institute of Medical Sciences (PIMS) in Islamabad, Pakistan, from Jan 2007 to Dec 2021.

Methodology: The study analyzed 155 pediatric HL cases treated at study setting over a period of 15 years retrospectively. Cases were reviewed for age, gender distribution, clinical presentation, histological subtypes, disease staging, treatment response, and survival outcomes. Findings were compared with national and international literature.

Results: The mean age at diagnosis was 7.4 years, with 56.1% of cases between 6–10 years and a male-to-female ratio of 4:1. Classical HL (96.1%) was predominant, with mixed cellularity (63.2%) as the most common subtype. Advanced-stage disease (Stage III–IV) was observed in 75.0% of patients, and B symptoms were present in 63.2%. Despite late presentation, event-free survival (EFS) and overall survival (OS) were 89.0% and 93.5%, respectively. The relapse rate was 7.1%, with limited salvage success due to a lack of advanced therapeutic modalities.

Conclusion: This study highlights significant diagnostic and systemic delays contributing to advanced-stage presentation in pediatric HL. Despite resource limitations, survival outcomes were comparable to international standards, reflecting effective treatment protocols. Measures are needed to work on early detection, referral systems, and oncology infrastructure to further improve paediatric HL outcomes in Pakistan and similar poor countries.

Keywords: B symptoms, Classical Hodgkin Lymphoma, Delayed Diagnosis, Epidemiology, Mixed Cellularity, Pediatric Hodgkin Lymphoma, Resource Limited Setting, Survival Outcomes.

How to Cite This Article: *Rafique N, Laique MH, Yasmeen N, Zulfiqar S, Manzoor R, Shaheen H. Comparison of GRACE Score and SYNTAX Score in Predicting Complexity of Coronary Artery Disease in Patients with NON-ST ACS. Pak Armed Forces Med J 2026; 76(Suppl-8: S1266-S1270. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-8.13844*

INTRODUCTION

Hodgkin's lymphoma (HL) is a type of childhood cancer with the most favorable prognosis. It makes up 6–10% of all cancers in children around the world.[1,2] It is a lymphoid neoplasm and is identified by the presence of Reed-Sternberg cells. It is an equal cause of concern for cancer in both young children and adolescents.[3] In children, HL is mainly divided into two types: Classical Hodgkin Lymphoma (cHL) and Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL). cHL is by far the most common, seen in more than 90% of cases.[4] cHL is further subdivided into four subtypes: nodular sclerosis, mixed cellularity, lymphocyte-rich, and lymphocyte-depleted. Each Subtype has its own clinical and pathological characteristics. Among these, nodular sclerosis and mixed cellularity are the most common in children. However, the prevalence of each type varies depending on the child's geographical location and the involvement of Epstein-Barr virus (EBV).[5] The way HL is treated in children varies in different countries. In the Western world, children are usually diagnosed early, and treatments have success rates of over 90%. This success is early detection, clear treatment plans, and good supportive care.[6] On the other hand, in low- and middle-income countries (LMICs) like Pakistan, diagnosis is often delayed. This is mostly because of not having easy access to hospitals and low awareness among families and healthcare workers.[7]

There is a scarcity of data available on Hodgkin lymphoma (HL) in children from Pakistan. Comparative studies analyzing different parameters in national and international populations are very limited. Because each population has its own unique mix of environmental factors, infections, and

Correspondence: Dr Muhammad Hassan Laique, Department of Pediatric Oncology, Pakistan Institute of Medical Sciences, Pakistan
Received: 13 Sep 2025; revision received: 08 Apr 2026; accepted: 09 Apr 2026

demographics, it is imperative to have research based on local patients and compare it with international studies. This kind of evidence can help physicians make better treatment decisions as per individual patient needs.[8]

This research was carried out at a large tertiary care hospital and regional pediatric hematology and oncology center in Pakistan. The primary objective was to evaluate the epidemiological characteristics, clinicopathological features, and treatment outcomes of pediatric patients diagnosed with HL, and to compare these findings with national and international literature to identify trends and variations in clinical presentation and treatment outcomes. The rationale behind this study was to bridge the important gaps in our literature and help improve the overall understanding of pediatric HL in our region.

