International Journal of Contemporary Pediatrics
*Anny IJ et al. Int J Contemp Pediatr. 2026 Sep;13(9):2409-2414*
https://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20264305

**Original Research Article**

# Clinical and biochemical profile of non-Hodgkin's lymphoma in children: a hospital-based study

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**Received:** 15 July 2026
**Accepted:** 14 August 2026

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## ABSTRACT

**Background:** Non-Hodgkin's lymphoma (NHL) is a diverse lymphoproliferative condition exhibiting differing clinical behavior and geographic differences in the distribution of subtypes. This research sought to assess the clinical features, stage at diagnosis, and biochemical characteristics of NHL in children hospitalized in a tertiary hospital, with the goal of outlining the disease pattern at presentation in the pediatric demographic.
**Methods:** This study, based in a hospital, was carried out in the Paediatric Haemato-Oncology Department at Bangabandhu Sheikh Mujib Medical University in Dhaka, from July 2022 to June 2023. Thirty successive children diagnosed with NHL were included. Diagnosis and staging were conducted using the St. Jude system, complemented by clinical assessment, imaging studies, and laboratory tests. The diagnosis was confirmed by biopsy, while metastatic involvement was evaluated through bone marrow aspiration and CSF analysis.
**Results:** The average age was 7.73 years, with a higher percentage of males (76.7%). The most prevalent symptoms were fever (93.3%) and abdominal pain (66.7%), whereas the most common sign was an abdominal mass (60%). LDH levels were elevated in 73.3% of the patients. Abnormalities in liver and kidney function were noted in some cases. The majority of patients (60%) arrived with stage III disease.
**Conclusions:** Childhood NHL typically appears in males approximately 7 years old, accompanied by fever and an abdominal mass. The majority of cases were identified at Stage III with raised LDH levels, showing significant tumour load and delayed detection, underscoring the importance of earlier diagnosis.

**Keywords:** Non-Hodgkin's lymphoma, Children, Clinical profile, Biochemical profile

## INTRODUCTION

Non-Hodgkin's lymphoma (NHL) is a diverse collection of lymphatic tumors that originate from T, B or unspecified cell sources.[1,2] It represents about 10–13% of newly diagnosed cancers in children, placing second behind acute lymphoblastic leukemia and brain tumors.[3] The illness exhibits a male dominance with a ratio roughly of 2.5:1 and the majority of instances arise between the ages of 5 and 15 years.[4]

The existing WHO classification categorizes different NHL subtypes based on unique morphological, immunophenotypic, and genetic characteristics and precise diagnosis necessitates the combination of all these factors.[5,6] NHL in childhood consists of four main types:

lymphoblastic lymphoma, Burkitt/small noncleaved cell, anaplastic large cell and large B-cell lymphoma. It could be without symptoms and discovered unintentionally during a CBC or chest X-ray. Location, platform, and category influence presentation. It often happens extranodally, usually impacting the abdomen, head and neck, and mediastinum.[7,8]

Laboratory results encompass CBC, blood chemistry (electrolytes, uric acid, calcium, phosphorus, LDH), CSF analysis, and bilateral bone marrow biopsy to identify dissemination. CT scans of the chest, abdomen, and pelvis, along with bone scans, are utilized as well. Staging adheres to Murphy's classification considering disease dissemination, extranodal involvement and central nervous system/bone marrow disease.[9,10]

Meena JP et al noted children with NHL, primarily appearing with a predominance of males. The majority of cases presented with an abdominal mass and advanced-stage disease (III–IV), frequently of the B-cell (Burkitt) type. Even with a delayed start, risk-adapted chemotherapy resulted in positive survival rates and manageable toxicity.[11] Marginean CO et al discovered that pediatric NHL often manifests late with vague symptoms, necessitating a biopsy for diagnosis, and that the prognosis primarily relies on stage and treatment response, showing improved outcomes in early-stage disease. Nahar K et al stated that the majority of pediatric NHL cases in Bangladesh emerge at an advanced stage with abdominal masses and systemic symptoms, predominantly of B-cell variety, highlighting that late diagnosis is frequent and that prompt histopathological confirmation is essential for improved outcomes.[12]

In Bangladesh, information regarding childhood non-Hodgkin's lymphoma is scarce and disorganized, with a majority of research emphasizing clinical characteristics and lacking thorough biochemical analysis. This study seeks to evaluate the clinical and biochemical characteristics of pediatric NHL and their relationship to enhance early diagnosis and treatment.

