Primary Extranodal Non-Hodgkin’s Lymphomas: A Single Center Experience

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ABSTRACT

Background: Primary extranodal non-Hodgkin’s lymphoma is emerging as a common entity that presents with diverse clinical features, morphology and immunophenotyping patterns.

Aim: The aim of this study is to analyze the clinicopathological and immunohistochemical features in patients with primary extranodal non-Hodgkin’s lymphoma.

Settings and Design: This is a retrospective observational study from pre-recorded hospital data.

Materials and Methods: The data of all histologically confirmed patients with non-Hodgkin’s lymphoma were retrieved to identify those confirmed as primary extranodal non-Hodgkin’s lymphoma among patients attending King Abdulaziz University Hospital, Jeddah, Saudi Arabia over the last 12 years (January 2003 - May 2015). Retrieved data was analyzed with regards to the demography, clinical features, histopathological and immunohistochemical features. Lymphoma of the study group were classified according to World Health Organization classification of lymphomas 2008.

Result: A total of 218 patients with histologically confirmed non-Hodgkin’s lymphoma were identified. Seventy-nine (36.2%) had primary extranodal non-Hodgkin’s lymphoma. The most common age group affected was 20-39 years for both genders. Gastrointestinal system was the most frequently involved system for both genders. Colon was the most common site involved among males, while thyroid and thymus were the most common sites involved among females. Diffuse large B cell lymphoma was the most common histological type.

Conclusion: Primary extranodal non-Hodgkin’s lymphoma is common in Saudi Arabia affecting males and females almost equally in the third and fourth decades of life, with diffuse large B cell lymphoma being the most common histologic subtype.

Keywords
Extranodal lymphoma; Diffuse large B cell; non-Hodgkin’s lymphoma


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INTRODUCTION

Primary extranodal non-Hodgkin's lymphoma (PENHL) is a group of diverse and challenging presentations of non-Hodgkin’s lymphoma. Factors contributing to the significant degree of challenge are the large variety of lymphoma subtypes occurring at extra nodal sites, the variation in their morphology and expression of immunohistochemical markers, variability of genetic profile and clinical presentations. These variations not only cause limitations in distinguishing within and between them but also in distinguishing them from other malignancies. The necessity of such distinction is essential due to the different clinical implications of lymphomas with primary versus secondary involvement of extranodal sites[3].

Literature is replete with controversies regarding the definition of PENHL, especially given the scenario of co-existent nodal and extranodal disease. Proposed definitions of PENHL vary from lymphoma localized to a single extranodal site with involvement of its regional lymph nodes to lymphoma in which extranodal organ is the dominant presenting site of the disease although it may otherwise be widespread[1]. In the latter case therapy is primarily aimed at the dominant site[2].

As per Dawson criteria[2], lymphoma is said to be primarily extranodal if 1) On the first physical examination performed there is no palpable superficial lymph nodes; 2) Plain chest X-ray shows no evidence of mediastinal lymphadenopathy; 3) Major bulk of the disease is at the extranodal sites; 4) Involvement of regional lymph nodes near the primary lesion; and 5) Normal range of white blood cell (WBC) count. The extranodal site at which lymphoma arises is an important predictor of its biological behavior, pathological features, clinical presentation, dissemination pattern, genetic profile and outcome[13]. Applying the existing definitions and the available epidemiological data the PENHL constitute 25-50% of all non-Hodgkin lymphomas[5-9].

According to the most recent Saudi Cancer Registry report non-Hodgkin’s lymphoma ranks second among male population accounting for 8.5% and seventh among female population accounting for 4%. The most common age group affected is between 60-69 years[10]. To the best of our knowledge, no substantially large population based study has considered incidence patterns for the PENHL subtypes in Saudi Arabia as defined by the WHO classification.