METHODOLOGY

This retrospective study was conducted in the Pediatric Oncology Unit, Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. Data collection and analysis were done between Nov 2024 and Apr 2025, based on a review of medical records covering 15 years from Jan 2007 to Dec 2021. After obtaining approval from the Ethical Review Board of PIMS (ERC No: F.1-1/2015/ERB/SZAMBU/1331) on 23.10.2024. The Head of the Pediatric Oncology Department also granted permission to access patient records.

A sample size calculation was not performed due to the exploratory nature of the study and variability in reported epidemiological estimates of Hodgkin lymphoma across comparable settings. Instead, all eligible pediatric patients diagnosed with Hodgkin lymphoma during the study period were included, yielding a total of 155 participants. A consecutive non-probability sampling technique was employed to ensure comprehensive inclusion of cases presenting within the study timeframe.

Inclusion Criteria: Records of children aged 1 to 13 years with a Histopathologically confirmed diagnosis of HL who had undergone complete staging and received full treatment at the study center over the past 15 years were analyzed.

Exclusion Criteria: Records were excluded if any essential clinical or treatment information was missing, or if patients discontinued treatment against medical advice.

Of the 192 records reviewed, 155 fulfilled the criteria and were then included in the final analysis. As this was a retrospective record-based study, the requirement for informed consent was waived. Pediatric HL patients were identified from the hospital admission register, and then their medical records were retrieved and reviewed for data extraction.

Data were collected using a structured, pre-tested Questionnaire. To ensure accuracy, all entries were cross-checked manually by the principal investigator. The questionnaire included demographic and epidemiological details, clinical features, histopathological classification, disease stage, treatment information, and outcomes. Operational definitions were used as follows: demographic and epidemiological variables included age at diagnosis, sex, presence of B symptoms (fever >38°C for more than three consecutive days, drenching night sweats, or weight loss >10% within six months), and family history of malignancy.

Clinical and pathological parameters included erythrocyte sedimentation rate (ESR), site of primary lymph node involvement, histological type of HL (classical HL or nodular lymphocyte predominant HL), and classical HL subtypes (mixed cellularity, nodular sclerosis, lymphocyte-rich, lymphocyte-depleted). Disease staging was done according to the Ann Arbor classification.

Treatment outcomes were categorized as complete remission, relapse, or mortality. Complete remission was defined as the absence of clinical or radiological disease after treatment. Relapse was defined as the recurrence of disease after initial remission. Among relapsed patients, outcomes were further classified as remission after relapse or death due to relapse. All-cause mortality was recorded and categorized as refractory disease, relapse-related death, or death due to sepsis. Event-free survival (EFS) was defined as the proportion of patients who achieved and maintained remission without relapsing, while overall survival (OS) was defined as the proportion of patients alive at the last follow-up, regardless of disease status. Patients were followed for at least 3 to 5 years after treatment.

Data was analyzed using IBM Statistical Program of Social Sciences (SPSS) Statistical version 23. The normality of distribution for continuous variables was assessed using the Shapiro–Wilk test. Age at diagnosis was found to be approximately normally distributed and was therefore expressed as mean ± standard

deviation. Other continuous variables, where applicable, did not demonstrate normal distribution and were summarized using appropriate descriptive measures. All categorical variables, including sex, erythrocyte sedimentation rate (ESR), primary site of lymph node involvement, histological subtype, Ann Arbor stage, presence of B symptoms, family history of malignancy, and treatment outcomes, were non-normally distributed by nature and were summarized as frequencies and percentages.

RESULTS

A total of 155 pediatric patients diagnosed with HL and treated. Mean age at diagnosis was 7.4 ± 2.56 years. Most of the patients in the study group were male (80%) as compared to females (20%). B symptoms were present in 98 out of 155 (63.2%) patients, and 128 patients (82.6%) had no family history of malignancy. The demographic and epidemiological characteristics are summarized in Table-I.

