

## **AIM OF THE WORK**

The aim of the present work is to determine the demographic parameters, clinical presentation and the most common causes of pediatric lymphadenopathy.

## **SUBJECTS**

The study comprised 170 prospective cases of pediatric significant lymphadenopathy presenting to the department of pediatrics, Alexandria University Children's Hospitals during the year January 2011 through December 2012, aged one month to 18 years. An informed consent was taken from all patients.

## METHODS

This prospective, descriptive study was conducted at Alexandria university children's Hospital at El Shatby, during the period from January through December 2012. The population was children with Lymphadenopathy aged from one month-18 years attending the outpatient clinic or admitted in the inpatient ward.

The work protocol entails the following:

### 1. Clinical data collection:

A detailed history with thorough general and systemic physical examination together with lymph node examination.

- Relevant personal data as age, sex and residence.
- Duration of lymphadenopathy of the studied patients were divided into less than two weeks in the acute category, two weeks or more up to six weeks in the subacute category and lastly more than six weeks in the chronic group.
- Relevant complaints such as fever, sorethroat, rash, cough, weight loss and night sweats.
- Relevant signs during complete physical examination such as presence of pallor, petechial rash, dental caries, tonsillitis, skin rash or hepatosplenomegaly.
- Lymph node examination including location, localized or generalized ,size, consistency, fixation and tenderness.

### 2. Lab investigations:

Initial work up:

- CBC: total and differential blood count.<sup>(54)</sup>
- Peripheral Blood smear: for atypical cells.
- ESR.
- LDH level.

Whenever needed, other tests were resorted to according to the case:

- Mantoux test: T.B.<sup>(55, 56)</sup>
- Throat swab.
- Skin swab from infected area.
- Blood culture.
- Serological tests:
  - EBV and CMV antibodies.<sup>(57, 58)</sup>
  - Toxoplasmosis serology.
  - HHV-6 serology.
  - HIV serology.
  - Brucellosis standard agglutination test.
  - Bone marrow biopsy.
  - Lymph node biopsy for Tuberculosis and Actinomycosis.
  - Liver biopsy.

All necessary investigations were done to ensure the safety of the patients before obtaining liver biopsy such as PT and PTT.

### **3. Radiological investigations:**

- Plain Chest X ray.
- Ultrasonography of the neck and abdomen.
- CT chest and abdomen (If malignancy is suspected).

### **4. Pathological study was done when indicated to 44 cases.**

- FNA smears and immunophenotyping by flow cytometry for T and B cell markers.
- Excisional biopsy:
  - Histopathological examination and flow cytometry if FNA failed.
  - Immunohistochemical profile.
- Molecular cytogenetic study:
  - was resorted to if required.

### **Statistical analysis of the data<sup>(59)</sup>**

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0.<sup>(60)</sup>

Qualitative data were described using number and percent. Quantitative data were described using minimum and maximum, mean and standard deviation.

Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Monte Carlo correction.

The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agostino test, also Histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used.

For abnormally distributed data Kruskal Wallis test was used to compare between different groups. Significance of the obtained results was judged at the 5% level.

## **RESULTS**

The present study was conducted at Alexandria University Children's Hospitals during the period from January 2011 through December 2012 on 170 patients who presented with lymphadenopathy aged from 1 month-18 years .

### **Out of the 170 patients:**

- a) Sixty of the patients (35.2%) were admitted in the pediatric ward of the Shatby Children Hospital.
- b) Hundred and ten patients (64.7%) were attending the outpatient clinic.

According to the final diagnosis of the studied cases, they were categorized into three main groups:

- Infectious group representing 50.6% of the cases (cases = 86).
- Non infectious -non neoplastic cases were representing 23.5% (cases = 40).
- Neoplastic group representing 25.9% of the cases (cases = 44).

### **I. Demographic data of studied cases:**

Table (3) shows that studied groups included 109 males and 61 females who fulfilled the inclusion criteria of the study with overall mean age of  $6.1 \pm 4.6$  years, the most commonly presenting age was between 1 to 5 years and the youngest patient was one month old. The majority (64.7%) of them were from urban residence.

### **II. Clinical data:**

Table (4) shows that the mode of onset of the disease whether acute or gradual were approximately in the same percentage.

The duration of lymphadenopathy was less than 2 weeks in 65 (38.2%) patients, 2- 6 weeks in 70 (41.1%) patients and the remaining 30 (20.7%) patients had lymphadenopathy for more than 6 weeks.

The main presenting symptoms were either mass (90%) or fever (50%) with only 10% of cases had history of weight loss and 7 % had night sweats.

Whereas 18.2% of patients had sorethroat, skin rash was noticed in 12.4 % of patients and 15.9% had cough as preceding symptom, while history of ear discharge was present in 4 cases.

Table (5, 6) represents the exposure of the patients to a number of risk factors including 12 cases (7.1 %) had contact with cats , 12 patients (7.1%) to insect bites , 4 (2.4%) cases had history of drinking unpasteurized milk, one case(0.6%) had history of eating undercooked meat.

Drug history of the studied patients includes 8 patients had antibiotics as trial for regression of the LN size , one patient had antiviral treatment and three patients were receiving anti-epileptic therapy which was the cause of the enlarged LN.

Table (7) demonstrates the clinical findings of the patients: pallor was noticed among 13 cases, 5 cases had jaundice and one leukemic patient was down syndrome.

Table (8) illustrates important finding of patient's physical examination such as head, neck, abdominal and skin findings.

Table (9) describes the distribution of studied lymph nodes which were mainly of the cervical LNs counting 87 in number, followed by 33 inguinal LNs, 22 axillary LNs, 12 submandibular LNs, 9 suboccipital LNs, 6 submental LNs, 3 preauricular and same postauricular as well.

### III. Laboratory investigations :

**Table (10) represents the hematologic parameters of the studied cases:**

Anemia was diagnosed in 70 cases (about 40%) of which 56 cases had normocytic normochromic anemia and 14 cases had microcytic hypochromic type.

Leucocytosis was present in 41 (24.1%) of the cases, whereas 11 (6.5%) patients had leucopenia and normal WBC. In the remaining 118 cases (75.9%).

Platelet count was normal in 129 patients (75.9%), in contrast to 22 (12.9%) patients with thrombocytopenia and 19 (11.1%) patients had thrombocytosis.

The differential WBC revealed lymphocytosis in 29 (17.1%) patients and 31 (18.2%) patients had lymphocytopenia, as regards neutrophil count, 15 (8.8%) of the patients had neutrophilia and 27 (15.9%) had neutropenia in their differential count, and lastly eosinophilia was noted in two cases.

The blood films of the CBCs showed toxic granules in 15 patients (8.8%), reticulocytosis in 17 patients (10%), activated lymphocytes in 18 (10.6%), and lastly 16 patients (9.4%) had blast cells in their blood film examination.

Table (11) represents the needed investigation for a number of patients: ESR results showed elevated level in 78 patients (45.9%) and 90 patients had elevated CRP (52.9%).

Hb electrophoresis was done to 5 patients of which 3 patients had elevated HbF and HbA<sub>2</sub> with decreased HbA, and one patient electrophoresis showed elevated HbS.

EBV IgM and IgG antibodies were done to 63 & 57 of patients respectively showing EBV positive IgM in 11 patients and positive CMV IgM in 10 patients.

Tuberculin test was done to 46 of the patients and was positive in 4 cases of them (8.7%), whereas PCR for TB was positive in one patient and negative result in the three other cases.

