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PEDIATRIC NON-HODGKIN LYMPHOMA IN NINEVAH GOVERNORATE: AN EPIDEMIOLOGICAL, CLINICAL AND HISTOPATHOLOGICAL STUDY

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ABSTRACT

Background: In contrast to adult non-Hodgkin lymphoma (NHL), which is typically indolent, childhood NHL is characteristically high-grade, aggressive, and highly proliferative. Objective: To evaluate the epidemiological parameters, clinical presentation, histopathological subtypes, and therapeutic outcomes of pediatric NHL at a specialized oncology unit in Mosul. **Materials and Methods:** A retrospective randomized study reviewed 60 pediatric patients aged 1–14 years admitted to the Pediatric Oncology Unit of Ibn Al Atheer Hospital from April 1, 2017, to February 28, 2018. Patients were treated using the FAB/LMB 96 protocol. **Results:** The study cohort had a mean age of 5 years, with 71.6% (n = 43) aged <=5 years. Males predominated with a male-to-female ratio of 2.75:1. The mean duration of symptoms prior to diagnosis was 4 weeks, with 75% presenting within 4–6 weeks. The primary site of involvement was the abdomen in 61.6% (n = 37) of cases, presenting as an abdominal mass (43.4%) or abdominal pain (18.4%). Peripheral lymphadenopathy was the primary feature in 28.4% (n = 17). Major associated clinical findings included pallor (56.7%), fatigue (26.7%), and anorexia (21.7%). Anemia was present in 38.4% (n = 23), with a mean hemoglobin of 8 g/dl. All patients presented with advanced disease (91.7% in Stage III and 8.3% in Stage IV). Histopathologically, Burkitt lymphoma was the dominant subtype, accounting for 91.6% (n = 55) of cases, followed by lymphoblastic lymphoma (6.7%, n = 4) and diffuse large B-cell lymphoma (1.7%, n = 1). Therapeutic evaluation demonstrated a successful completion rate of 86.7% (n = 52), while the mortality rate was 11.7% (n = 7). The primary causes of death were bacterial sepsis/neutropenic fever (8.3%, n = 5) and tumor lysis syndrome (3.4%, n = 2). **Conclusion:** Pediatric NHL in Nineveh is highly aggressive, predominantly affects males under 5 years of age, and presents almost exclusively at advanced stages. Burkitt lymphoma is the dominant variant. Despite the aggressive presentation, multi-agent chemotherapy protocols yield high remission rates.

KEYWORDS: Non-Hodgkin Lymphoma, Burkitt Lymphoma, Pediatric Oncology, FAB/LMB 96, Mosul.

INTRODUCTION

Non-Hodgkin's Lymphoma (NHL) results from the malignant proliferation of cells of the lymphocytic lineage. Although malignant lymphomas are generally restricted to lymphoid tissue such as lymph nodes and the spleen, bone marrow involvement is not uncommon in children.[1] Pathophysiologically, NHL represents a progressive clonal expansion of B-cells, T-cells, or natural killer (NK) cells arising from an accumulation of genetic lesions affecting proto-oncogenes or tumor suppressor genes.[2, 3]

As a group, non-Hodgkin lymphomas are the third most common childhood cancer, accounting for approximately 7 percent of all pediatric malignancies. In contrast to adult NHL, which is typically indolent, pediatric NHL is

usually high-grade, aggressive, and highly proliferative. Although more than 70% of pediatric patients present with advanced disease at the time of initial clinical evaluation, the prognosis has improved dramatically over recent decades, with survival rates rising to 90-95% for localized disease and 70-95% for advanced stages.[4, 5]

Epidemiologically, pediatric NHL shows a strong male predominance, with an overall male-to-female ratio of 2.3:1, and a median age at presentation of 10 years; cases under 3 years of age are rare in Western literature.[1] Etiological risk factors include congenital immunodeficiency states (e.g., severe combined immunodeficiency, Wiskott-Aldrich syndrome), acquired immunodeficiencies (e.g., HIV/AIDS), and induced immunosuppression (e.g., post-transplant regimens). Aggressive subtypes are also linked to viral agents like the Epstein-Barr virus (EBV), chronic inflammatory states such as celiac disease, and environmental exposures like pesticides and solvents.[1, 2, 7]

Childhood and adolescent NHL is categorized into four major histopathological subtypes: Burkitt lymphoma (small non-cleaved cell), lymphoblastic lymphoma (LL), diffuse large B-cell lymphoma (DLBCL), and anaplastic large cell lymphoma (ALCL).[10] The clinical presentation is closely linked to the site of the primary tumor mass. Abdominal primaries represent the most common presentation globally, often involving the bowel wall, mesentery, or omentum, and can cause pain, palpable masses, intussusception, or ascites.[4, 12]