Table-I: Demographic and Epidemiological Characteristics of Pediatric HL Patients (n = 155)

Variable	Category	Frequency (%)
Age at diagnosis (years)	1–5	43 (27.8)
	6–10	87 (56.1)
	11–13	25 (16.1)
Gender	Male	124 (80.0)
	Female	31 (20.0)
Presence of B-symptoms	Present	98 (63.2)
	Absent	57 (36.8)
Family history of malignancy	Yes	27 (17.4)
	No	128 (82.6)

Elevated ESR (> 30 mm/hr) was observed in 106 patients (68.4%) while 49 patients (31.6%) had ESR below 30 mm/hr. indicating that the majority presented with raised inflammatory markers at diagnosis. The most common primary site of lymph node involvement was cervical lymph nodes (85.5%), followed by mediastinal (5.8%), axillary (5.2%), and inguinal nodes (3.2%). Regarding histological type, classical HL constituted the vast majority of cases (96.1%), while nodular type accounted for only 3.9%. Among the CHL subtypes, mixed cellularity was the most common subtype (63.2%), followed by nodular sclerosis (29.7 %), lymphocyte-rich (2.0%), and lymphocyte-depleted (1.3%). Most patients are presented with advanced-stage disease (stage 111 and IV, 50.3% and 25.2%, respectively). These clinical and pathological features of pediatric HL patients are summarized in Table-II.

Despite the predominance of advanced-stage disease at presentation, treatment outcomes were largely favorable in our study. A total of 149 patients (96%) achieved complete remission following initial therapy. The tabular representation of different treatment outcomes is in Table-III.

Table-II: Clinico-Pathological features of Pediatric HL Patients (n = 155)

Variable	Category	Frequency (%)
ESR	< 30 mm/hr.	49 (31.6)
	≥ 30 mm/hr.	106 (68.4)
Primary site of lymph node involvement	Cervical	133 (85.8)
	Mediastinal	9 (5.8)
	Axillary	8 (5.2)
	Inguinal	5 (3.2)
Histologic Type	cHL	149 (96.1)
	NLPHL	6 (3.9)
cHL subtype (n=149)	Mixed cellularity	98 (63.2)
	Nodular sclerosis	46 (29.7)
	Lymphocyte-rich	3 (2.0)
	Lymphocyte-depleted	2 (1.3)
Ann Arbor stage	I	3 (1.9)
	II	35 (22.6)
	III	78 (50.3)
	IV	39 (25.2)

**ESR – Erythrocyte Sedimentation Rate, NLPHL - Nodular Lymphocyte-Predominant Hodgkin Lymphoma, cHL - Classical Hodgkin Lymphoma*

Table-III: Treatment Outcomes of Pediatric HL Patients (n = 155)

Outcome variable	Category	Frequency (%)
EFS	Achieved and maintained remission post-treatment	138 (89.0)
Relapse outcomes	Experienced relapse	11 (7.0)
	Achieved remission post-relapse	7 (63.6)
	died post-relapse	4 (36.4)
Mortality	Total deaths	10(6.5)
	Due to sepsis	1 (10.0)
	Due to disease progression	5 (50.0)
	Relapse-related	4 (40.0)
OS	Alive at last follow-up	145 (93.5)

EFS = Event-free survival rate, OS = Overall survival

DISCUSSION

Pediatric Hodgkin lymphoma (HL), though highly curable, continues to present significant clinical challenges in low- and middle-income countries (LMICs) like Pakistan due to delayed diagnosis, limited access to specialized care, and resource-constrained healthcare systems. This retrospective study highlights the urgent need to enhance diagnostic infrastructure, improve referral systems, and implement integrated care models tailored to local needs. The mean age at diagnosis was 7.4 ± 2.56 years, and most patients were aged 6–10 years (56.1%),

consistent with other Pakistani cohorts.9 In contrast, developed nations exhibit a later peak age, often >10 years, with a bimodal distribution likely influenced by differences in healthcare access, environmental exposure, and genetics.[10] Elevated ESR (≥30 mm/hr.) was found in 68.4% of cases, much higher than reported in some local studies, i.e., 26% in a retrospective analysis. While ESR is a known inflammatory marker in HL, the high rate may also have been influenced by concurrent anemia or malnutrition, requiring further investigation.

A marked male predominance (4:1) was observed in a study conducted by Mousavi et al., which is consistent with local studies.[11] While Western and Arab literature has shown a more balanced gender distribution. This disparity may reflect biological factors and gender-based differences in healthcare-seeking behavior as reported by Ashraf *et al*.[12] A positive family history of malignancy was reported by Sherief *et al.,* in which 17% of patients were reported, higher than the international data.[13] This may be due to broader inclusion criteria, underreporting, or consanguineous marriages. A study by Linabery et al., shows a strong familial association, with up to a 13-fold increased risk in families with multiple affected first-degree relatives, emphasizing the need for detailed family history and genetic counselling in such populations.[14]