It is evident that since PENHL can arise at any site in the body, collection of a single site population based series for the purpose of study is difficult. The comparison between various reported series is further limited by the absence of consistent criteria for both the definition and enrollment of PENHL and the use of different systems for clinical staging and histologic sub-typing. Despite the relative prevalence of PENHL, detailed data on the subject is scant in literature especially in this region. This retrospective study aimed to examine the pattern of PENHL among patients attending King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia from January 2003 until May 2015, with a view to determine their various clinicopathological and immunohistochemical features.

AIM

Study Setting and Population

We performed a retrospective evaluation of all histologically confirmed cases of non-Hodgkin’s lymphoma (NHL) from the departmental archives of Anatomic Pathology. Out of these cases, we then identified PENHL among patients attending KAUH, Jeddah, KSA from January 2003 to May 2015 for this study. The inclusion criteria were all histologically diagnosed PENHL in all ages and nationalities. We excluded from the study cutaneous T cell lymphoma, plasmacytoma and nodal NHL with secondary extranodal involvement. Non-Hodgkin’s lymphomas with predominant involvement of extranodal sites with no or only trivial lymph node involvement were considered as PENHL[1]. Non-Hodgkin’s lymphomas with clinically predominant and generalized lymph node involvement were considered as nodal. Involvement of Waldeyer’s ring and spleen were considered nodal sites[11]. The study was carried out in accordance with the Principles of Helsinki Declaration of 1975, as revised in 2000.

Data Collection

A computerized search was performed to filter the required data using Systematized Nomenclature of Human Medicine (SNOWMED) morphologic codes indicating following parameters: Date of receiving biopsy, demographics, clinical diagnosis, morphology and radiography. Relevant and necessary medical information was obtained from the medical records. Data regarding clinical staging was obtained partly from the medical records and partly from the clinical teams involved. Patients were staged according to the Ann Arbor classification by performing clinical examination of palpable lymph nodes, radiological evidence using computerized tomography scan, histopathological confirmation and bone marrow biopsy. All the data obtained was rechecked manually to filter duplications. Computerized search was then exported to Microsoft Office 2010, EXCEL - Service Pack 2, (Microsoft Inc., Redmond, WA USA) which was used for analysis.

Paraffin embedded Hematoxylin and Eosin (H & E) stained tissue sections were analyzed and reviewed by two histopathologist to reach a consensus diagnosis and reclassified based upon morphologic and immunophenotypic criteria according to World Health Organization 2008 classification[12]. Immunohistochemical (IHC) analysis was performed initially to classify the lymphomas into B and T cell type and then to further subclassify them into more specific
types. Immunohistochemical analysis was performed on the paraffin embedded tissue sections, using a panel of antibodies by Peroxidase-antiperoxidase method. Antigen retrieval was done as required. All antibodies used were "ready to use" kits (Ventana, Rocklin, CA, USA). An automated immunostainer (BenchMark XT, Ventana Medical Systems Inc., Tucson, AZ, USA) was used to perform IHC staining according to the manufacturer's instructions. Subsequently, slides were washed, counterstained with Mayer's hematoxylsin, and mounted. Negative and positive controls were used. The panel of antibodies used for IHC, based upon morphological analyses, anatomic sites and panel selection guidelines from Higgins et al.[13], included leukocyte common antigen (LCA), B cell markers such as CD20 and CD 79a, T cell markers such as CD 3 and CD 8, CD 4, CD 8, CD 30, CD 23, CD 43, CD 10, CD 99, CD 38, CD 56, TdT (terminal deoxynucleotidyl transferase) Bcl-2 & 6, anaplastic large cell lymphoma kinase-1 (ALK-1), Cyclin D1, epithelial membrane antigen (EMA), neuron specific enolase (NSE), synaptophysin (SYN) and pan cytokeratin (CK-PAN). Mitosis was counted in areas with the highest reactivity after staining with the MIB1 antibody detecting the Ki67 antigen. Combined scoring criteria used were according to Higgins et al.[13] and Rao[14].

Statistical Analysis

Data was analyzed using the program statistical package for the SPSS for Windows, Version 15.0 (SPSS Inc., Chicago, IL USA). Descriptive and frequency statistics were obtained for the variables studied. Different parameters were compared and analyzed for frequencies using the chi-square test or other appropriate tests as determined by the type of data.

