DISCUSSION

Lymphadenopathy is one of the most common clinical problems encountered in pediatrics. The precise incidence of lymphadenopathy is not known, however Larsson et al stated that 38- 45% of otherwise healthy children have palpable cervical lymph nodes in USA. [69]

Park states that 90% of children aged 4-8 yrs have palpable cervical lymph nodes. [70]

The evaluation of the child with lymphadenopathy is a common clinical scenario for the pediatrician. Most of the cases result from a benign, self-limited disease and most resolve without any sequelae within a limited period. Since it can be the manifestation of a serious systemic disease or malignancy, it is critical to understand the differential diagnosis in directing an appropriate and timely evaluation. [71]

The patients are often referred to a specialist with delay and even more often they are referred to unneeded diagnostic and therapeutic procedures. [72]

After reaching the final diagnosis, all studied patients were divided into 2 groups according to the etiology neoplastic and non- neoplastic, the later was further divided into infectious and non infectious.

The present study was directed toward classifying the etiology of pediatric lymphadenopathy after full detailed history, clinical examination of each case and lymph node examination. Relevant laboratory studies was done according to the propable diagnosis.

The present study was conducted on 170 patients including 109 (64.1%) males and 61 (35.88%) were females with male to female ratio of 1.8:1.

In concordance with our study, the demographics of several studies showed male predominance as well [72,73]. Other studies found no sex predilection for lymphadenopathy. [71,72,74-78]

In the present study, the gender of the studied patients had no statistical significant difference (p=0.204) between the two groups, although 75% of the diagnosed as malignant etiologies were males.

This is like the study by Adelusola et al [79] and Tanteo et al [80] who showed lymphomas to be more common in males. They suggested that though gender is not a risk factor for lymphadenopathy, certain etiologies for lymphadenopathy are more prevalent in one gender over the other.

In the present study, the age range was between one month and 18 years old with overall mean age 6.1± 4.6 years.. The majority of the studied patients were in the preschool age (1≤ 5 years) (52.9%). This is in concordance with Reddy MP et al, [81] where the majority of children were in the age group of 4-8 years . In contrast to other studies by Mahesh et al[82], Annam et al [78] Kumar et al [83] Al-Nazer et al[84] , and Adelusola et al [79] in which most of the children were presenting in the age group of 6 to 10 years showing that the majority of cases were school aged children, probably due to increased

exposure to surrounding environment . However, Knight et al emphasized in one of the largest studies relating age to lymphadenopathy that age is not important in predicting the incidence of significant lymphadenopathy. [85]

In the current study, on comparing both groups there was no significant difference as regards age between the non-neoplastic and neoplastic categories. Several other studies similarly found that age is not important in predicting the etiology of lymphadenopathy. [76,77] On the other hand, the study by Yaris et al [75] reported a mean age to be 86 ± 55 months with higher values in malignant cases compared to other causes. In the study by Tanteo et al [80] , the children's age varied according to the different etiologies with a tendency towards benign etiology in younger ages (6.5 ± 3.8 years) and towards malignant etiology in older ages (12.4± 4.2 years). [80]

Regarding the residence, 64.7% of cases in this study came from urban areas while 35.2% came from rural areas. No significant difference was found regarding the residence between the non-neoplastic and the neoplastic categories (P= 0.171). Most of the cases within the neoplastic category (54.5%) and those within the non-neoplastic category (68.3%) came from urban areas. This difference may be explained by the referral of the cases to the Main University hospitals with better diagnostic and therapeutic facilities and not due to an actual increase in the incidence of lymphadenopathy in the urban areas. By reviewing the literature, no previous studies have compared the incidence of lymphadenopathy in rural and urban areas.

In the present study, the cases were distributed nearly equal along the different seasons of the year. This is in accordance with other study done by Larsson et al.[69]

Regarding the duration of symptoms, the majority of the patients in the current study had duration of symptoms between two to six weeks as observed in 41.1% of cases followed by the duration of less than two weeks which was observed in 38.2% of cases. Few cases had a duration of symptoms of more than 6 weeks which was observed in only 20.7% of cases.