MATERIALS AND METHODS

A retrospective study was conducted on 60 randomly selected pediatric patients aged 1–14 years who were admitted to the Pediatric Oncology Unit of Ibn Al Atheer Hospital in Mosul city, Iraq, over a 11-month period from April 1, 2017, to February 28, 2018. Medical records were reviewed to extract detailed data regarding referral origin, age, sex, symptom duration prior to diagnosis, primary tumor site, and presenting symptoms.

Diagnostic and staging workups performed before initiating treatment included a complete blood count (CBC), biochemical markers (renal and liver function tests), cerebrospinal fluid (CSF) cytology, chest X-rays, abdominal ultrasonography, bone marrow aspiration/biopsy, and computed tomography (CT) or magnetic resonance imaging (MRI) scans where clinically indicated. Anemia was defined using age-specific hemoglobin lower limits according to standard reference guidelines.[5] Histopathological diagnoses were confirmed via excisional or incisional tissue biopsies, fine needle aspiration (FNA), or malignant ascites fluid cytology, processed through the pathology laboratories of Al-Salam Teaching Hospital and specialized private reference centers. Clinical staging was determined according to the St. Jude staging system, and therapeutic management followed the international mature B-cell FAB/LMB 96 multi-agent chemotherapy protocol.[15]

RESULTS AND DISCUSSION

Geographic referral analysis indicated that 63.4% (n = 38) of the patients originated from urban areas within Mosul city, while 36.6% (n = 22) came from rural districts. The age distribution showed that the disease predominantly affected younger cohorts, with 71.6% (n = 43) of the patients aged 5 years and below. The overall mean age was 5 years. This contrasts with a median age of 10 years reported in international series, but aligns with a previous study by Yehya (2008) in Mosul, which showed a similar early childhood clustering.[18] These regional variations may reflect random selection patterns or shifting demographic conditions in the post-conflict period.

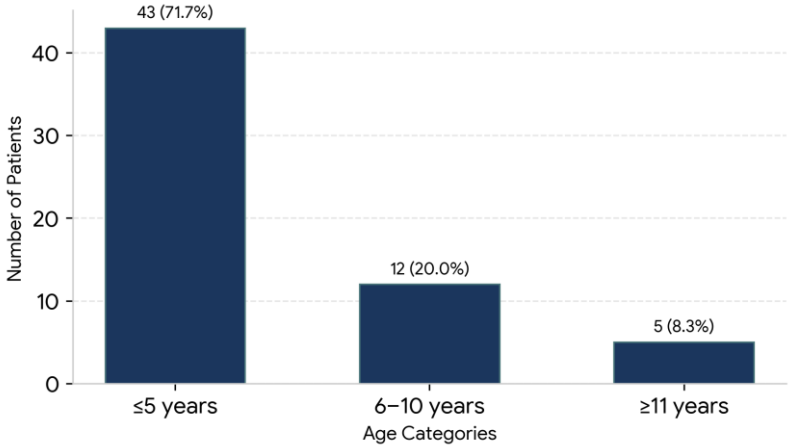

Fig. 1: Age distribution of pediatric NHL patients at presentation (n = 60)

Biological sex distribution showed a marked male predominance, with 44 males (73.4%) and 16 females (26.6%), establishing a male-to-female ratio of 2.75:1. This is highly consistent with the male predominance reported by Klumb in Brazil (2.8:1) and Burkhardt in Germany (2.7:1).[20, 21] The mean duration of clinical symptoms before definitive diagnosis was 4 weeks, with 75% (n = 45) presenting within a narrow 4–6 week

window, reflecting the rapid growth fractions characteristic of pediatric NHL.[19]

Table 1: Primary sites of involvement and initial presenting symptoms.