RESULTS

There were 218 cases of NHL out of which 138 (63.3%) were nodal and 79 (36.2%) were PENHL. Among the patients who had PENHL, 34 (43%) were Saudi and 45 (56.9%) were non-Saudi. The most common age group involved by PENHL was 20-39 years. No case was recorded below 2 years of age. One (1.2%) case was recorded above 80 years of age in a female patient. Male to female ratio was 1.2:1. On histological examination 75 (95%) were B cell type and 4 (5.3%) were T cell type. The most common system involved among both genders was the gastrointestinal system. Head and neck region and musculoskeletal system were the second most commonly involved systems among males while endocrine system was the second most common system involved among females. The detailed age, sex, system, histological type and immunohistochemical expression are presented in Tables 1, 2, 3, and Figures 1 and 2.

DISCUSSION

About one third of PENHL develops in extranodal sites[15,16]. It is also encountered frequently in Saudi Arabia. Al Diab et al.[17] reported an incidence of 41.4% from Riyadh, Saudi Arabia with notable differences in the pattern among

**TABLE 1.**

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>B Cell Type</th>
<th>T Cell Type</th>
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<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
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<tr>
<td>N</td>
<td>%</td>
<td>N</td>
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<tr>
<td>0-19</td>
<td>4</td>
<td>5.00%</td>
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<tr>
<td>20-39</td>
<td>11</td>
<td>13.75%</td>
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<tr>
<td>40-59</td>
<td>14</td>
<td>17.50%</td>
</tr>
<tr>
<td>60-79</td>
<td>11</td>
<td>13.70%</td>
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<tr>
<td>More than 80</td>
<td>None</td>
<td>None</td>
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</tbody>
</table>

**FIGURE 1A, B.** Percentage of histological subtypes of PENHL at KAUH, Jeddah, KSA among both genders.

DLBCL: Diffuse large B-cell lymphoma; BL: Burkitt lymphoma; MALTL: Mucosal associated lymphoid tissue lymphoma; FL: Follicular lymphoma; MCL: Mantle cell lymphoma; SLL: Small lymphocytic lymphoma; BCLL: B cell lymphoclastocytic lymphoma; T/NK CL: T cell/Natural killer cell lymphoma; ATCL ALK POS: Anaplastic T cell lymphoma ALK positive; ATCL ALK NEG: Anaplastic T cell lymphoma ALK negative; PENHL: Primary extranodal non-Hodgkin’s lymphomas; KAUH: King Abdulaziz University Hospital; KSA: Kingdom of Saudi Arabia
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Saudi patients compared to other nationalities. These findings are similar to our results and to reports from the neighboring Arab countries like Kuwait (52% of all NHL) indicating the possible role of common transmissible and demographic factors in the etiology of PENHL in this region. In Table 4 we present the analytical comparison of our study with recent studies from Asian[5-7,17,19-24] and Western countries[15,25-27]. Extranodal disease is also frequent in patients from France (42%), Denmark (33%) and Israel (34%)[29]. Increasing trend has also been reported from developing countries, especially in Middle East and Far East[20,21]. A study from Nigeria[26] reported an enormous increase in the prevalence of PENHL from 9.8% during 1981-1998 to 46.4% during 1991-2005 in their study. Interestingly most of the PENHL (52.1%) cases in the Nigerian study were among children less than 17 years[26]. Minor epidemiological variations are reported in terms of extranodal sites that are predominantly involved: for instance the frequency of intestinal PENHL ranges from 1% in Italy to 10% in Kuwait while gastric PENHL ranges from 3% of all NHL in Costa Rica to 10% in Kuwait, Italy, and Spain[18,30,31]. The jaw is one of the common locations of PENHL (23.5%) reported from Nigeria[26]. This regional variation in common sites of PENHL may be explained partly by variability of ethnic factors and partly by the use of diverse definition criteria.

