

Outcome and survival in children with Non-Hodgkin's lymphoma

Abstract

Background Non-Hodgkin lymphoma is the third most common malignant tumor in children. It includes four major subtypes: Burkitt Lymphoma (BL), Lymphoblastic Lymphoma (LL), Diffuse Large B-cell Lymphoma (DLBL) and Anaplastic Large Cell Lymphoma (ALCL). The use of multidrug chemotherapy, radiation therapy, biologic agents, and improved diagnostic and supportive care resulted in better cure rates.

Objective This study is to report prognosis and outcome of Non-Hodgkin lymphoma (NHL) patients at tertiary health care facility in King Faisal Specialist Hospital and Research Center, Jeddah (KFSHRC-J).

Materials and Method A retrospective cross-sectional study of all eligible patients with Non-Hodgkin lymphoma (NHL), admitted, diagnosed and managed at King Faisal Specialist Hospital and Research Center, Jeddah from Jan 2005 to December 2016, previously untreated, with biopsy proven NHL and Age \leq 15 years at diagnosis. Clinical data Research Form used to collect patient's data from medical records. Demographic, Clinical and Survival data analysed using Statistical Package for Social Sciences.

Results Thirty-one pediatric patients with biopsy proven Non-Hodgkin lymphoma (NHL) fulfilled the inclusion criteria. Twenty-six (80.6%) were males. Nineteen (61.3%) patients were \leq 10 years of age at diagnosis, while 12 (38.7%) were $>$ 10 years of age. The mean age at diagnosis was 8.1 years. The commonest primary site is abdomen (n=19, 61.3%), followed by Head & Neck (n=9, 28.1%), mediastinum (n=1, 3.1%), primary CNS (n=1, 3.1%), bone (n=1, 3.1%) and skin (n=1, 3.1%). Regarding histology 19 (61.3%) had Burkitt Lymphoma (BL), 6 (19.4%) had Diffuse Large B-cell Lymphoma (DLBL), 2 (6.4%) had T-cell Lymphoblastic Lymphoma, 2 (6.4%) had T-cell rich B Cell Lymphoma, 1 (3.1%) had B-cell Lymphoma not otherwise specified and 1 (3.1%) had Cutaneous Anaplastic Large Cell Lymphoma (ALCL). Predominantly, patients presented in advanced stages III (n=18, 60%) and IV (n=10, 33%). Twenty-five (77.8%) patients completed treatment and are well to date while six of the patients (18.6%) died during the study period.

Conclusion Children admitted to the (KFSHRC-J) appeared affected by non-Hodgkin Lymphoma at a younger age, with a higher incidence of Burkitt's Lymphoma. The predominant presenting site is abdomen followed by head/neck. They present mostly with advanced disease. Survival rates are similar to those described in the literature of developed countries.

Keywords: Cancer, childhood, developing countries, epidemiology, lymphoma, Saudi Arabia, survival

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Introduction

Non-Hodgkin lymphoma (NHL) is the third most common malignant tumor in children representing approximately 8–10% of all childhood cancers in patients between 5 and 19 years.¹ Data from the US National Cancer Institute's Surveillance Epidemiology and End Results program have demonstrated a steady increase in Non-Hodgkin Lymphoma (NHL) with age. The annual incidence per million inhabitants ranges from 5.9 in children less than 5 years of age to about 10 in children between 5 and 14 years old, and 15 in adolescents.²

Non-Hodgkin Lymphoma (NHL) is a heterogeneous group of lymphoid malignancies, but the WHO classification of lymphoma, revised 2016, is now widely used, and it provides clinicians with a common language and valuable comparisons.³

Pediatric NHL is mostly (more than 95%) high-grade and includes four major subtypes: Burkitt Lymphoma (BL), Lymphoblastic Lymphoma (LL), Diffuse Large B-cell Lymphoma (DLBL). And

Anaplastic Large Cell Lymphoma (ALCL).⁴

Improvement in the outcomes of pediatrics-NHL has been seen over the past few decades. The use of multidrug chemotherapy and radiation therapy, intensification of treatment, improved supportive care, and better imaging and staging systems have resulted in the cure of more than 75% of patients, representing one of the most significant success stories in Pediatric Oncology. More recently, tremendous progress in the understanding of cancer cell biology and its microenvironment has resulted in the development of biologic agents, also called "target" therapies, that are more specific in targeting cancer cells either directly or via enhancement of the immune system.⁵

Rationale of the study

Specific studies about clinical presentations, histopathology, chemotherapy, complications, prognosis and outcome of NHL pediatric patients are lacking from this region, and the majority of data are derived from studies performed either on adults or in combination.

Objective

The primary End-point: to report the prognosis and outcome of NHL patients at our tertiary health care facility.

Secondary Endpoints

- 1) To determine the demographic features, histological subtypes and staging of NHL.
- 2) Describe the tolerance and effect of different chemotherapy protocols used in our setting.
- 3) Describe associations between survival rates, clinical and demographic characteristics.