Primary Anatomic Site	Presenting Clinical Symptom	Case Frequency (n = 60) [%]
Abdomen	Abdominal Mass	26 [43.4%]
Abdomen	Abdominal Pain	11 [18.4%]
Lymphadenopathy	Palpable Lymph Nodes	17 [28.4%]
Jaw Mass	Jaw Swelling	4 [6.6%]
Mediastinal Mass	Acute Dyspnea	1 [1.6%]
Paraspinal Mass	Sudden Paraplegia	1 [1.6%]

The abdomen was confirmed as the most common primary site of involvement, accounting for 61.8% of cases ($n = 37$). Within this abdominal cohort, the small bowel wall was the primary location in 20.0% ($n = 12$) of cases, large bowel involvement occurred in 11.6% ($n = 7$), and 5.0% ($n = 3$) presented with intussusception. Hepatomegaly was identified in 16.7% ($n = 10$) and splenomegaly in 5.0% ($n = 3$) of cases. Peripheral or deep lymphadenopathy was present in 56.7% ($n = 34$) of the total cohort, with cervical nodes being the most frequent peripheral site (21.6%, $n = 13$). The commonest associated clinical features were pallor (56.7%), fatigue (26.7%), anorexia (21.7%), and fever (15.0%).[23]

Laboratory investigations identified anemia in 38.4% ($n = 23$) of the children, with a mean hemoglobin level of 8 g/dl. Normocytic normochromic anemia was seen in 23.4% ($n = 14$), and microcytic hypochromic patterns occurred in 15.0% ($n = 9$). Baseline white blood cell and platelet counts were normal in all patients at presentation. Advanced disease extension was confirmed by positive CSF cytology in 3.3% ($n = 2$) and bone marrow infiltration in 5.0% ($n = 3$). Staging according to the St. Jude system showed that 91.7% ($n = 55$) of patients presented with Stage III disease, and 8.3% ($n = 5$) with Stage IV. No patients presented with localized Stage I or II disease, highlighting the aggressive and rapidly spreading nature of these malignancies.[18, 24]

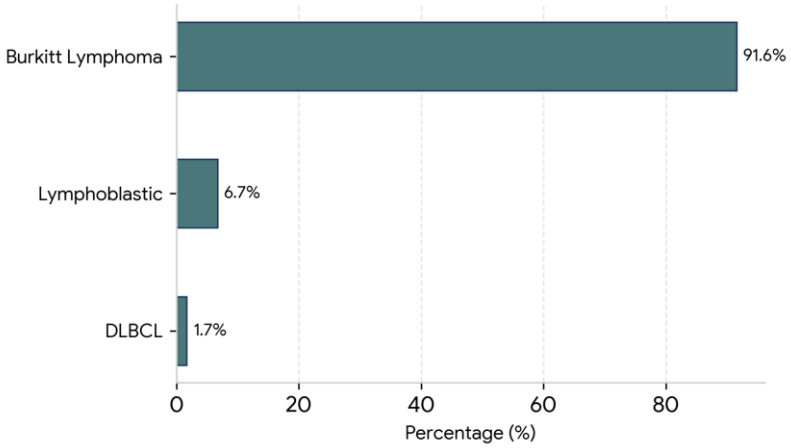

Fig. 2: Histopathological subtype distribution showing Burkitt lymphoma dominance.

Histopathological distribution showed that Burkitt lymphoma (small non-cleaved cell) was the dominant subtype, accounting for 91.6% ($n = 55$) of cases. Lymphoblastic lymphoma was identified in 6.7% ($n = 4$), and diffuse large B-cell lymphoma occurred in 1.7% ($n = 1$). This high prevalence of Burkitt lymphoma aligns with data from Sahar (88.4%) and Klumb (80%).[19, 21]

Regarding therapeutic outcomes, 86.7% ($n = 52$) of the patients successfully completed the FAB/LMB 96 multi-agent chemotherapy protocol. One patient (1.6%) refused therapy, and seven patients died, resulting in an induction mortality rate of 11.7%. This outcome compares favorably with the 82.6% survival rate reported by Sahar in 2014.[19] The primary causes of death were neutropenic fever and bacterial sepsis in 8.3% ($n = 5$) of cases, and acute tumor lysis syndrome (TLS) in 3.4% ($n = 2$). These findings demonstrate that while advanced pediatric NHL can be highly responsive to intensive chemotherapy, metabolic and infectious complications present significant clinical challenges during induction.[18, 19]

CONCLUSION

1. Childhood NHL in Nineveh is highly aggressive, predominantly affects males under 5 years of age, and has an overall mean age of 5 years.
2. The abdomen is the most common primary site of involvement, with abdominal masses and pain being the main presenting symptoms.

3. Burkitt lymphoma is the dominant histopathological subtype, accounting for over 90% of pediatric cases.
4. The majority of cases present at advanced stages (St. Jude Stage III and IV), with no localized Stage I or II presentations observed.
5. The FAB/LMB 96 protocol achieved a high therapeutic success rate of 86.7%, with bacterial sepsis and tumor lysis syndrome identified as the primary causes of mortality.

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