In the present study a significant difference was found in the duration of symptoms between the non-neoplastic and neoplastic categories (P= 0.001). Most of the cases within the neoplastic category (65.9%) had duration of symptoms between 2-6 weeks while most of the cases within the non-neoplastic category (42.9%) had duration of symptoms of less than 2 weeks. This is concordant with the studies by Tanteo et al [80] and Granado et al [76]. The study by Bazemore et al [86] concluded that lymphadenopathy which lasts less than 4 weeks or more than one year without change in size, should be considered benign.

The age and duration of lymph node enlargement are two risk factors reported in malignant disease. In the current study, only duration of symptoms was statistically significant. However Soldes et al [87] reported increasing age, while Bazemore et al & Smucker [86] found older age and duration of greater than two weeks to be associated with increased risk for malignancy.

As regards the presenting symptom(s), the most frequent presenting symptom in the present study was swelling as observed in 85% of the cases. These findings were comparable to the findings of Reddy et al [81], Mahesh et al [82] and Tanteo et al [80] who reported swelling as the commonest presenting symptom in 52%, 71.8% and 82%

respectively. However, the study done by Niedzielska et al[88] showed fever to be the commonest presenting symptom (24.1%) of cases. [88]

In the present study, the major presenting symptom was neck swelling followed by fever then loss of weight. while in the study by Reddy MP et al [81] & Mahesh et al,[82] the predominant symptom were neck swelling followed by fever & cough. In another study, the predominant symptoms were swelling in the neck followed by loss of appetite and fever [89].

In the current study there was significant difference as regard constitutional symptoms, fever (p=0.037) and weight loss (<0.001), but as regard night sweating no significance (^{MC}p=0.129) was found between the neoplastic and non-neoplastic category or between the infectious and non-infectious categories. Similarly in the study of Tanteo et al [80], fever was observed more commonly in the non-neoplastic category, This is in contrast with Soldes et al[87] who showed no significant difference in the presence of fever between benign and malignant etiology. In contrast a study done by Darnal et al [90] noted that the commonest symptom in children with chronic non- specific lymphadenitis was abdominal pain followed by loss of weight and appetite, while the commonest symptom among children with tuberculosis was fever.

Regarding the systemic findings, varying grades of pallor was seen in 7.6 % of children, which, together with the finding of anemia on laboratory testing in 41.2% of children reflected the prevalence of anemia in the pediatric population. Studies by Redely et al [81] on lymphadenopathy's association with anemia revealed an incidence of 45%, an observation comparable to our study. [81]

In the present study, head and neck findings were observed in 32.3% of cases, out of which follicular tonsillitis and tonsillar enlargement were detected in 11.1% of cases and pharyngitis in 7.6% of cases. Chest findings were observed in 7.4% of cases and abdominal findings were detected in 24 % of cases, abdominal organomegaly was detected in 19.4% of cases, out of which, hepatomegaly was detected in 9.4% of cases, splenomegaly in 10% of cases. According to Reddy et al [81], abdominal organomgaly and chest findings were observed in 15% and 21% of cases respectively.

As regards, lymph nodes characteristics in the present study, Cervical LN enlargement was the most prevalent among the localized peripheral lymphadenopathy accounting for 51.1% of the involved cases. This is in accordance with the observation of Reddy et al [81], Mahesh el al[82],Annam el al [78] , Kumar et al[83], Al Nazer et al[84] and Yaris et al [75] who found that localized lymphadenopathy constituted the predominant finding with cervical LN involvement forming the majority of the involved groups. Lymph nodes in the cervical region drain areas that are common portals of entry for a large variety of infectious agents As children have a high incidence of oropharyngeal, dental and scalp infections which results in enlargement of the cervical lymph nodes, draining the above regions, and this makes them the most commonly involved nodes and as expected reactive hyperplasia occurred most frequently in the cervical LNs. However, the study by Darnal et al [90] on the profile of lymphadenopathy in both children and adults showed cervical lymphadenopathy to be the commonest site among adults and generalized lymphadenopathy to be the commonest site among children.