Rheumatoid factor was elevated in 2 out of 3 patients who had the test done, whereas 2 out of 6 patients had positive Antids DNA and positive ANA results.

LDH level was elevated in 33 (20.3%) out of 162 patients. Toxoplasma IgM was positive in one patient out of 22 patients and two IgG positive results.

## Results

Brucella IgM positive result in two patients and the same for the widal test result. Blood culture yielded positive growth in 6 patients.

Lymph node biopsy was performed to 42 patients who needed further investigation for the diagnosis, the results showed 15 patients with Non Hodgkin lymphoma, 8 diagnosed with Hodgkin lymphoma, 13 showed reactive lymphadenitis, 4 with granulomatous lymphadenitis, three cases were progressive transformation of germinal centers and one case was sinus histiocytosis.

Bone marrow aspiration biopsy was done to 28 patients showing hypocellular BM with blast cells in 18 cases, it was hypercellular in 2 cases, lymphomatous cells in 4 cases, neuroblastoma cells in 2 cases and one case was myelodysplastic syndrome.

### IV. Radiological investigations

Chest x ray was done to 69 patients showing mediastinal mass in 17 cases(24.6%) and pleural effusion in 5 cases(7.2%).

US of the neck of 76 cases showed lymph nodes in 70 cases(92.1%), US of the abdomen was done to 109 patients demonstrates 52 cases(47.7%) with abdominal lymph nodes, 11 cases(20.8%) with significant hepatomegaly and 13cases (16.7%) with significant splenomegaly.

**Table (3): Demographic characteristics of the studied patients with lymphadenopathy**

Personal characteristics	Studied patients (n=170)	
	No.	%
<b>Age (years)</b>		
Less than 1	7	4.1
1-<5	90	52.9
5-<10	50	29.4
10-<15	23	13.5
Min-Max	0.1-18.0	
Mean±SD	6.1±4.6	
<b>Gender</b>		
Male	109	64.1
Female	61	35.88
<b>Residence</b>		
Urban	110	64.7
Rural	60	35.2

Table (4): Medical history of the studied patients with lymphadenopathy

Medical history of lymphadenopathy	Studied patients (n=170)	
	No.	%
<b>Onset and duration</b>		
<b>Time of onset</b>		
Winter	38	22.4
Spring	39	22.9
Summer	37	21.8
Autumn	56	32.9
<b>Mode of onset</b>		
Acute	86	50.6
Gradual	84	49.4
<b>Duration of lymphadenopathy (weeks)</b>		
Min-Max	1 day – 102.9 week	
Mean±SD	16.62 ± 26.26	
<2 weeks	65	38.2%
≥2 ws-6 weeks	70	41.1%
>6ws	35	20.7%
<b>Constitutional manifestations</b>		
<b>Fever</b>		
Absent	83	48.8
Present	87	51.1
<b>Weight loss</b>		
Absent	153	90
Present	17	10
<b>Night sweating</b>		
Absent	158	92.9
Present	12	7.1
<b>Sore throat</b>		
Absent	139	81.8
Present	31	18.2
<b>Preceding symptoms</b>		
<b>Ear ache or discharge</b>		
Absent	166	97.6
Present	4	2.4
<b>Skin rash</b>		
Absent	149	87.6
Present	21	12.4
<b>Cough</b>		
Absent	143	84.1
Present	27	15.9

Table (5): History of exposures before occurrence of lymphadenopathy among the studied patients

Exposures	Studied patients (n=170)	
	No.	%
<b>Cats</b>		
Absent	158	92.9
Present	12	7.1
<b>Insect bite</b>		
Absent	158	92.9
Present	12	7.1
<b>Unpasteurized milk</b>		
No	166	97.6
Yes	4	2.4
<b>Undercooked meat</b>		
No	169	99.4
Yes	1	0.6
<b>Drug history</b>		
Absent	156	91.8
Present	14	8.2
<b>Type of drugs (n=14)</b>		
Antibiotics	8	57.1
Anti-viral	1	7.1
Immune vitie capsules	1	7.1
Drugs for bronchial asthma	1	7.1
Anti-epileptics	3	1.8
<b>BCG vaccine</b>		
Incomplete	0	0.0
Complete	170	100.0

Table (6): Past history of the studied patients with lymphadenopathy

Past history	Studied patients (n=170)	
	No.	%
<b>Allergy</b>		
Absent	156	76.7
Present	14	23.3
<b>Family history of similar problem</b>		
Absent	165	91.7
Present	5	8.3
<b>Previous treatment</b>		
Absent	163	88.3
Present	7	11.7

## Results

**Table (7): Clinical findings among the studied patients with lymphadenopathy**

Physical examination		Studied patients (n=170)	
		No.	%
<b>General appearance</b>	Normal	151	88.8
	Abnormal	19	11.1
	Pallor	13	7.6
	Jaundice	5	2.9
	Down syndrome	1	0.6

#Categories are not mutually exclusive

**Table (8): Physical examination among the studied patients with lymphadenopathy**

Physical examination		Studied patients (n=170)	
		No.	%
<b>Head and neck examination</b>	<b>Scalp</b>		
	Normal	165	97.1
	Abnormal (Pediculosis, Tinea, Discoid lupus)	5	2.9
	<b>Conjunctivitis</b>		
	Absent	165	97.1
	Present	5	2.9
	<b>Oropharynx</b>		
	Normal	129	75.9
	Abnormal	41	24.1
	Pharyngitis	13	7.6
	Tonsillitis	19	11.1
	Dental caries/ gum infection/gingivitis	7	4.1
	Painless oral ulcers	2	1.8
	<b>Otitis media</b>		
	Absent	169	99.4
Present	1	0.6	
<b>Other findings</b>			
Absent	167	98.2	
Present (mouth ulcers/eyelids/mallar flush)	3	1.8	
<b>Abdomen</b>	<b>Liver</b>		
	Not enlarged	154	90.6
	Enlarged	16	9.4
	<b>Spleen</b>		
	Not enlarged	153	90.0
	Enlarged	17	10.0
	<b>Abdominal masses</b>		
	Absent	164	96.5
	Present	6	4.5
<b>Skin examination</b>	<b>Rash</b>		
	Absent	159	93.5
	Present	11	6.5
	<b>Petechiae/ecchymosis</b>		
	Absent	161	94.7
Present	9	5.3	