Ethical Approval

The Institutional Review Board (IRB) of KFSH&RC-J, approved the study proposal and patients information Confidentiality is maintained.

Materials and method

Study Design: This is a retrospective cross-sectional study of all eligible patients.

Study Setting: Paediatric Hematology, Oncology and Bone Marrow Transplantation Unit, King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia.

Patients: Patients with NHL admitted, diagnosed and managed at King Faisal Specialist Hospital and Research Center, Jeddah from Jan 2005 to December 2016.

Inclusion Criteria: Previously untreated patients, with biopsy proven NHL and Age \leq 15 years at diagnosis.

Exclusion Criteria: Previously treated patients, NHL not biopsy proven and Age $>$ 15 years at diagnosis.

Data collection: Clinical data Research Form (CRF) designed and used to collect patient's data from medical records and included the following sections: **Section 1**-demographic data and the date of primary diagnosis. **Section 2**-clinical presentation, primary site, metastatic work-up and staging. **Section 3**-type of tissue obtained for diagnosis and Histopathological subtype. **Section 4**-treatment protocol, evaluation of response and toxicity report (Grade 3 or above toxicities reported based on the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. **Section 5**-outcome (dead or alive), date and cause of death, date and treatment of relapse.

Data retrieval: Medical record number of all eligible patients identified from the Oncology Data Unit of the Department of Oncology and then transferred from to the CRF.

Statistical analysis: Dataset was prepared using Statistical Package for Social Sciences (SPSS for windows) and the 5-year overall survival and disease-free survival rates will be calculated.

Results

Results of demographics

Thirty-one patients were included in this study. Twenty-six were males and only five were females with male to female ratio of 4.3:1. Nineteen patients (61%), of the total analyzed patients were \leq 10 years of age at diagnosis, while 12 (39%) were $>$ 10 years of age. The average age at time of diagnosis was 8.1 years.

Results of clinical presentation

The commonest primary site is abdomen (n=19, 61.3%), followed by Head & Neck (n=9, 28.1%), mediastinum (n=1, 3.1%), primary CNS (n=1, 3.1%), bone (n=1, 3.1%) and skin (n=1, 3.1%).

Results of histology

The most frequent histological subtype was Burkitt's Lymphoma in 20 of the patients (62.5%), DLBL in 6 patients (19.4%), T-cell Lymphoblastic Lymphoma in 2 (6.4%), T-cell rich B Cell Lymphoma in 2 (6.4%), B-cells in 1 patient (3.1%) and 1 patient (3.1%) had cutaneous ALCL.

Results of staging

Predominantly, patients presented in advanced stages III (n=18, 60%) and IV (n=10, 33%) of Murphy's Classification

Results of treatment

Follow-up duration ranges between 1.6 and 10 years with a mean follow-up duration of 5 years. Six out of 31 patients had expired during the study period. Two patients died due to infection after completion of treatment; one with SCID died due to Cytomegalovirus pneumonia and the other was splenectomized and died due to overwhelming sepsis within the 1st year of completion of treatment. Four patients died during treatment, two were stage IV and died due to sepsis. The other 2 died due to primary disease, one presented with spontaneous tumor lysis complicated by severe renal impairment which required hemodialysis and died in PICU, the other PT had primary CNS disease and died due DI.

Result of survival

Overall survival in this study was approaching 80%, which is comparable with data from developed countries.

Discussion

NHL incidence in children and adolescents depends upon age, gender, race and histopathology. Childhood NHL is more common in males as compared to females in this study, which is evident also from other studies.^{6,7}

In the present study, the mean age at diagnosis was 8.1 years & the majority of children presented were below 10 years of age, which correlates with other studies.^{8,9}

BL is the most common histological subtype as mentioned in literature and as manifested in this study and commonest presenting sign described in literature was abdominal mass as it is evident in this study as well.^{10,11}

NH-Lymphomas are rapidly growing tumors and patients present late with widespread disease, majority of patients ($>$ 90%) in this study also presented in advanced stage i.e. in stage, 3 or 4.¹²

During the last two decades, the survival outcome of children with B-NHL has shown marked improvement owing to consecutive clinical trials in large study groups, with the cure rate of childhood B-NHL reaching 90%.¹³⁻¹⁸ Overall survival in this study is approaching 80%, which is comparable with data from developed countries.

Limitations of the Study

This is a single center study involving small number of patients. There is a need for a large multi-center study will help delineate

clinical features, exact disease behaviour and more understanding of the disease.

Conclusion

Children admitted to the (KFSHRC) appeared affected by non-Hodgkin lymphoma at a younger age, with a higher incidence of Burkitt's lymphoma. The predominant presenting site is abdomen followed by head/neck. They present mostly with advance disease. Survival rates are similar to those described in the literature of developed countries. A large multi-center study will help delineate clinical features, exact disease behaviour and more understanding of the disease.

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Conflicts of interest

Author declares that there is no conflicts of interest.

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