## METHODS

### *Study settings*

This was a prospective observational clinical study based in a hospital, carried out in the Pediatric Hemato-Oncology Unit, Department of Pediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU). The study was conducted over a span of one year, from July 2022 to June 2023.

### *Study population*

This study included a total of 30 consecutive patients who were admitted to the Pediatric Haemato-Oncology Department of the hospital during the study period.

### *Selection criteria*

Children aged 1–15 years of both genders admitted to the Paediatric Haemato-Oncology Unit of BSMMU, who were diagnosed with lymphoma through history, clinical assessment, and pertinent tests such as bone marrow examination and cerebrospinal fluid (CSF) analysis, were part of this study. Patients under 1 year and over 18 years old, along with those who were critically ill upon admission or had incomplete medical records, were not included in the study.

### *Data collection procedure*

A formatted data collection sheet was utilized for every participant. A comprehensive history and complete clinical examination were conducted in every case, with a focus on significant presenting characteristics. Pertinent evaluations comprised complete blood count, peripheral blood smear, abdominal ultrasonography, chest radiography, CT scan, bone marrow analysis, and cerebrospinal fluid examination to determine disease involvement. Extra laboratory tests including serum electrolytes, renal and liver function tests, and serum LDH were conducted for disease evaluation and treatment. All information was documented in a case record form for evaluation.

### *Data analysis procedure*

Data analysis was conducted using SPSS (Version 23.0) statistical software (SPSS, Inc, Chicago, Ill). The outcome was represented as frequency distribution; percentages were calculated, and the mean and standard deviation were determined.

### *Ethical considerations*

Before carrying out the study, the study protocol was presented to the ethics committee for approval. The study's aim, objectives, procedures, risks and benefits were explained to the patients, and informed consent was then obtained from each patient. This was an observational study and no intervention took place. A sterile single-use syringe and method were utilized for blood sampling. It was confirmed that the patient did not undergo any additional blood sampling or further investigations. It was guaranteed that all information and records remained confidential.

## RESULTS

Table 1 shows the majority of patients were aged between 6 and 10 years (40%), with an average age of 7.73±3.51 years. A distinct male dominance was observed, with males comprising 76.7% and a male-to-female ratio of 3.2:1, suggesting a greater prevalence among males.

Table 2 presents the most prevalent symptom was fever (93.3%), with abdominal pain (66.7%) and weight loss (40%) following. The most common symptom was abdominal mass (60%), whereas lymphadenopathy, dyspnoea, and ascites were observed in 23.3% each. In general, the main presenting symptoms were abdominal and systemic characteristics.

Table 3 shows most patients showed abdominal involvement (60%), then mediastinal/chest (23.3%), nodal (13.3%), and head & neck (3.3%) presentations. At the time of diagnosis, the majority of cases were at advanced stages, with 60% categorized as Stage III and 16.6% as Stage IV, and no patients classified in Stage I, highlighting a late-stage presentation in most instances.

Table 4 shows the gastrointestinal tract was the most frequently observed primary tumor site (60%), followed by the mediastinum (23.3%) and lymph nodes (13.3%). The majority of gastrointestinal and mediastinal cases were found in advanced stages (III & IV), while every lymph node case was detected in early stages (I & II). In general, most patients showed signs of advanced disease, suggesting that diagnosis was often delayed.

Table 5 presents the majority of patients exhibited increased LDH levels (73.3%), suggesting significant tumour burden. Liver function showed moderate impairment, with increased ALT in 36.7% and abnormal serum albumin levels in 43.3% of instances. Renal function assessments indicated elevated urea in 36.7% and creatinine in 33.3% of individuals. Uric acid levels were high in 23.3% of instances. In general, biochemical irregularities were prevalent, indicating considerable disease activity in a segment of patients.