## Results

**Table (9): Lymph nodes characteristics among the studied patients with lymphadenopathy**

Lymph nodes characteristics	Studied lymph nodes (n=175)															
	Submental (n=6)		Submandibular (n=12)		Cervical (n=87)		Suboccipital (n=9)		Periauricular (n=3)		Postauricular (n=3)		Axillary (n=22)		Inguinal (n=33)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<b>Number</b>																
Single	6	100.0	5	41.7	15	17.9	6	66.7	3	100.0	1	33.3	18	82.4	12	35.5
Multiple	0	0.0	7	58.3	72	82.1	3	33.3	0	0.0	2	66.7	4	17.6	21	64.5
<b>Size</b>																
< 1cm	1	16.7	8	66.7	51	59.0	8	88.9	0	0.0	1	33.3	16	70.6	23	71.0
≥ 1cm	5	83.3	4	33.3	36	41.0	1	11.1	3	100.0	2	66.7	6	29.4	10	29.0
<b>Consistency</b>																
Soft	2	33.3	7	58.3	60	69.2	8	88.9	0	0.0	2	66.7	16	70.6	26	77.4
Firm	2	33.3	5	41.7	20	23.1	1	11.1	2	66.7	1	33.3	6	29.4	7	22.6
Hard	1	16.7	0	0.0	2	2.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Fluctuant	1	16.7	0	0.0	2	2.6	0	0.0	1	33.3	0	0.0	0	0.0	0	0.0
Matted	0	0.0	0	0.0	3	2.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
<b>Fixation</b>																
Not fixed	6	100.0	12	100.0	83	94.9	9	100.0	3	100.0	2	66.7	21	94.1	33	100.0
Fixed	0	0.0	0	0.0	4	5.1	0	0.0	0	0.0	1	33.3	1	5.9	0	0.0
<b>Tenderness</b>																
Not tender	1	16.7	9	75.0	69	79.5	8	88.9	1	33.3	2	66.7	21	94.1	30	90.3
Tender	5	83.3	3	25.0	18	20.5	1	11.1	2	66.7	1	33.3	1	5.9	3	9.7
<b>Overlying skin</b>																
Normal	4	66.7	12	100.0	85	97.4	9	100.0	1	33.3	3	100.0	22	100.0	33	100.0
Inflamed	2	33.3	0	0.0	2	2.6	0	0.0	2	66.7	0	0.0	0	0.0	0	0.0

**Results**

**Table (10): Hematologic parameters among the studied patients with lymphadenopathy**

Hematologic parameters		Studied patients (n=170)	
		No.	%
<b>RBC count</b> ( ×10 <sup>6</sup> /mm <sup>3</sup> )	Min-Max	2.5-5.7	
	Mean±SD	4.2±0.7	
<b>Hemoglobin</b> (gm/dl)	No anemia	100	58.8
	Anemia	70	41.2
	Min-Max	5.0-13.5	
	Mean±SD	10.3±2.6	
<b>MCV</b> (FL)	Min-Max	53.5-85.5	
	Mean±SD	72.6±8.7	
<b>MCH</b> (PG)	Min-Max	16.2-29.7	
	Mean±SD	24.8±3.6	
<b>MCHC</b> (g/dl)	Min-Max	27.8-38.2	
	Mean±SD	34.1±2.2	
<b>HCT</b>	Min-Max	5.5-40.5	
	Mean±SD	30.0±7.8	
<b>Anemia</b> (n=70)	Normocytic normochromic	56	80
	Microcytic hypochromic	14	20
<b>WBC count</b> (×10 <sup>3</sup> /mm <sup>3</sup> )	Normal	118	75.9
	Leucocytosis	41	24.1
	Leucopenia	11	6.5
	Min-Max	2.6-65.2	
	Mean±SD	11.6±11.2	
<b>Platelets</b> (×10 <sup>3</sup> /mm <sup>3</sup> )	Normal	129	75.9
	Thrombocytopenia	22	12.9
	Thrombocytosis	19	11.1
	Min-Max	9.0-670.0	
	Mean±SD	339.8±153.0	
<b>Differential leukocyte count</b>			
<b>Lymphocytes</b>	Normal	110	64.1
	Lymphocytosis	29	17.1
	Lymphocytopenia	31	18.2
<b>Neutrophils</b>	Normal	128	75.3
	Neutrophilia	15	8.8
	Neutropenia	27	15.9
<b>Eosinophils</b>	Normal	168	98.8
	Eosinophilia	2	1.2
<b>Blood film</b>			
<b>Toxic granules</b>	Absent	155	91.2
	Present	15	8.8
<b>Reticulocytosis</b>	Absent	153	90.0
	Present	17	10.0
<b>Activated lymphocytes</b>	Absent	152	89.4
	Present	18	10.6
<b>Blast cells</b>	Absent	154	90.6
	Present	16	9.4

## Results

**Table (11): Results of laboratory investigations among the studied patients with lymphadenopathy**

Laboratory investigations		Studied patients	
		No.	%
<b>Hb electrophoresis (n=5)</b>	Normal	1	20.0
	Elevated HbF and A <sub>2</sub> , decreased HbA	3	60.0
	Elevated HbS	1	20.0
<b>ESR result (n=170)</b>	Normal	92	54.1
	Elevated	78	45.9
<b>CRP (n=170)</b>	Normal	80	47.1
	Elevated	90	52.9
	Min-Max (Mean±SD)	1.2-103.0 (35.7±32.8)	
<b>EBV IgM (n=63)</b>	Negative	52	82.5
	Positive	11	17.5
<b>IgG (n=57)</b>	Negative	46	80.7
	Positive	11	19.3
<b>CMV IgM (n=63)</b>	Negative	53	84.1
	Positive	10	15.9
<b>IgG (n=49)</b>	Negative	33	67.3
	Positive	16	32.7
<b>Tuberculin test (n=46)</b>	Negative	42	91.3
	Positive	4	8.7
<b>Rheumatoid factor (n=3)</b>	Negative	1	33.3
	Elevated	2	66.7
<b>Antids DNA (n=6)</b>	Normal	4	66.7
	Elevated	2	33.3
<b>ANA (n=6)</b>	Normal	4	66.7
	Elevated	2	33.3
<b>LDH level (n=162)</b>	Normal	129	79.6
	Elevated	33	20.4
	Min-Max (Mean±SD)	353.0-485.0 (422.3±66.3)	
<b>Toxoplasma IgM (n=22)</b>	Negative	21	95.5
	Positive	1	4.5
<b>IgG (n=10)</b>	Negative	6	60.0
	Positive	4	40.0
<b>Brucella IgM (n=12)</b>	Negative	10	83.3
	Positive	2	16.7
<b>Widal test (n=9)</b>	Negative	7	77.8
	Positive	2	22.2
<b>Blood culture (n=8)</b>	Negative	2	25.0
	Positive	6	75.0
<b>PCR for TB (n=4)</b>	Negative	3	75.0
	Positive	1	25.0

Table (12): Results of biopsy and radiologic investigations among the studied patients with lymphadenopathy

Biopsy and radiologic investigations		Studied patients	
		No.	%
<b>Biopsy</b>			
<b>Lymph node biopsy (n=44)</b>	Hodgkin lymphoma-Reed Sternberg cells	8	18
	Granulomatous lymphadenitis	4	9
	Non Hodgkin lymphoma	15	34
	Reactive follicular hyperplasia and sinus histiocytosis	1	2.3
	Reactive lymphadenitis	13	29.5
	Progressive transformation of germinal centers	3	6.8
	<b>Bone marrow aspiration biopsy (n=28)</b>	Normal	1
	Hypocellular -blast cells	18	64.3
	Hypercellular	2	7.1
	Neuroblastoma cells	2	7.1
	Lymphomatous cells	4	14.3
	Myelodysplastic syndrome	1	3.6
<b>Radiological investigations</b>			
<b>Chest X-ray</b>	<b>Chest X-ray (n=69)</b>		
	No mass	52	75.4
	Mass	17	24.6
	Pleural effusion	5	7.2
	No effusion	64	92.8
<b>Ultrasound neck</b>	<b>Ultrasound neck (n=76)</b>		
	No Lymph nodes	6	7.9
	Lymph nodes	70	92.1
<b>Ultrasound abdomen</b>	<b>Lymph nodes(n=109)</b>		
	No Lymph nodes	57	52.3
	Lymph nodes	52	47.7
	<b>Liver (n=24)</b>		
	Normal	98	79.2
	Enlarged	11	20.8
	<b>Spleen (n=24)</b>		
Normal	96	83.3	
Enlarged	13	16.7	