In the present study, there was no significant difference regarding the spread of LN groups involved between the non-neoplastic and neoplastic categories (P=0.297). Most

cases of both groups presented by generalized lymphadenopathy. Therefore, the spread of LN groups was not considered one of the factors associated with malignancy. This is in concordance with a study by Oguz et al [91] which stated that most of the patients had generalized lymphadenopathy.[91]

Moreover Leung et al [92,93] reported that generalized lymphadenopathy were often caused by a viral infection and less frequently by malignancies, collagen vascular diseases and medications.

Regarding the distribution of LNS, most of the cases were bilateral in distribution (68.8%) with no significant difference between the diagnostic categories (p=0.204).

Regarding LN number, multiple LNs were present in the majority of cases with a significant difference between the non- neoplastic and the neoplastic categories (p<0.001). Therefore, LN number was considered one of the factors associated with malignancy.

Lymph node size is important factor in evaluating children with peripheral lymphadenopathy. In the present study, a LN size greater than 1 cm in diameter of the different LN groups or more than 1.5 cm in the inguinal LNs was regarded as being clinically significant which is also in accordance with other studies.[73,79,84,91] A study by Karadeniz et al & Oguz [91] reported a maximum diameter of more than 2 cm as the appropriate limit to distinguish malignant or granulomatous disease from the others. A study by Al Nazeer et al [84] observed that only 8% of reactive hyperplasia had a LN diameter of more than 2 cm while all those with a specific diagnosis had LNs with a maximum diameter greater than 2 cm. Thus, a LN size of more than 1 cm can be considered an appropriate limit to distinguish those with specific diagnosis those with reactive hyperplasia. However, this is not the case for those with supraclavicular lymph nodes where the majority, based on published literature, have a specific diagnosis even if less than 2 cm in diameter. [73,87]

There was a significant difference regarding LN size between the non- neoplastic and neoplastic categories (P< 0.001). In this study, most of cases (85 %) within the neoplastic category had a LN size of more than 1 cm. This is in accordance with Karadeniz et al [73] and El Nazeer et al. [84] However, the studies by Kumral et al [94], Vargas- Vallejo et al [95] and Yaris et al [75] found a LN size more than 3 cm to be associated with increased risk of malignancy.

In another study, the size of the node was not of diagnostic value when it was between 1 and 3 cm. Nodes that were smaller than 1 cm were suggestive of benign disorders and nodes that were larger than 3 cm were of diagnostic value in differential diagnosis for malignant disorders. Although the relevant studies mostly avoid giving a definite size for differential diagnosis, a maximum diameter of >2 cm was considered to be the limit to distinguish malignant or granulomatous disorder from other causes. [94]

Regarding the character of LNs, discrete LNs were found in the majority of cases (85.2%) while matted LNs were found in (14.7%) of cases. A significant difference regarding LN character was found between the non- neoplastic and the neoplastic categories (P<0,001). Discrete LNs were found in both non-neoplastic and neoplastic cases, while matted amalgamated LNs were found in the neoplastic cases. Therefore, amalgamated LNs were considered as one of the factors associated with malignancy.

Matted LNs are characteristic but not pathognomonic of tuberculous lymphadenitis, a fact stated by other studies. [81,82]

Regarding the consistency of LNs, most of the LNs were firm (52.9%) which is in accordance with the studies of Reddy et al [81] and Mahesh et al[82]. A significant difference was found in LN consistency between the non-neoplastic and neoplastic categories (P<0.001) for solid and cystic LNs and P<0.001 for soft, firm and hard LNs). Cystic LNs were found only in the non-neoplastic category while solid LNs were found in both the non- neoplastic and neoplastic categories. As for solid LNs, firm LNs were found in both the non-neoplastic and neoplastic categories, soft LNs were found mainly in the non-neoplastic category while hard LNs were found mostly in the neoplastic category. Therefore, hard LNs were regarded as one of the factors associated with malignancy. This is in concordance with the study of Bazemore et al & Smucker. [86]