Table 6 shows Bone marrow aspiration and cerebrospinal fluid analysis were conducted on all patients (100%), revealing involvement in 13.3% of cases each. Abdomen ultrasound (90%) and chest X-ray (80%) were the imaging studies conducted most often. CT abdomen was performed in 53.3% of instances, while chest CT was conducted in 23.3% of cases. Lymph node biopsy/FNAC was conducted on merely 16.6% of patients, whereas imaging of the skull and orbit was infrequently necessary (3.3%). In general, fundamental examinations were extensively utilized, whereas advanced imaging was conducted selectively according to clinical necessity.

**Table 1: Demographic characteristics of patients (n=30).**

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| **Age (years)** | 1–5 | 11 | 36.7 |
| | 6–10 | 12 | 40.0 |
| | 11–15 | 7 | 23.3 |
| | Mean ± SD | 7.73±3.51 | — |
| **Sex** | Male | 23 | 76.7 |
| | Female | 7 | 23.3 |
| | M:F ratio | 3.2:1 | — |

**Table 2: Presenting symptoms and signs (n=30).**

| Features | Frequency | Percentage |
|---|---|---|
| **Symptoms** | | |
| Fever | 28 | 93.3 |
| Abdominal pain | 20 | 66.7 |
| Weight loss | 12 | 40.0 |
| Abdominal distension | 10 | 33.3 |
| Altered bowel habit | 8 | 26.7 |
| Respiratory difficulty | 4 | 13.3 |
| Visual disturbance | 1 | 3.3 |
| **Signs** | | |
| Abdominal mass | 18 | 60.0 |
| Lymphadenopathy | 7 | 23.3 |
| Dyspnoea | 7 | 23.3 |
| Hepatomegaly | 5 | 16.7 |
| Pleural effusion | 5 | 16.7 |
| Ascites | 7 | 23.3 |
| Splenomegaly | 2 | 6.7 |
| Proptosis | 1 | 3.3 |

**Table 3: Disease presentation and stage (n=30).**

| Parameters | Category | Frequency | Percentage |
|---|---|---|---|
| **Site of presentation** | Abdominal | 18 | 60.0 |
| | Mediastinal/chest | 7 | 23.3 |
| | Nodal | 4 | 13.3 |
| | Head & neck | 1 | 3.3 |
| **Stage at diagnosis** | Stage I | 0 | 0 |
| | Stage II | 7 | 23.3 |
| | Stage III | 18 | 60.0 |
| | Stage IV | 5 | 16.6 |

**Table 4: Anatomical distribution of primary tumor sites and relationship with clinical stage (n=30).**

| Primary site | Stages I and II | Stages III and IV | Total (%) |
|---|---|---|---|
| **Gastrointestinal tract** | 1 | 17 | 18 (60.0) |
| **Mediastinum** | 2 | 5 | 7 (23.3) |
| **Lymph nodes** | 4 | 0 | 4 (13.3) |
| **Head & Neck** | 0 | 1 | 1 (3.3) |
| **Total** | 7 | 23 | 30 (100) |

**Table 5: Laboratory findings (n=30).**

| Investigations | Category | Frequency | Percentage | Mean±SD |
|---|---|---|---|---|
| **LDH** | Normal | 8 | 26.7 | 2546±2311 |
| | Elevated | 22 | 73.3 | — |
| **ALT** | Normal | 19 | 63.3 | 146.00±150.23 |
| | Elevated | 11 | 36.7 | — |
| **Albumin** | Normal | 17 | 56.7 | — |
| | Abnormal | 13 | 43.3 | — |
| **Urea** | Normal | 19 | 63.3 | 13.53±6.43 |
| | Elevated | 11 | 36.7 | — |
| **Creatinine** | Normal | 20 | 66.7 | 1.71±2.23 |
| | Elevated | 10 | 33.3 | — |
| **Uric acid** | Normal | 23 | 76.7 | 3.58±1.28 |
| | Elevated | 7 | 23.3 | — |