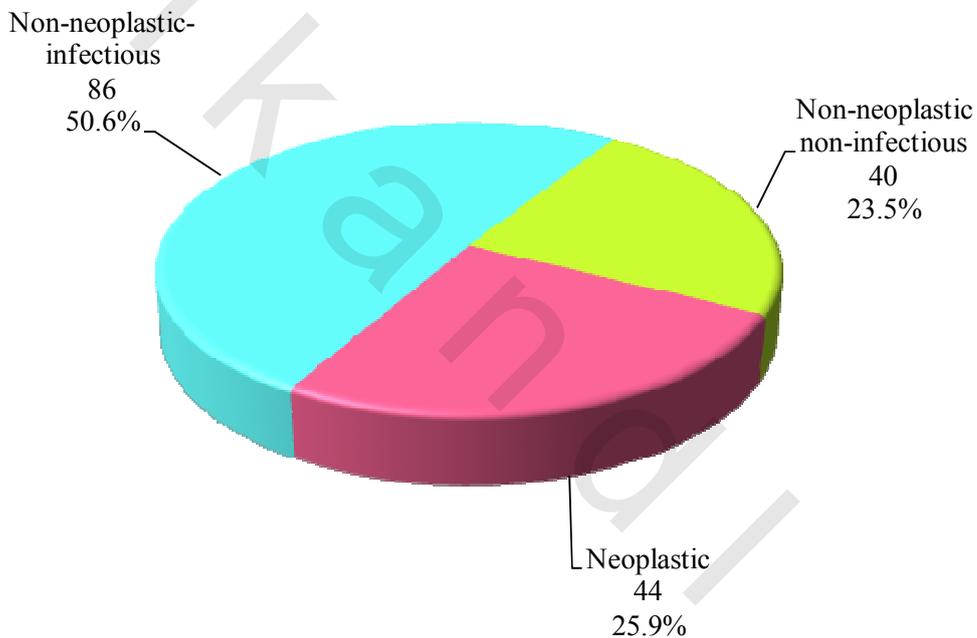
## Results

Table (13a) and Figure (5) demonstrate the final diagnosis of the studied cases divided into three main categories:

- Infectious cases represent 86 cases (50.6%)
- Non-infectious non –neoplastic cases were 40 (23.5%)
- Neoplastic cases represent 44 cases (25.9%)

**Table (13a): Final diagnosis among the studied patients with lymphadenopathy**

Diagnosis	Studied patients (n=170)	
	No.	%
• Infectious	86	50.6
• Non-infectious non-neoplastic	40	23.5
• Neoplastic	44	25.9



**Figure (5):** Demonstrates the final diagnosis of the 170 cases divided into three main categories or the final diagnosis of the 170 studied cases.

## **Results**

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Table (13b) shows that 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.

As regards the non-infectious non-neoplastic cases, miscellaneous causes such as non diagnostic reactive category represented the upper hand 15.3%, whereas autoimmune diseases and blood diseases each represented 3%, 1.7% drug induced and 0.6% storage diseases.

The neoplastic cases constituted 25.9% of the studied cases. Lymphomas constituted 14.1% of them, followed by Leukemias 10.7% and 1.2% were Neuroblastoma .

Table (13b): Diagnostic categories among the studied patients with lymphadenopathy (n=170)

	NO.	%
<b>I. Infectious</b>	86	50.6
1-bacterial lymphadenitis		
<b>a)Non specific</b>		
1.Abscess	5	2.9
2.Tonsillitis	21	12.4
3.Local infection	14	8.2
4.Sepsis	3	1.8
<b>b)Specific</b>		
1.Tuberculosis	10	5.9
2.Salmonellosis	1	0.6
3.Brucellosis	2	1.2
2-Viral lymphadenitis	26	15.3
3-Parasitic lymphadenitis:toxoplasmosis	4	2.4
<b>II. Non neoplastic non infectious</b>	40	23.5
1-Autoimmune		
a. SLE	2	1.2
b. Rheumatoid arthritis	2	1.2
c. Kawasaki disease	1	0.6
2-Blood diseases		
a. Thalassemia major	3	1.8
b. Sickle cell anemia	1	0.6
c. Hereditary spherocytosis	1	0.6
3-Storage disease :mucopolysaccharidosis	1	0.6
4-Drug induced	3	1.7
5-Miscellaneous		
a. Non diagnostic reactive hyperplasia	22	12.9
b. PTGC	3	1.8
c. Sinus histiocytosis	1	0.6
<b>III. Neoplastic</b>	44	25.9
1-Primary Lymphomas		
a. Hodjkin disease	8	4.7
b. Non -hodjkin lymphoma	16	9.4
2-Secondary		
a. Leukemias		
ALL(B-cell)	12	7.1
ALL(T-cell)	3	1.8
AML	2	1.2
Burkitt's lymphoma	1	0.6
b. Neuroblastomas	2	1.2

PTGC= Progressive transformation of germinal centers

## Results

Table 14 compares age, gender and residence of the three groups showing no significant difference statistically between them ( $^{MC}p=0.874$ ), ( $p=0.204$ ) and ( $p=0.171$ ) respectively.

**Table (14): Demographic characteristics among the studied patients with lymphadenopathy according to the etiology**

Personal characteristics	Non-Neoplastic (n= 126)				Neoplastic (n= 44)		Test of sig.
	Infectious (n=86 )		Non-infectious (n= 40)		No.	%	
	No.	%	No.	%			
<b>Age (years)</b>							
Less than 1	4	4.7	2	5.0	1	2.3	$^{MC}p = 0.874$
1-<5	45	52.3	22	55.0	23	57.5	
5-<10	28	32.6	10	25.0	12	27.3	
10-<15	9	1.2	6	15.0	8	18.2	
Min-max	2 month–13.0year		7month-13.0year		9month-15 year		$^{KW}p = 0.321$
Mean $\pm$ SD (year)	4.64 $\pm$ 3.07		4.74 $\pm$ 3.38		5.77 $\pm$ 3.89		
<b>Gender</b>							
Male	51	59.3	25	62.5	33	75.0	$\chi^2 = 3.177$ $p = 0.204$
Female	35	40.7	15	37.5	11	25.0	
<b>Residence</b>							$\chi^2 = 3.533$ $p = 0.171$
Urban	61	70.9	25	62.5	24	54.5	
Rural	25	29.1	15	37.5	20	45.5	

p: p value for comparing between the three studied groups

$\chi^2$ : Chi square test

$^{KW}$ p: p value for Kruskal Wallis test

## Results

Table (15), Figures (6 and 7) illustrate the difference in the medical history between the Three categories : there is statistical difference as regards mode of onset of the disease ( $p<0.001$ ) and the duration of lymphadenopathy ( $p<0.001$ ).

As regards the associated symptoms there was significant difference between the three groups in relation to fever ( $p=0.037$ ), weight loss ( $p<0.001$ ) and skin rash ( $p=0.002$ ), but no significance statistically as regards the other associated manifestations.