In our study, B symptoms were present in 63.2% of patients, indicating advanced disease at diagnosis. Comparable rates were reported by Rehaman *et al.,* in Pakistan from Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH& RCC), Lahore, while lower rates were reported in western literature. This variation likely reflects late presentation and higher EBV prevalence in South Asia.[15]

Cervical lymphadenopathy was the most common site (85.8%), aligning with similar studies as reported by Bhurani *et al.* Though mediastinal involvement was less common clinically, imaging often revealed bulky disease, highlighting the need for radiographic evaluation.[16]

Classical HL (cHL) constituted 96.1% of cases, with nodular lymphocyte-predominant HL (NLPHL) making up 3.9%, similar to global patterns.[17] Mixed cellularity was the most frequent cHL subtype (63.2%), consistent with South Asian studies like a study conducted by Kaseb *et al.,* whereas nodular sclerosis predominates in high-income countries. This difference represents a high prevalence of EBV infection in our population.18 Late-stage disease was common, with 75% of patients presenting in Stage III or IV. This is consistent with local data and contrasts sharply with earlier-stage diagnoses in developed nations (Sweden: 30%, UK: 42%). Misdiagnosis as tuberculosis was common, suggesting a need to train general practitioners for early recognition and referral.[13]

Despite a large number of cases with advanced disease, survival outcomes were favorable: event-free survival (EFS) was 89% and overall survival (OS) 93.5%, in comparison to both national (EFS 91%, OS 94%) and international studies (Sweden: OS 97%, South Africa: OS 91–100%. These results reflect strong treatment adherence and high-quality care despite limitations in early diagnosis and referral.[11]

The relapse rate was 7.1%, similar to both local (6–11.3%) and international data (UK: 8%). Among relapsed cases, 63.6% achieved remission, while 36.4% died, indicating limited access to more effective therapies such as autologous stem cell transplant (ASCT) or immune-based treatments.[19] Mortality in our study cohort was 6.5%, primarily due to refractory disease (50%), relapse (40%), and sepsis (10%). Comparable death rates have been reported in other studies from Pakistan (5–8%), while European studies report lower rates (Sweden: 3%, UK: 0%).[20] Improved infection control and availability of advanced therapies are needed to reduce mortality.

LIMITATION OF STUDY

This study offers important insights into the epidemiology and clinical profile of paediatric Hodgkin lymphoma in a resource-limited setting, based on one of Pakistan's largest single-center cohorts over 15 years. Strengths include long-term follow-up and comparison with national and international data. While limited by its retrospective design and single-center scope, the study points towards critical gaps in care, particularly delayed diagnosis and limited access to specialized care.

CONCLUSION

In summary, this study highlights persistent challenges in early diagnosis and referral in Pakistan. Advanced-stage presentation remains a major barrier, yet survival rates are encouraging due to effective treatment protocols. Addressing diagnostic delays and integrating risk-adapted therapies with improved healthcare infrastructure will be key to further improving outcomes.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

NR & MHL: Data acquisition, data analysis, critical review, approval of the final version to be published.