The incidence of PENHL has increased more rapidly than the nodal type[23,39] and it represents much of the increase in NHL incidence observed in the past thirty years in United States[39]. Non-Hodgkin’s lymphoma ranks fifth among the most commonly diagnosed cancer in United States, with an estimated 70,130 new cases in 2012[20]. The incidence rates for PENHL increased at a rate of 4.1% annually, compared with a slower rate of 1.4% for nodal NHL according to the data from the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) Program United Sates, from 1975 to 2003[20]. Extranodal disease is also frequent in patients from France (42%), Denmark (33%) and Israel (34%)[29]. Increasing trend has also been reported from developing

<table>
<thead>
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<th>TABLE 2.</th>
<th>Detailed site distribution of PENHL at KAUH, Jeddah, KSA (n = 79).</th>
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</thead>
<tbody>
<tr>
<td>Site of PENHL</td>
<td>Number</td>
</tr>
<tr>
<td>Colon, Thymus, Thyroid Gland</td>
<td>9 (each)</td>
</tr>
<tr>
<td>Stomach, Neck</td>
<td>7 (each)</td>
</tr>
<tr>
<td>Nose and Nasopharynx</td>
<td>5 (together)</td>
</tr>
<tr>
<td>Ileum</td>
<td>4</td>
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<tr>
<td>Mouth, Scalp</td>
<td>3 (each)</td>
</tr>
<tr>
<td>Parotid Gland, Lumbar Vertebra, Brain, Breast, Ovary, Thigh</td>
<td>2 (each)</td>
</tr>
<tr>
<td>Chest Wall, Ilium, Femur, Lung, Kidney, Esophagus, Duodenum, Retropertitonium, Cervix, Vagina, Adrenal gland</td>
<td>1 (each)</td>
</tr>
</tbody>
</table>

PENHL: Primary extranodal non-Hodgkin’s lymphomas; KAUH: King Abdulaziz University Hospital; KSA: Kingdom of Saudi Arabia

FIGURE 2A, B. Percentage of histological subtypes of PENHL at KAUH, Jeddah, KSA among both genders.

DLBCL: Diffuse large B-cell lymphoma; BL: Burkitt lymphoma; MALTL: Mucosal associated lymphoid tissue lymphoma; FL: Follicular lymphoma; MCL: Mantle cell lymphoma; SCLL: Small lymphocytic lymphoma; BCLL: B-cell lymphoblastic lymphoma; PL: Plasmablastic lymphoma; T/BCL: T cell rich B cell lymphoma; BCLU: B cell lymphoma unclassified; TNK CL: T cell/Natural Killer cell lymphoma; ATCL ALK POS: Anaplastic T cell lymphoma ALK positive; ATCL ALK NEG: Anaplastic T cell lymphoma ALK negative; PENHL: Primary extranodal non-Hodgkin’s lymphomas; KAUH: King Abdulaziz University Hospital; KSA: Kingdom of Saudi Arabia
**TABLE 3.**

Immunohistochemical expression of markers against histological subtypes of PENHL at KAUH, Jeddah, KSA.

<table>
<thead>
<tr>
<th>IHC Marker</th>
<th>N= 79(%)</th>
<th>LCA</th>
<th>CD 20</th>
<th>CD 79a</th>
<th>CD3</th>
<th>CD5</th>
<th>CD 23</th>
<th>CCND1</th>
<th>Bcl2</th>
<th>CD10</th>
<th>CD45</th>
<th>Bcl6</th>
<th>TdT</th>
<th>CD99</th>
<th>CD 38</th>
<th>CD8</th>
<th>CD 4</th>
<th>Alk</th>
<th>CD 30</th>
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<tr>
<td>DLBCL</td>
<td>54 (68.3)</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<td>-</td>
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<td>+</td>
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<tr>
<td>MALT L</td>
<td>8(10)</td>
<td>+</td>
<td>+</td>
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<td>BKL</td>
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<td>FL</td>
<td>4(5)</td>
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<td>SLI</td>
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<td>MCL</td>
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<td>PL</td>
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<td>T/BCL</td>
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<td><strong>T CELL TYPE</strong></td>
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<td>T/NK CL</td>
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</table>