Regarding LN mobility, most of the LNs were mobile (88.2%). A significant difference was found regarding mobility between the non-neoplastic and the neoplastic categories (P< 0.001). Mobile LNs were found in both non-neoplastic and neoplastic categories while fixed LNs were found only in the neoplastic category. Therefore, fixed LNs were considered as one of the factors associated with malignancy. This is in concordance with Soldes et al [87] and Bazemore et al & Smucker. [86]

Regarding LN tenderness, most of the LNs were non-tender (77%). This is in accordance with the studies of Reddy et al [81] and Mahesh et al [82]. A significant difference was found regarding LN tenderness between the non-neoplastic and the neoplastic categories (P<0.001). Non tender LNs were found in both the non-neoplastic and neoplastic categories while tender LNs were found only in the non-neoplastic category. Therefore, tender LNs were considered as one of the factors not associated with malignancy. This is in accordance with Soldes et al [87] who reported LN tenderness as one of the factors not associated with malignancy.

Regarding the inflammatory changes were observed in the skin overlying the lymph nodes of the non neoplastic category, with significant difference between the neoplastic and the non neoplastic categories (p=0.009) . This is in accordance with Kumral et al [94] who reported also that skin changes were noted among the non neoplastic category

As regard laboratory investigations, anemia was detected in 41.2% of cases which is in accordance with Reddy et al [81] where anemia was detected in 45% of cases. Total WBCs count was normal in 75.9% of cases which is slightly lower than the finding of Reddy et al [81] (92%). Lymphocytosis was detected in 17.1% of cases unlike Reddy et al [81] where lymphocytosis was detected in 50% of cases. Raised ESR/CRP was detected in 45.9 % and 52.9% of cases respectively which is in accordance with Reddy et al [81] where ESR was elevated in 62% of cases.

In the present study, 80% of anemic cases had normocytic normochromic anemia, while only 20% presented by microcytic hypochromic anemia

A significant difference was found between the non-neoplastic and the neoplastic categories regarding anemia (p=0.001), some items of the differential WBCs count (abnormal lymphocyte count p=0.002), platelet count (P= 0.002), some items of blood film (toxic granules in neutrophils (P=0.001) and blast cells (P< 0.001) and LDH level

($p<0.001$). This is in accordance with Bazemore et al & Smucker [86] who reported abnormal CBC findings as one of factors associated with malignancy. Yaris et al [75] and Granado et al [76] reported elevated LDH level as one of the factors associated with malignancy.

A significant difference was found between the neoplastic and the non neoplastic categories as regard the abdominal ultrasound findings including the presence of abdominal LNs ($p=0.001$), hepatomegaly ($p=0.004$) and/or splenomegaly ($p=0.001$). This is in accordance with several studies.[91,94,96]

It has been accepted that imaging studies have a higher accuracy than palpation in the diagnosis of neoplastic lymphadenopathy. The relative accuracy of each modality, however, is an area of continuing study. In 2005, Ahuja et al [89] described the use of ultrasound to differentiate reactive from pathologic lymphadenopathy. Reactive lymphadenopathy had the following characteristics: size less than 1 cm, oval shape with short: long ratio less than 0.5, normal hilar vascularity and a low resistance index with high bood flow when using Doppler technology. Pathologic lymphadenopathy had the characteristics: size greater than 1 cm, round with a short: long ratio greater than 0.5, necrotic center, no echogenic hilus and a high resistive index with low blood flow. Evaluation of the vascular pattern of lymph nodes is useful to differentiate benign from malignant nodes. Using these parameters, they found a sensitivity of 95% and a specificity of 83% success rate of differentiating reactive from pathologic lymph nodes.[89] In the present study, neck imaging was done on 76 cases, out of which 6 cases (16.7%) showed non-pathologic LNs and 70 cases (83,3%) showed pathologic LNs.