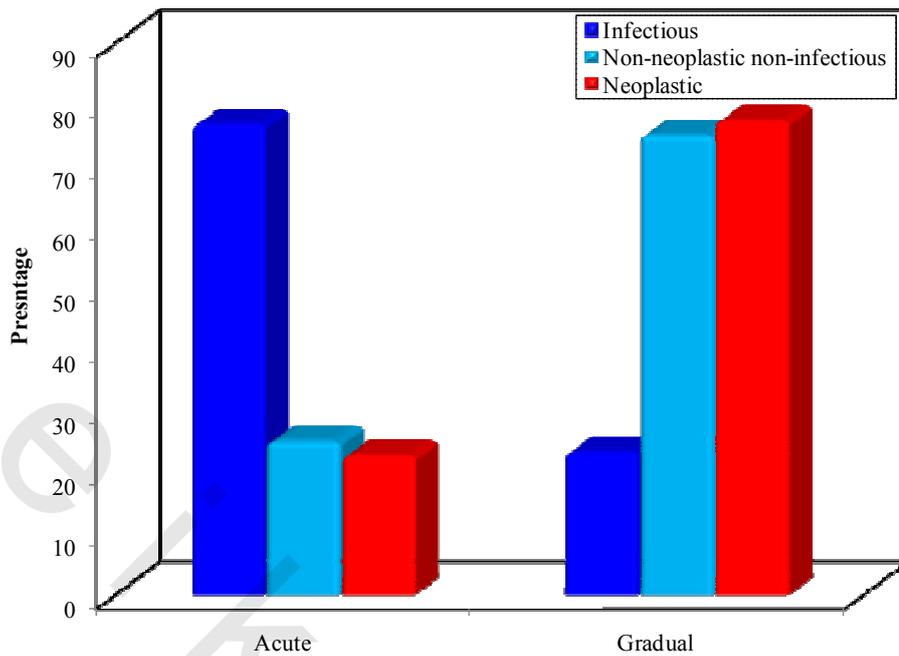
**Table (15): Present medical history among the studied patients with lymphadenopathy according to the etiology**

Medical history	Non-neoplastic (n=126)				Neoplastic (n=44)		Test of sig.
	Infectious (n= 86)		non-infectious (n=40)		No.	%	
	No.	%	No.	%			
<b>Mode of onset</b>							
Acute	66	76.7	10	25.0	10	22.7	$\chi^2=47.679^*$ $p<0.001$
Gradual	20	23.3	30	75.0	34	77.3	
<b>Duration of lymphadenopathy</b>							
Less than 2 weeks	49	57.0	5	12.5	11	25.0	$\chi^2=38.549^*$ $p<0.001$
2-6 weeks	21	24.4	20	50.0	29	66.0	
More than 6 weeks	16	18.6	15	37.5	4	9.1	
<b>Constitutional manifestations</b>							
<b>Fever</b>							
Absent	60	69.8	27	67.5	39	88.6	$\chi^2=6.596^*$ $p=0.037$
Present	26	30.2	13	32.5	5	11.4	
<b>Weight loss</b>							
Absent	36	41.9	38	95.0	42	95.0	$\chi^2=34.917^*$ $p<0.001$
Present	30	34.9	2	5.0	2	5.0	
<b>Night sweating</b>							
Absent	81	94.1	39	97.5	38	86.4	MC $p=0.129$
Present	5	5.9	1	2.5	6	13.7	
<b>Sore throat</b>							
Absent	68	79.1	33	82.5	39	88.6	$\chi^2=1.834$ $P=0.400$
Present	18	20.9	7	17.5	5	11.4	
<b>Preceding symptoms</b>							
<b>Ear ache or discharge</b>							
Absent	84	97.7	38	95.0	44	100.0	MC $p=0.267$
Present	2	2.3	2	5.0	0	0.0	
<b>Skin rash</b>							
Absent	80	93.0	37	92.5	32	72.8	$\chi^2=12.212^*$ $p=0.002$
Present	6	7.0	3	7.5	12	27.2	
<b>Cough</b>							
Absent	69	80.2	34	85.0	40	91.0	$\chi^2=2.514$ $p=0.285$
Present	17	19.8	6	15.0	4	9.0	

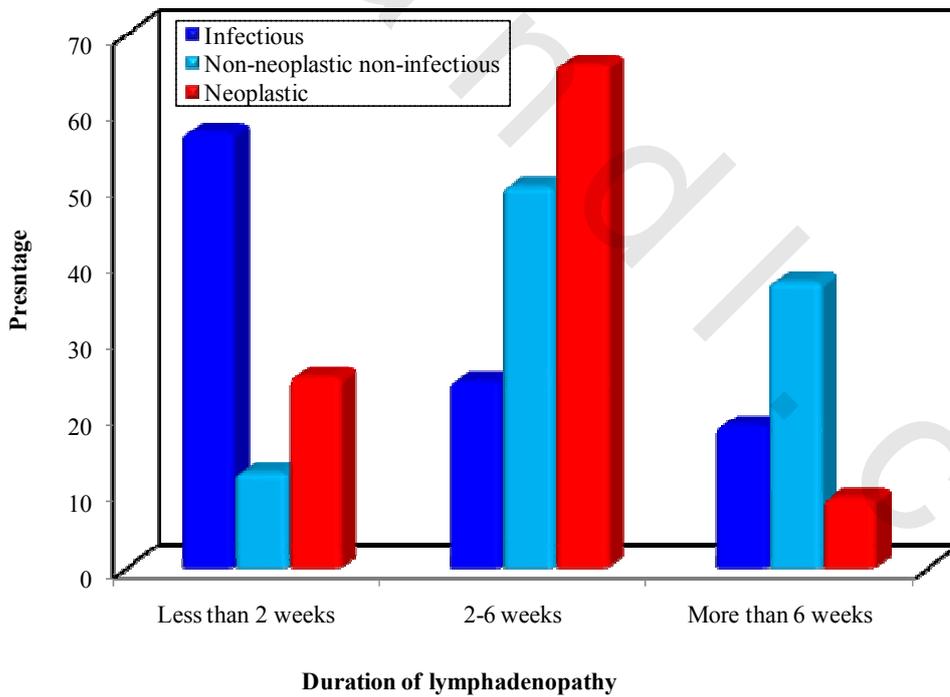
p: p value for comparing between the three studied groups

$\chi^2$ : Chi square test MC: Monte Carlo test

\*: Statistically significant at  $p \leq 0.05$



**Figure (6):** Medical history of the studied patients with lymphadenopathy according to the Mode of onset



**Figure (7):** Medical history of the studied patients with lymphadenopathy according to the duration of lymphadenopathy

## Results

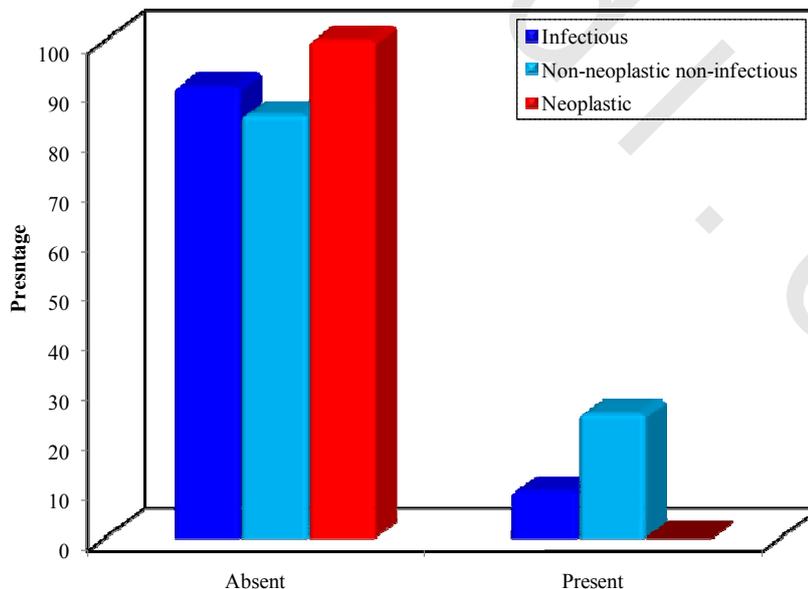
Table (16) and Figure (8) illustrate the past history of the different patients and demonstrates that there is no significant difference between the three groups as regards exposures to cats, insect bites and allergies ( $p=0.061$ ,  $0.075$  and  $0.251$ ). Although exposure to drugs was statistically significant ( $p=0.039$ ).