DLBCL: Diffuse large B-cell lymphoma; BL: Burkitt lymphoma; MALT L: Mucosal associated lymphoid tissue lymphoma; MCL: Mantle cell lymphoma; FL: Follicular lymphoma; SCLL: Small lymphocytic lymphoma; BCLL: B-cell lymphoblastic lymphoma; PL: Plasmablastic lymphoma; T/BCL: T cell rich B cell lymphoma; BLCL: B cell lymphoma unclassified; T/NK CL: T cell/Natural Killer cell lymphoma; ATCL ALK POS: Anaplastic T cell lymphoma ALK positive; ATCL ALK NEG: Anaplastic T cell lymphoma ALK negative; TdT: Terminal deoxynucleotidyl transferase; CCND1: Cyclin D1; PENHL: Primary extranodal non-Hodgkin’s lymphomas; KAUH: King Abdulaziz University Hospital; KSA: Kingdom of Saudi Arabia

Immunohistochemical expression scoring: +, >50%; −, >5%; +/-, 5–25%; +/−, 25–50%; v *, not performed
as the most common system involved followed by head and neck and central nervous system (CNS) in other frequent sites[35,37]. Some studies indicate stomach as the most common organ involved[9] followed by the head and neck[9]. On the contrary a study from India reported central nervous system (CNS) as the most common extranodal site (20/68, 29.5%) followed by stomach (17/68, 25%), and nose/nasopharynx (5/68, 7.3%). Th e etiology of PENHL is dependent on multiple factors such as immune suppression, infections and exposure to pesticides or other environmental agents[38]. The anatomic location of PENHL may suggest specific disorders such as systemic lupus erythematosus (SLE)[42], Celiac disease[42], inflammatory bowel disease (IBD)[42], Sjogren syndrome[42], rheumatoid arthritis[42], Hashimoto thyroiditis[43], immunodeficiency syndrome (HIV/AIDS, organ transplant)[44] has been reported. Regarding prognosis Chen et al.[9] reported that PENHL had worse outcomes with significant variation in survival rates when compared to nodal, clarifying the applicability and prognostic significance of the WHO 2008 lymphoma classification system. A population based study examining the relevance of sites of PENHL (DLBCL type) to the prognosis concluded that sites associated with worse overall survival rates were gastrointestinal, pulmonary and liver/pancreas, whereas those arising in head and neck were associated with better survival[20]. The association of PENHL with the mentioned autoimmune disorders may also contribute to poor prognosis.

The most common histological type of PENHL is the diffuse large B-cell lymphoma[9]. We found similar results in the present study and other studies from the region[17]. A rising trend of diffuse histological pattern over nodular is seen particularly in developing countries, especially in the Middle and Far East, with an increase in more aggressive biological behavior[20]. A population based study examining the histological pattern of PENHL