The study by Ying et al[74] also recommended ultrasonography as a useful imaging tool for the initial investigation of cervical lymphadenopathy in children. However, Ultrasound guided FNAC or biopsy may still be necessary for confirmation if the ultrasound findings are equivocal.[74] The study by Jenssen[97] on the clinical value of lymph node sonography also recommended ultrasound, whether percutaneous or endoscopic, as a useful complementary imaging tool in the assessment of lymphadenopathy in almost all anatomical regions of the body.

Furthermore, ultrasound guided biopsy permits histological diagnosis of pathological lymph nodes with minimal risk, low cost and high diagnostic accuracy.[97] Imaging techniques such as US, CT and MRI have a 20-28% higher sensitivity for the detection of lymphadenopathy than clinical assessment. However, they have a low specificity for differentiating benign from malignant lymphadenopathy and lymphoma from metastatic disease. A tissue diagnosis remains a standard requirement.[97]

In the present study as only 44 cases (25.8%) underwent LN sampling whether fine needle or excisional biopsy, the number of children requiring a LN sampling is correspondingly low. That was explained by the high frequency of non-neoplastic self-limited disorders.[80,98-100]

Nevertheless, automatic core biopsy systems have found little attention in the head and neck region as yet.

This may be due to the concern to use an automated spring-loaded cutting-needle biopsy-gun in an anatomic region, which comprises numerous large vessels and major

nerves. Reviewing the international medical literature, we found only a few reported series evaluating the usefulness of core-needle biopsy devices in the head and neck. [101-104]

Regarding the final etiologic diagnosis of lymphadenopathy in the present study, non-neoplastic etiologies outnumbered the neoplastic ones. Out of the 170 studied patients 74.1% were non-neoplastic and only 25.9% were neoplastic. This is in accordance with most of the reported studies stating non-neoplastic etiologies as the predominant cause of pediatric lymphadenopathy.[69-71,73,75-79,81-84,88,94,105,106]

In the present study, the neoplastic cases constituted 25.9% of the studied cases. This is in accordance with the study by Lovera et al [106], Kumral et al [94] and Yaris el al [75] where the neoplastic etiologies represented 48%, 30% and 23.5% of the studied cases. However, this is much higher than the study by Reddy et. Al [81], Annam et al [78], Benesch et al [77], Puiu et al [71] and Granado et al[76] where, the neoplastic etiologies represented 4%, 4.6%, 7.7% and 16% of the studied cases respectively.

The high percentage of neoplastic cases (25,9%) in the present study may be explained by a partial selection bias due to referral of neoplastic cases from nearby areas to Alexandria Main University Hospitals for better diagnostic and therapy facilities. This was evident from the demographic parameters stating that almost half of the neoplastic cases came from rural areas. The predominance of malignancy in the studied Lovera et al[106], Kumral et al[94]and Yaris et al[75] may also be explained by the fact these studies were conducted in hematology - oncology referral hospitals so there may selection bias in these studies as well.

In the present study, out of the 126 non-neoplastic cases, 50.6% were of infectious etiology and 23.5% were of non-infectious etiology. Bacterial lymphadenitis, whether specific or non- specific was the commonest etiology in the infectious group representing 33% of the studied cases followed by viral lymphadenitis in 15.3% and parasitic (Toxoplasmosis) in 2.4%. Non-specific bacterial lymphadenitis accounted for 25.3% of cases, mycobacterial lymphadenitis represented 5.9% of the cases while Salmonellosis and Brucellosis represented each 0.6% and 1.2% respectively. This was in accordance with most of the reported studies stating infectious etiology as a predominant cause of pediatric lymphadenopathy. [69,70,75-78, 81, 82, 88,105]

In the current study, there was high percentage of non diagnostic reactive LN hyperplasia 12.9%, which was also relevant in a number of other studies.[80,105]