**Table (16): Past history among the studied patients with lymphadenopathy according to the etiology**

Past history	Non-neoplastic (n =126)				Neoplastic (n=44)		$\chi^2$ (p)
	Infectious (n= 86)		non-infectious (n=40)		No.	%	
	No.	%	No.	%			
<b>Exposure to cats</b>							
Absent	81	94.2	34	85.0	43	97.7	<b>5.584 (0.061)</b>
Present	5	5.8	6	25.0	1	2.3	
<b>Insect bite</b>							
Absent	81	94.2	34	85.0	39	88.6	<b>5.193 (0.075)</b>
Present	5	5.8	6	25.0	1	2.4	
<b>Drug history</b>							
Absent	78	90.7	34	85.0	44	100.0	<b>6.500* (0.039)</b>
Present	8	9.3	6	25.0	0	0.0	
<b>Allergy</b>							
Absent	78	90.7	35	87.5	39	88.6	<b>2.764 (0.251)</b>
Present	8	9.3	5	12.5	1	2.4	

p: p value for Monte Carlo test for comparing between the three studied groups

\*: Statistically significant at  $p \leq 0.05$



**Figure (8):** Past history of the studied patients with lymphadenopathy according to the drug history

### **Lymph node characteristics:**

Table (17) and Figures (9-16) illustrate that 37.2 % of the lymph nodes were localized in the infectious category and 62.8 % were generalized , 75% of the lymph nodes were generalized in the non infectious non neoplastic category.

27.3% of the lymph nodes were localized in the neoplastic category and 72.7% of the cases were generalized As regards consistency : 17.4 % of the infectious lymph nodes were fluctuant and % 82.6 were solid of which 54.9 % were soft ,42.3% were firm and 2.8 % were hard whereas all of the non infectious non neoplastic lymph nodes 100% were solid of which 32.5% were soft and 67.5% were firm with no hard lymph nodes.

In the neoplastic category 100 % of the lymph nodes were solid of which 6.8 % were soft , 75% firm and 18.2% were hard As regards tenderness 40.7% of the infectious lymph nodes were tender and 59.3% were non tender , but 10 % of the non infectious non neoplastic category were tender .

All of the neoplastic cases had non tender lymph nodes As regards fixation and character of the examined lymph nodes: all the infectious and the non- infectious non-neoplastic lymph nodes were mobile and discrete but 45.5% of the neoplastic lymph nodes were fixed, and 54.5% were matted.

Skin changes were present in 10.5% cases of the infectious etiology and no skin changes were noticed in the other two group of cases there was significant difference statistically between the three studied groups as regards multiplicity ( $p<0.001$ ), size ( $p<0.001$ ), character ( $p<0.001$ ), consistency (MCP $<0.001$ ), tenderness ( $p<0.001$ ), fixation ( $p<0.001$ ) and skin changes (MCP=0.009).

But no significance was found as regards spread ( $p=0.297$ ) and distribution ( $p=0.204$ ) of the LNs in the studied groups.

**Results**

**Table (17): Characteristics of LN among the studied patients with lymphadenopathy according to the etiology**

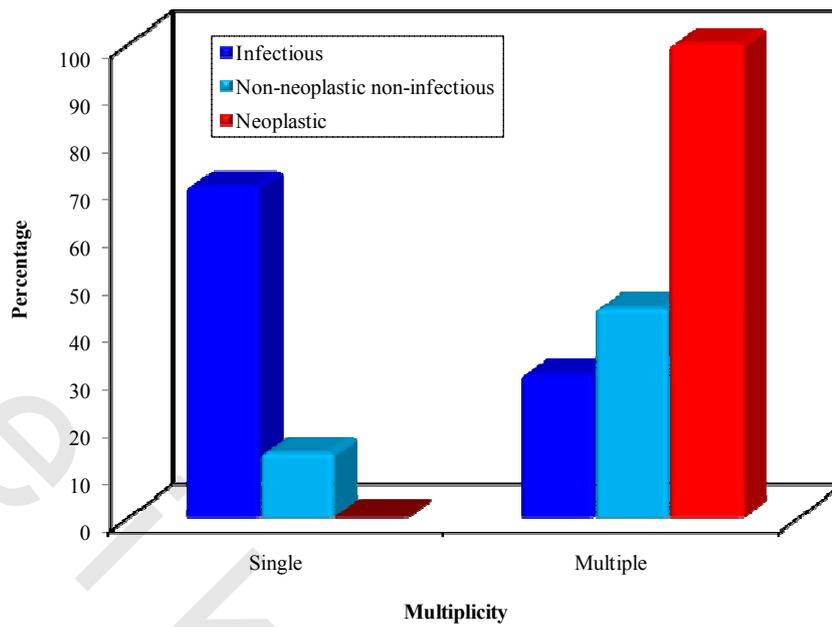
Characteristics of LN	Non- neoplastic (n=126)				Neoplastic (n=44)		Test of sig.
	Infectious (n=86)		non-infectious (n=40)		No.	%	
	No.	%	No.	%			
<b>Spread</b>							$\chi^2=2.430$ p=0.297
Localized	32	37.2	10	25.0	12	27.3	
Generalized	54	62.8	30	75.0	32	72.7	
<b>Multiplicity</b>							$\chi^2=72.153^*$ p<0.001*
Single	60	69.8	6	15.0	0	0.0	
Multiple	26	30.2	34	85.0	44	100.0	
<b>Distribution</b>							$\chi^2=3.181$ p=0.204
Unilateral	30	34.9	14	35.0	9	20.5	
Bilateral	56	65.1	26	65.0	35	79.5	
<b>Size (of largest LN )</b>							$\chi^2= 19.120^*$ p<0.001*
<1	21	24.4	22	55.0	6	13.6	
≤1	65	75.6	18	45.0	38	86.4	
<b>Character</b>							$\chi^2=75.149^*$ p<0.001*
Discrete	85	98.8	40	100.0	20	45.5	
Matted	1	1.2	0	0.0	24	54.5	
<b>Consistency</b>							MC p<0.001*
Solid	71	82.6	40	100.0	44	100.0	
Fluctulant	15	17.4	0	0.0	0	0.0	
<b>Consistency of solid LN</b>	n=71		n= 40		n= 44		MC p<0.001*
Soft	39	54.9	13	32.5	3	6.8	
Firm	30	42.3	27	67.5	33	75.0	
Hard	2	2.8	0	0.0	8	18.2	
<b>Tenderness</b>							$\chi^2=32.227^*$ p<0.001
Tender	35	40.7	4	10.0	0	0.0	
Not tender	51	59.3	36	90.0	44	100.0	
<b>Fixation</b>							$\chi^2= 64.909^*$ p<0.001*
Fixed	0	0.0	0	0.0	20	45.5	
Not fixed	86	100.0	40	100.0	24	54.5	
<b>Skin changes</b>							MC p=0.009*
Absent	77	89.5	40	100.0	44	100.0	
Presnt	9	10.5	0	0.0	0	0.0	