### TABLE 4.

Analytical comparison of PENHL pattern with other Asian and Western countries.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year/Country of Study</th>
<th>NHL</th>
<th>PENHL n (%)</th>
<th>Duration of Study</th>
<th>Most Common Anatomic Sites in Order of Frequency</th>
<th>Most Common Histological Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian countries</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fujita et al.[10]</td>
<td>2009, Japan</td>
<td>847</td>
<td>395 (46.60%)</td>
<td>7</td>
<td>GIT, WR, Orbit</td>
<td>DLBCL,MALT</td>
</tr>
<tr>
<td>Chen et al.[11]</td>
<td>2010, Taiwan</td>
<td>278</td>
<td>125 (44.99%)</td>
<td>1</td>
<td>Stomach, WR, Eye, Sino nasal Cavity, and Small Intestine</td>
<td>MZBCL,DLBCL</td>
</tr>
<tr>
<td>Kim et al.[12]</td>
<td>2011, Korea</td>
<td>3807</td>
<td>2650 (69.90%)</td>
<td>1</td>
<td>Stomach, WR, Eye, Sino nasal Cavity, and Small Intestine</td>
<td>MZBCL,DLBCL</td>
</tr>
<tr>
<td>Al Diab et al.[13]</td>
<td>2011, KSA</td>
<td>855</td>
<td>354 (41.40%)</td>
<td>5</td>
<td>GIT, Head and Neck, Skin</td>
<td>DLBCL,MALT</td>
</tr>
<tr>
<td>Padi et al.[14]</td>
<td>2012, India</td>
<td>308</td>
<td>68 (22.00%)</td>
<td>5</td>
<td>Brain, GIT, NPNS</td>
<td>DLBCL,MALT,BCLU</td>
</tr>
<tr>
<td>Yang et al.[15]</td>
<td>2011, China</td>
<td>5549</td>
<td>2968 (53.50%)</td>
<td>9</td>
<td>WR, GIT, NPNS, Skin</td>
<td>DLBCL,ENKTCL,MALT</td>
</tr>
<tr>
<td>Yaqo et al.[16]</td>
<td>2011, Iraq</td>
<td>205</td>
<td>99 (48.30%)</td>
<td>7</td>
<td>Intestine, WR, Nose, Stomach Skin</td>
<td>DLBCL,BL,MALT</td>
</tr>
<tr>
<td>Nagi et al.[17]</td>
<td>2010, SA</td>
<td>386</td>
<td>147 (38.80%)</td>
<td>13</td>
<td>GIT, NPNS, Salivary Gland, Bone</td>
<td>DLBCL,FLC,LB,</td>
</tr>
<tr>
<td>Lal et al.[18]</td>
<td>2008, Pakistan</td>
<td>557</td>
<td>235 (42.00%)</td>
<td>16</td>
<td>GIT</td>
<td>DLBCL</td>
</tr>
<tr>
<td>Temmam et al.[19]</td>
<td>2004, Kuwait</td>
<td>2077</td>
<td>935 (45.00%)</td>
<td>16</td>
<td>Stomach, Skin</td>
<td>DLBCL,DL</td>
</tr>
<tr>
<td>Western countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu et al.[20]</td>
<td>2009, USA</td>
<td>30,444</td>
<td>30,444</td>
<td>5</td>
<td>GIT, WR, Orbit, Skin (other than MF), Stomach, Oral Cavity Nasopharynx and Brain (men), Stomach, Skin (other than MF), Oral Cavity Pharynx and Brain (women)</td>
<td>DLBCL,MALT</td>
</tr>
<tr>
<td>Cabrera et al. et al.</td>
<td>2012, Chile</td>
<td>195</td>
<td>74 (38.00%)</td>
<td>2</td>
<td>Stomach</td>
<td>DLBCL,MALT</td>
</tr>
<tr>
<td>Olusowalo et al.[21]</td>
<td>2011, Nigeria</td>
<td>558</td>
<td>235 (33.50%)</td>
<td>15</td>
<td>Jaw, Nasopharynx and Nasal Cavity, Breast, Ovary</td>
<td>SNCCL,DLBCL,SLL</td>
</tr>
<tr>
<td>Holler et al.[22]</td>
<td>2009, Germany</td>
<td>116</td>
<td>28 (24.13%)</td>
<td>Stomach, Thyroid, Small and Large Intestine</td>
<td>DLBCL</td>
<td></td>
</tr>
<tr>
<td>Present study</td>
<td>2015, KSA</td>
<td>218</td>
<td>79 (36.20%)</td>
<td>12</td>
<td>GIT, Endocrine, Head and Neck</td>
<td>DLBCL</td>
</tr>
</tbody>
</table>