In the present study, lymphoma was the predominant cause of neoplastic lymphadenopathy accounting for 56.8% of the neoplastic cases. This is in accordance with most of the reported studies.[80,84,107] Non- Hodgkin's lymphoma constituted 68% of the lymphomatous cases while HL constituted 32% of the lymphomatous cases which is in accordance with what has been reported in the literature that the vast majority of pediatric lymphomas are of NHL type.[108,112]

In the current study, leukemia was the second common cause of neoplastic lymphadenopathy accounting for 38.6% of the neoplastic cases. In the leukemia group, ALL represented the majority (88.2%) of leukemia cases while AML represented two cases only (11.7%). This is in accordance with what has been reported in the literature that ALL accounts for the vast majority of pediatric leukemia (about 77%) [108,113,114] The

majority of ALL, cases were of the B cell type as observed in 75% of the ALL cases compared to only 25 % of the T cell type. This is in accordance with what has been reported in the literature that the vast majority of pediatric ALL (85%) is of B cell origin.[108,113,114]

The results of this study showed that the following factors were useful in determining the risk of malignancy: the presenting symptoms (weight loss, abdominal and multiple symptoms), the duration of lymph node enlargement (2-6 weeks), number (multiple LNs), size (> 2 cm), character (amalgamated), consistency (hard), mobility (fixed) and tenderness (non-tender), abnormal CBC findings (anemia, thrombocytopenia, and lymphocytopenia), blast cells in blood film and elevated LDH level.

In the present study, the factors associated with infectious lymphadenitis were: duration of symptoms (less than 2-6 weeks), fixation (not fixed), consistency of LNs (cystic/soft), tenderness of LNs (tender), presence of overlying skin inflammation, abnormal CBC findings (lymphocytosis, activated lymphocytes, toxic granules in neutrophils) and increased ESR/CRP levels.

Several studies conducted to evaluate the diagnosis of pediatric lymphadenopathy such as that of Soldes et al [87], Bazemore et al[86], Kumral et al[94], Vargas-Vallcjo et al[95], and Wang et al[115] reported age, size and number of sites of adenopathy, location and duration of LN enlargement, presence of certain signs and symptoms such as fever and weight loss and response to initial antibiotic treatment as being factors determining the risk of malignancy.[86,87,94,95,115] Soldes et al noted increasing node size, number of sites of adenopathy and age as factors associated with increased risk of malignancy. Additional factors included supraclavicular LN location, abnormal chest X-ray and fixed nodes. However, the duration of adenopathy, the presence of fever, cough, splenomegaly, skin involvement, tenderness and bilateral adenopathy were not associated with increased risk of malignancy[87].

The study by Yaris et al[75] found the risk of malignant change higher with increasing age, generalized lymphadenopathy, LN size greater than 3 cm, involvement of supraclavicular LNs, hepatosplcnomegaly and high lactate dehydrogenase level. The study by Granado et al[76] observed that all the cases with supraclavicular LN enlargement had lymphoma and the mean LDH level was higher in malignant cases than non-malignant ones. The study by Leung et al[92,93] also noted that supraclavicular and posterior cervical adenopathy carried a much higher risk for malignancy than anterior cervical adenopathy. These data should be helpful to supplement clinical judgment to predict the risk of malignancy.

Bazemore et al[87] noted older age, firm and fixed nodal character, duration greater than 2 weeks and supraclavicular location to be associated with increased risk of malignancy.[87] Kumral et al[94] noted location of lymphadenopathy (supraclavicular and postauricular), duration of adenopathy of more than 4 weeks, size of LNs of more than 3cm, abnormal CBC findings, abnormalities in chest x-ray and abdominal ultrasonography as factors associated with increased risk of malignancy.[94] Vargas-Vallejo et al[95] noted age, duration of adenopathy of less than 6 months, number of nodes involved (2 or more), size of LN(greater than 3 cm) and bilateral cervical adenopathy to be associated with increased risk of malignancy[95]. Wang et al[115] noted the ratio of maximal width to maximal length as the optimal parameter of size for malignancy, where a higher ratio

(greater than 0.5) is associated with increases risk of malignancy. Other factors were significant independent predictors of malignancy such as the number of involved regions (2 or more) and the location of the largest node (level II or III)[115].