**Table 6: Diagnostic and radiological investigations (n=30)**

| Investigations | Category | Number of patients | Percentage |
|---|---|---|---|
| **Lymph node biopsy and FNAC** | Yes | 5 | 16.6 |
| | No | 25 | 83.3 |
| **Chest X-ray** | Yes | 24 | 80.0 |
| | No | 6 | 20.0 |
| **USG abdomen** | Yes | 27 | 90.0 |
| | No | 3 | 10.0 |
| **Bone marrow aspiration** | Yes | 30 | 100.0 |
| | Normal | 26 | 86.7 |
| | BM involvement | 4 | 13.3 |
| **CT scan abdomen** | Yes | 16 | 53.3 |
| | No | 14 | 46.7 |
| **Chest CT** | Yes | 7 | 23.3 |
| | No | 23 | 76.7 |
| **Skull & orbit imaging** | Yes | 1 | 3.3 |
| | No | 29 | 96.7 |

Continued.

| Investigations | Category | Number of patients | Percentage |
|---|---|---|---|
| **CSF study** | Yes | 30 | 100.0 |
| | Involved | 4 | 13.3 |
| | Not involved | 26 | 86.7 |

## DISCUSSION

This study found that childhood non-Hodgkin lymphoma was mainly seen in children aged 6–10 years, with an average age of 7.73±3.51 years, and males were more commonly affected than females. Similar findings were noted by Tanzir Islam Brittoet al who observed that pediatric NHL in Bangladesh primarily affects school-aged boys and remains an underappreciated health issue due to insufficient diagnostic and treatment resources.[13]

Fever, abdominal discomfort, and loss of weight were the most frequently observed symptoms, whereas abdominal mass was the main clinical indicator in this research. Comparable results were noted by Deepinder Singh Sandhu et al who found that abdominal involvement and systemic symptoms were prevalent manifestations of non-Hodgkin lymphoma, indicating its aggressive extranodal characteristics.[14]

Abdominal involvement was the most frequent presentation in this study, followed by mediastinal/chest involvement, with the majority of patients presenting at advanced stages, notably Stage III and Stage IV. Comparable results have been observed in earlier research, where abdominal NHL was noted as the most common extranodal manifestation in children, and advanced-stage disease was prevalent at diagnosis, indicating late presentation and the aggressive characteristics of pediatric NHL.[15,16]

The current study revealed common biochemical irregularities, especially increased LDH, then heightened ALT, atypical albumin, and kidney dysfunction, suggesting a substantial tumour load. LDH serves as an important indicator of tumor activity and is linked to advanced, aggressive non-Hodgkin lymphoma. Comparable results were noted by Abdullah B Al-Naeeb et al who highlighted that increased LDH levels and other biochemical alterations are significant indicators of disease severity and are commonly utilized for lymphoma staging and prognosis.[17]

Every patient had bone marrow aspiration and CSF analysis, with 13.3% displaying involvement in both. The most frequently utilized investigations were ultrasound abdomen (90%) and chest X-ray (80%), whereas CT and FNAC were conducted selectively. This represents typical lymphoma staging procedures, where evaluating the marrow and using imaging are crucial for precise staging and treatment strategies, as advised by Bruce D Cheson et al.[18]

In summary, this study found that childhood non-Hodgkin lymphoma primarily impacted school-aged males, commonly appeared with advanced abdominal involvement, and exhibited notable biochemical irregularities, highlighting the necessity for earlier detection and better treatment strategies.

## CONCLUSION

In this study, non-Hodgkin's lymphoma in childhood primarily occurred in males approximately 7 years old, with fever and abdominal mass being the main characteristics. The majority of cases were identified at an advanced stage (Stage III) with increased LDH levels and other biochemical irregularities suggesting a significant tumor burden. The study underscores late disease presentation, stressing the importance of early detection and timely treatment.

## ACKNOWLEDGEMENTS

Authors would like to thank Dean, Smt. Kashibai Navale Medical College and General Hospital, Narhe, Pune.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Anny IJ, Islam A, Jannat F. Clinical and biochemical profile of non-Hodgkin's lymphoma in children: a hospital-based study. Int J Contemp Pediatr 2026;13:2409-14.