p: p value for comparing between the three studied groups

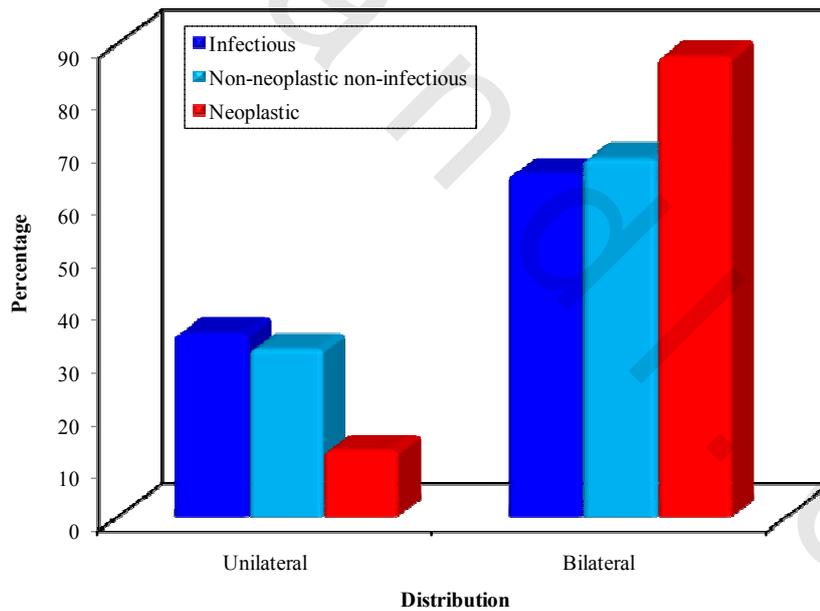
$\chi^2$ : Chi square test

MC: Monte Carlo test

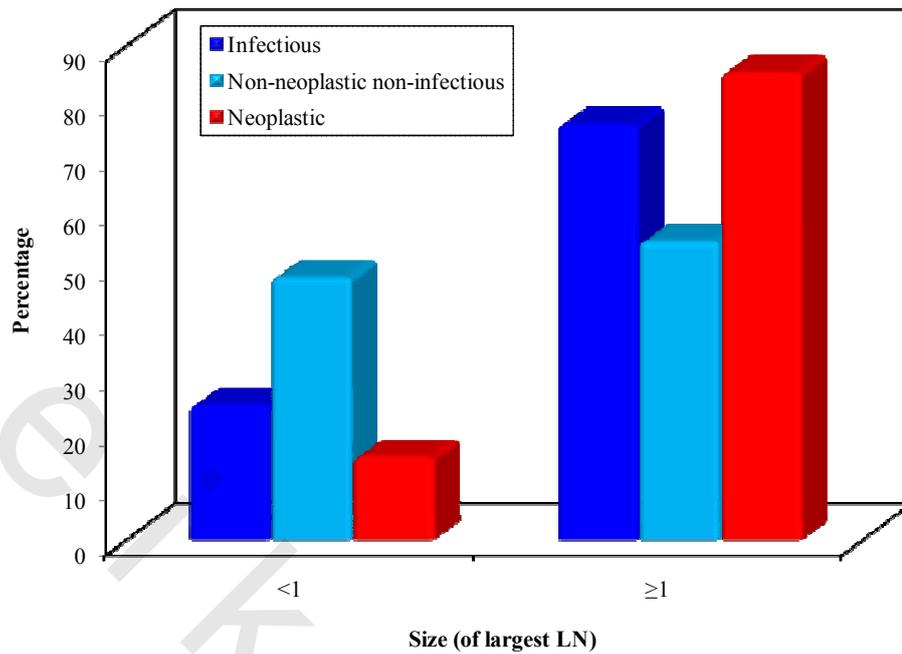
\*: Statistically significant at p ≤ 0.05



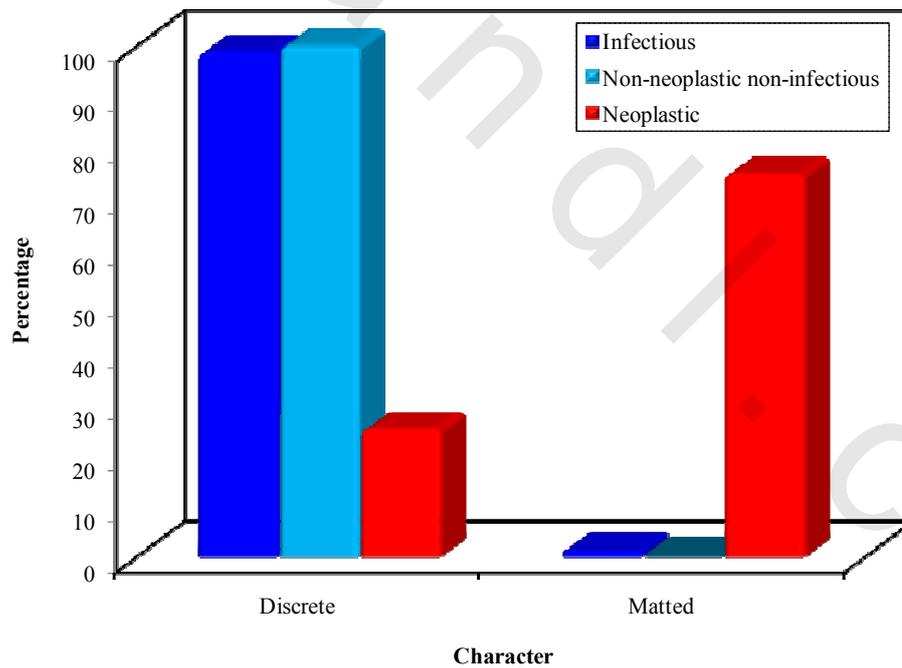
**Figure (9):** Characteristics of the studied LNs as regards multiplicity among the studied patients with lymphadenopathy



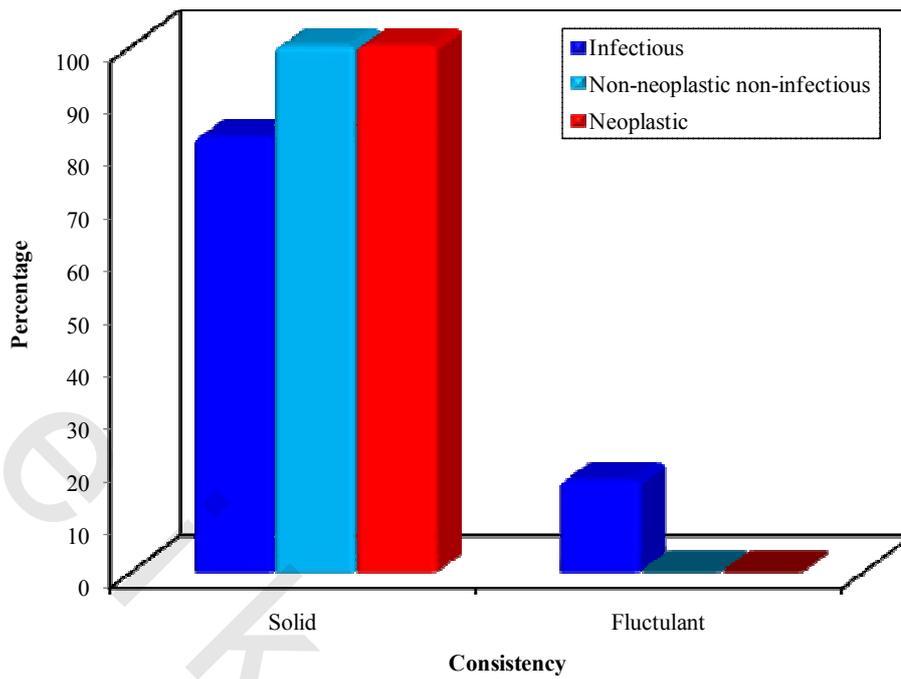
**Figure (10):** Characteristics of the studied LNs as regards distribution among the studied patients with lymphadenopathy