In the present study, a final etiologic diagnosis for pediatric lymphadenopathy was achieved after correlating information from the history and clinical findings with those of the laboratory, radiological, pathological and microbiological findings. In most cases, a careful history and physical examination identified a treatable etiology, such as tonsillitis or viral lymphadenitis and no further assessment was necessary. In a subset of patients, a presumptive diagnosis was made based on the clinical data but was confirmed by further tests or by follow up of the clinical course. Another subset of patients had localized lymphadenopathy with a reassuring clinical picture. In these cases a two-to-four week period of observation was adopted before investigation. In children with unexplained localized lymphadenopathy and a worrisome clinical picture and those with generalized lymphadenopathy, further diagnostic evaluation was needed.

In the present study, the etiology could not be ascertained in 12.9% of the studied cases even alter detailed laboratory, radiological, pathological and microbiological. This is in accordance with the study by Lovera el al[106], Annam et al[78], Kumral et al[94], Granado et al [76] and Benesch et al[77], since the etiology could not be ascertained in 5%, 9%, 10%. 11.6% and 12.6% of the cases respectively. However, in the study by Yaris et al[75], Reddy et al [82] and Puiu et al[74], the etiology could not be ascertained in 45.9%, 44% and 25% of the studied cases respectively. This may be explained by the use of different diagnostic facilities than the present study.

Further studies and a longer follow-up involving more sophisticated investigations for rarer causes of lymphadenopathy may decrease the fraction of these undiagnosed reactive hyperplastic conditions.

SUMMARY

Lymphadenopathy is one of the most common clinical problems encountered in pediatrics. The precise incidence of lymphadenopathy is not known, however estimates of palpable adenopathy in childhood vary from 38-45% in USA.

Lymphadenopathy refers to nodes that are abnormal in either size, consistency or number.or Lymphadenopathy refers to any disease process involving lymph nodes that are abnormal in size and consistency. A pathologic or abnormal lymph node is commonly quoted to be >1cm in size. Acute lymphadenopathy is 2 weeks duration, subacute is 2-6 weeks duration, and chronic is considered any lymphadenopathy that does not resolve by 6 weeks.

The aim of the present work was to determine the demographic parameters, clinical presentation and the most common causes of pediatric lymphadenopathy after a detailed history with thorough general and systemic physical examination together the required laboratory, radiologic, microbiologic and pathologic investigations.

This prospective study was performed on 170 cases of pediatric lymphadenopathy attending the department of pediatrics, Alexandria University Children's Hospitals during the year January 2011 through December 2012 aged from 1 month-18 years.

According to the final diagnosis of the studied cases, they were categorized into two main groups: non neoplastic and neoplastic. The non- neoplastic category was further divided according to the etiology of the LN into infectious and non- infectious groups. Out of the 170 studied patients, 74.1% were non neoplastic while 25.9% were neoplastic. The non- neoplastic group included 50.6% infectious causes and 23.5% non- infectious ones. Bacterial lymphadenitis was the commonest etiology in the non-neoplastic category. Mycobacterial lymphadenitis was the commonest cause of granulomatous lymphadenitis. Within the neoplastic category, lymphomas were the commonest etiology and NHLs were more common than HLs. However, the etiology of lymphadenopathy could not be ascertained in 12.9% of cases even after detailed clinical and investigative profile. The demographics of the present study showed a male predominance of 64%. No specific sex predilection to a certain diagnostic category could be found. Most of the children (52.9%) presented in the preschool age group (less than 5 years). No significant difference regarding the age was found between any of the diagnostic categories. Most of the children came from urban areas (64.7%) with no significant difference was found regarding the residence between the non-neoplastic and the neoplastic categories (P=0.101) where most of the cases within the neoplastic category (54.5%) and those of the non-neoplastic group (68.3%) came from urban areas.