NY & SZ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RM & HS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Ward E, DeSantis C, Robbins A, Kohler B, Jamal A. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin 2014; 64(2): 83-103. https://doi.org/10.3322/caac.21219
2. Heneghan MB, Belsky JA, Milgrom SA, Forlenza CJ. The pediatric approach to Hodgkin lymphoma. Semin Hematol 2024; 61(4): 245-252.
3. https://doi.org/10.1053/j.seminhematol.2024.05.003
4. Shanbhag S, Ambinder RF. Hodgkin lymphoma: A review and update on recent progress. CA Cancer J Clin 2018; 68(2): 116-132. https://doi.org/10.3322/caac.21438
5. Polyatskin IL, Artemyeva AS, Krivolapov YA. [Revised WHO classification of tumors of hematopoietic and lymphoid tissues, 2017 (4th edition): lymphoid tumors]. Arkh Patol 2019; 81(3): 59-65. https://doi:10.17116/patol20198103159.
6. Choi JK, Quintanilla-Martinez L. Pediatric lymphomas: overview and diagnostic challenges. Virchow's Arch 2025; 486(1): 81-100. https://doi.org/10.1007/s00428-024-03980-9
7. Lo AC, Dieckmann K, Pelz T, Gallop-Evans E, Engenhart-Cabillic R, et al. Pediatric classical Hodgkin lymphoma. Pediatr Blood Cancer 2021; 68: e28562. https://doi.org/10.1002/pbc.28562
8. Cotache-Condor C, Rice HE, Schroeder K, Staton C, Majaliwa E, Tang S, et al. Delays in cancer care for children in low- and middle-income countries: development of a composite vulnerability index. The Lancet Global Health. 2023; 11(4): e505-e515. https://doi.org/10.1016/S2214-109X(23)00053-0
9. Moleti ML, Testi AM, Al-Hadad S, Al-Jadiry MF, Foà R. Pediatric Hodgkin Lymphoma in Low-and Middle-Income Countries (LMICs). A Narrative Review. Mediterr J Hematol Infect Dis 2024; 16(1): e2024078. https://doi.org/10.4084/MJHID.2024.078
10. Castellino SM, Pei Q, Parsons SK, Hodgson D, McCarten K, et al. Brentuximab vedotin with chemotherapy in pediatric high-risk Hodgkin's lymphoma. N Engl J Med 2022; 387(18): 1649-1660. https://doi.org/10.1056/NEJMoa2206660
11. Bechara E, Eid T, El-Dhuwaib A, Tamim H, Noun D, Borghol R, et al. Outcome and Challenges in the Treatment of Pediatric Hodgkin Lymphoma With Euronet-PHL-C1 Protocol: Experience From a Resource-Limited Country. Cancer Med 2025; 14(15): e71095. https://doi.org/10.1002/cam4.71095
12. Mousavi SE, Najafi M, Aslani A, Ghasemi H, Yekta Z, Nejadghaderi SA. Population-based analysis of twenty-year incidence trends of pediatric Hodgkin lymphoma in the United States. Sci Rep 2025; 15(1): 22634. https://doi.org/10.1038/s41598-025-07472-x
13. Ashraf MS, Naz F, Yakoob MY. Characteristics and survival outcomes of children with Hodgkin lymphoma treated primarily with chemotherapy. J Pediatr Hematol / Oncol 2019; 41(6): 452-456. https://doi.org/0.1097/MPH.0000000000001496
14. Sherief LM, Elsafy UR, Abdelkhalek ER, Kamal NM, Elbehedy R, Hassan TH, et al. Hodgkin lymphoma in childhood: clinicopathological features and therapy outcome at 2 centers from a developing country. Med 2015; 94(15): e670. https://doi.org/10.1097/MD.0000000000000670
15. Linabery AM, Erhardt EB, Richardson MR, Ambinder RF, Friedman DL, Glaser Slet al. Family history of cancer and risk of pediatric and adolescent Hodgkin lymphoma: A Children's Oncology Group study. Int J Cancer 2015; 137(9): 2163-2174. https://doi.org/10.1002/ijc.29589
16. Rehman P, Wali RM. Response Assessment And Outcomes In Pediatric B-Cell Non-Hodgkin Lymphoma: Our Experience At Shaukat Khanum Memorial Cancer Hospital And Research Centre. Pak Armed Forces Med J 2020; 70(5): 1402-1407. https://pafmj.org/PAFMJ/article/view/5573
17. Bhurani D, Nair R, Rajappa S, Rao SA, Sridharan N, Boya RR, et al. Real-world outcomes of Hodgkin lymphoma: a multi-centric registry from India. Front Oncol 2022; 11: 799948. https://doi.org/10.3389/fonc.2021.799948
18. Kaseb H, Babiker HM. Hodgkin Lymphoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. [updated 2023 Jun 26; cited 2026 Jul 09]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499969/
19. Riaz S, Khan S, Badar F. Pediatric Hodgkin's Lymphoma: 5-Year Experience at a Single Center in Pakistan. https://doi.org/10.1182/blood.V124.21.5455.5455
20. Englund A, Glimelius I, Rostgaard K, Smedby KE, Eloranta S, Molin D, et al. Hodgkin lymphoma in children, adolescents and young adults–a comparative study of clinical presentation and treatment outcome. Acta Oncologica 2018; 57(2): 276-282. https://doi.org/10.1080/0284186X.2017.1355563
21. Geel JA, Hramyka A, Du Plessis J, Goga Y, Van Zyl A, et al. Machine learning to predict interim response in pediatric classical Hodgkin lymphoma using affordable blood tests. JCO Global Oncol 2024; 10: e2300435. https://doi.org/10.1200/GO.23.00435