GIT: Gastrointestinal tract including stomach, small and large intestine; NPNS: Nose, nasopharynx, and paranasal sinus; WR: Waldeyer’s ring; DLBCL: Diffuse large B cell lymphoma; ENKTCL: Extranodal natural killer/T cell lymphoma of nasal type; MALT: Extra nodal marginal zone lymphoma of mucosa associated lymphoid tissue type; BL: Burkitt lymphoma; MF: Mycosis fungoides; SNCCL: Small non cleaved cell lymphoma; SLL: Small lymphocytic lymphoma; PTCL: Peripheral T cell lymphoma, BCLU: B cell lymphoma unclassified, PENHL: Primary extranodal non-Hodgkin’s lymphomas; USA: United States of America; KSA: Kingdom of Saudi Arabia. * Not indicated in the study
among different whites, blacks and Asian/Pacific Islanders (APIs) classified the PENHL into B and T cell types. They reported that blacks and APIs showed the same or even lower incidence rates than whites for B–cell PENHL. The most common phenotype was the B-cell type (DLBCL followed by marginal zone lymphoma) among all races and both genders. A higher frequency was noted among white and API males (78%) and females (82%). However, the frequency was much lower among black males and females (69%). PENHL of T cell type were more common among blacks[8]. A cohort study examining the cytomorphological and immunohistochemical profile of high grade B-cell lymphomas performed genetic profiling using cDNA and oligonucleotide microarrays[27]. In this study two differentiation types of PENHL were delineated; one the germinal center B-cell like (GCBC) and the other activated B-cell like (ABC)[27]. The frequency of both types was similar. GCBC differentiation represented a favorable phenotype while immuno-expression of Bcl-2 and Bcl-6 (less than 20% of cells) represented an unfavorable one[27].

Limitations
The results in this study should be interpreted in the backdrop of its limitations. The first being due to existing confusions in literature regarding the categorization of Waldeyer’s ring and spleen as nodal or extranodal locations. We used Zucca et al.[11] criteria to consider these sites as nodal which might have led to the under estimation of this group and contributed to the differences in reporting the most common site when compared to other studies. The sample size is small and does not reflect a population based trend at large.

CONCLUSION
Primary extranodal non-Hodgkin’s lymphoma is fairly common in KSA affecting males and females with equal distribution. Diffuse large B cell is the most common histologic subtype. Gastrointestinal tract is the most frequently involved system. The most common site involved among males is the colon while among the females it is the thyroid gland. The heterogeneity of the pattern of PENHL suggests the importance of examining this malignancy by its histology, immunohistochemical expression and anatomic site of origin. Further study of distinct race and site-specific patterns in histology of PENHL will further explain racial differences in risk factor exposure and/or genetic predisposition and survival outcomes. Systematic large population based studies are recommended for this purpose. Since this is a single center experience it might not be generalizable to the experience in the Kingdom as a whole.

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Disclosure Statement
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Conflict of Interest
The authors have no conflict of interest.

Disclosure
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Ethical Approval
Obtained.

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Primary Extranodal Non-Hodgkin’s Lymphomas: A Single Center Experience
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المستخلص.

المعلومات الأساسية: يظهر ورم اللفوم اللاهدوفي كمرض نادر، به عدد سمات وأشكال وألمنا الكلينيكي.

الهدف: تهدف هذه الدراسة إلى تحلي البقاء الكلينيكي في المرضى المحتملين بورم اللفوم اللاهدوفي.

الإعداد والتصميم: هذه الدراسة مكونة مكليد معينة على بيانات المستشفى المسجلة سابقا.


النتائج: تم تحديد مجموعة من المرضى بلغ عددهم 218 مصابًا بورم اللفوم اللاهدوفي، واتضح إصابة 29 منهم بورم اللفوم اللاهدوفي خارج العقد اللفومية الأولية، حيث تراوحت أعمار أكثر إصابة بالمرض بين 20 و39 لكل الأسس، وتبين أن أكثر الأجهزة تعرضها للمريض هو الجهاز الهضمي، أما الفولان فقد كان الأكثر إصابة في الذكور، بينما كانت الغدة الدهنية والمعروفة (التوصية) الأكثر إصابة بين الإناث.

الخاتمة: أوضحت الدراسة أن ورم اللفوم اللاهدوفي خارج العقد اللفومية الأولية هو مرض نادر في السعودية لدى الذكور والإناث على السواء، وتكثر الإصابة به في العقود الثلاث والرابع من العمر.