The cases were distributed nearly equal along the four seasons of the year. Most of the children (41.1% of cases) had duration of symptoms more than two weeks but less than 6 weeks. A significant difference was found in the duration of symptoms between the non-neoplastic and neoplastic categories ($p<0.001$).

As regards the presenting symptom(s), the most frequent presenting symptom in the present study was swelling in 85% of the cases. Fever and loss of appetite came next. Constitutional symptoms were present in 68.2% of cases. Furthermore, a significant

difference in constitutional symptoms was found between the three diagnostic categories as regard fever (p=0.037) and weight loss (p<0.001). Abdominal findings was found in 24% of cases.

As regard lymph nodes examination, cervical LN enlargement was the most prevalent among the localized peripheral lymphadenopathy accounting for 51.1% of the involved cases. By comparing the LN status between the non-neoplastic (infectious and non-infectious) and the neoplastic categories, a significant difference was found regarding the number (P<0.001), size (P<0.001), character (P< 0.001), consistency (p<0.001), mobility (P< 0.001), tenderness of LNs (P<0.001) and skin changes (p=0.009) but no significant difference was found regarding the distribution and spread.

By comparing the initial laboratory investigations between the three diagnosed categories, a significant difference was found regarding presence anemia (p=0.001), platelet count (P=0.002), some items of the differential leukocytic count (abnormal lymphocyte count, P=0.002), some items in the blood film (toxic granules in neutrophils, P=0.001 and blast cells, P<0.001) and LDH level (P<0.001). Also, CRP and ESR values had statistical difference (p=0.001 and 0.002 respectively). But no significant difference was found regarding the WBCs count and neutrophil count.

The results of this study showed the following to be factors useful in determining the risk of malignancy: presenting symptoms (abdominal and multiple symptoms), duration of lymph node enlargement (2-6 weeks), number (multiple LNs), size (> 1or 1.5 cm), character (amalgamated), consistency (hard), mobility (fixed) and tenderness (non-tender) , abnormal CBC findings (anemia, thrombocytopenia, neutropenia and lymphocytopenia), blast cells in blood film and elevated LDH level.

In the present study, the factors associated with infectious lymphadenitis were: duration of symptoms (less than two weeks), number of LN groups involved (localized lymphadenopathy), consistency of LNs (cystic/soft), tenderness of LNs (tender), abnormal CBC findings (lymphocytosis), activated lymphocytes, toxic granules in neutrophils in blood film and increased ESR/CRP levels. In the present study, neck imaging was done on 76 cases, out of which 6 (16.7%) cases showed non-pathologic LNs and 70 (83,3%) cases showed pathologic LNs. Regarding the role of pathology in the workup, lymph node biopsy was required in 44 cases out of the 170 ones. The present study demonstrated that primary diagnostic evaluation of childhood lymphadenopathy is mainly based on clinical grounds. In most cases, a small number of additionally more sofisticated performed laboratory tests and longer duration of follow up allow to correctly identify the etiology of pediatric lymphadenopathy.

CONCLUSIONS

From the present study, we have concluded that:

1- Carefull detailed history and full examination can lead to diagnosis in wide number of cases.

2- Age, sex and residence are not important predicting factors for malignancy or for the etiology of lymphadenopathy.

3- Duration of Lymphadenopathy is important determinant of possible malignant etiology.

4- LNs clinical criterion can determine the probable diagnosis whether benign or malignant. Supraclavicular, posterior auricular and lymphadenopathies larger than 1 cm represent a greater risk for malignancy.

5- Abnormal CBC findings should alert for further diagnostic evaluation. While LDH is important screening tool in cases of generalized lymphadenopathy of suspicious malignancy.

6- Ultrasound of the suspicious LNs is more accurate than clinical examination to diagnose malignant LNs. However, Ultrasound guided FNAC or biopsy were necessary for the confirmation if the ultrasound findings are equivocal.

7- Pathologies identified in chest X-ray and abdominal US have a great diagnostic value.

8- The higher number of cases were in the non- neoplastic category and the commonest etiology were belonging to the infectious category.