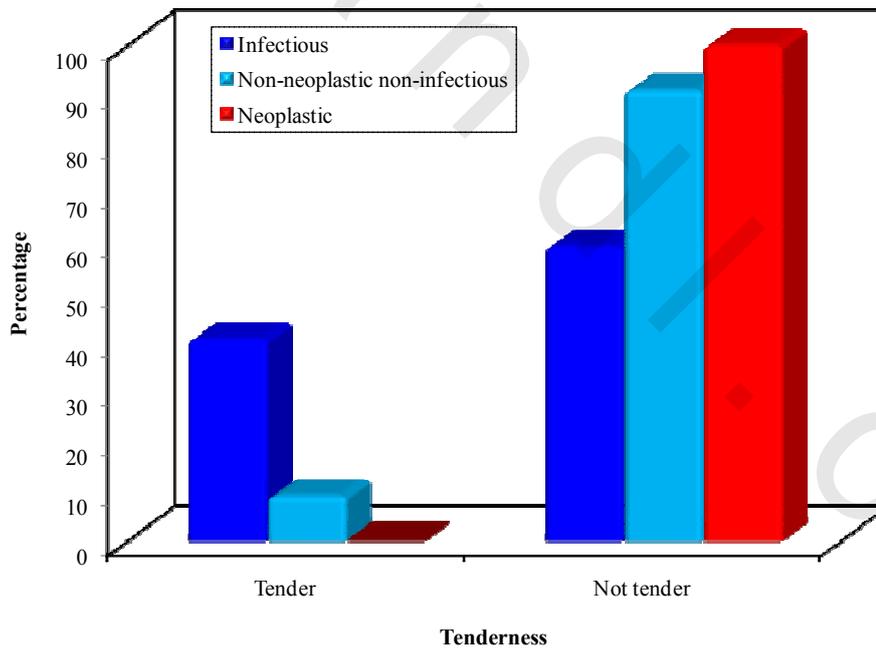
**Figure (11):** Characteristics of the studied LNs as regards size (of largest LN) among the studied patients with lymphadenopathy



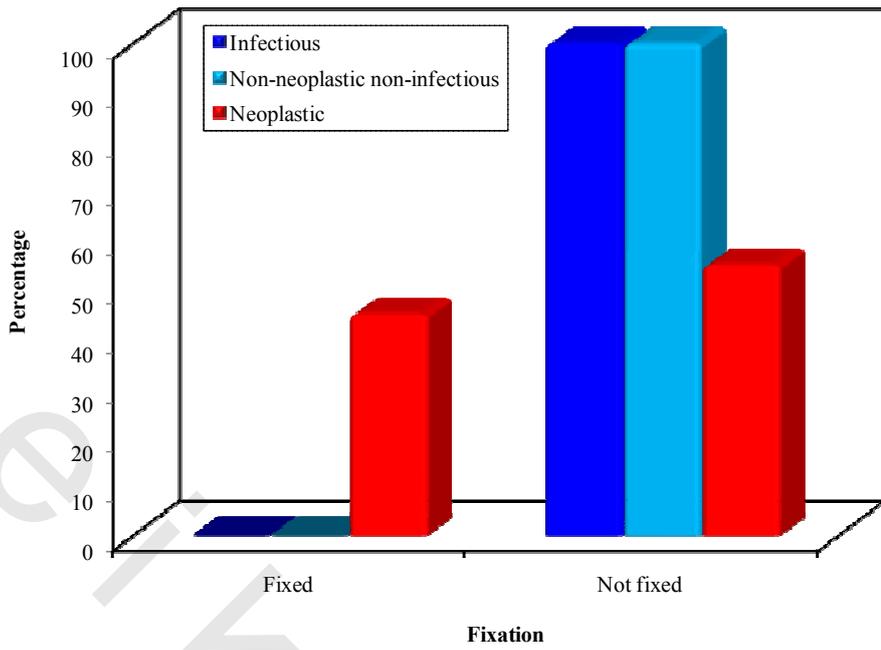
**Figure (12):** Characteristics of the studied LNs as regards character among the studied patients with lymphadenopathy



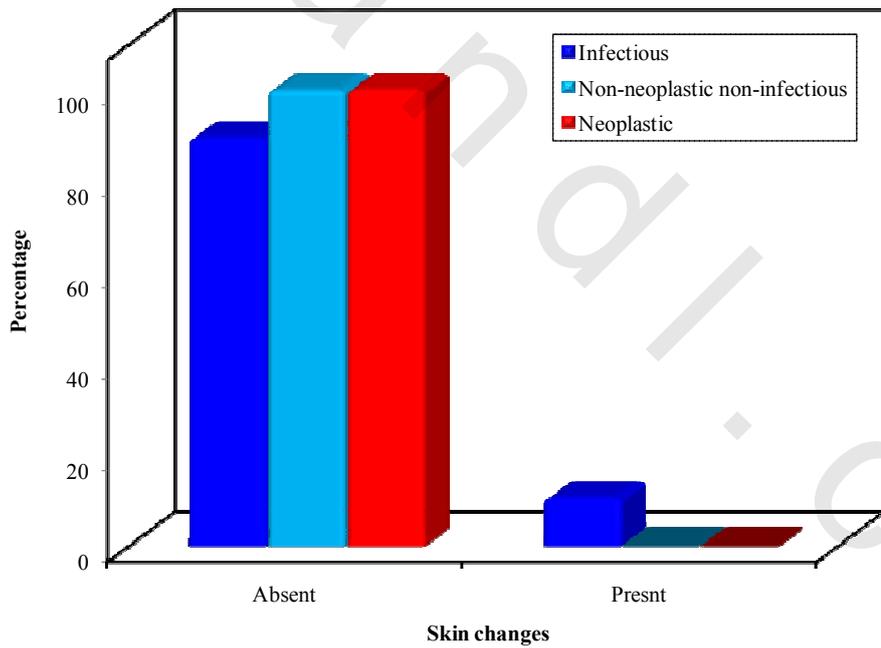
**Figure (13):** Characteristics of the studied LNs as regards consistency among the studied patients with lymphadenopathy



**Figure (14):** Characteristics of the studied LNs as regards tenderness among the studied patients with lymphadenopathy



**Figure (15):** Characteristics of the studied LNs as regards fixation among the studied patients with lymphadenopathy



**Figure (16):** Characteristics of the studied LNs as regards skin changes among the studied patients with lymphadenopathy

## Results

Table (18) and Figures (17-22) illustrate the laboratory investigation results among the three studied groups denoting no significance statistically as regards WBC ( $p=0.175$ ) and neutrophil count ( $p=0.128$ ) but there was significant difference regarding presence or absence of anemia ( $p=0.001$ ), lymphocyte count ( $p=0.002$ ), platelet count ( $p=0.002$ ) and lastly presence of activated lymphocytes ( $p=0.002$ ), toxic granules ( $^{MC}p=0.001$ ) and blast cells in the blood film ( $^{MC}p<0.001$ ).

LDH results were highly significant statistically as well ( $p<0.001$ ). There was significant difference statistically in the results of ESR ( $p=0.003$ ) and CRP ( $p=0.001$ ) values at the time of diagnosis of the three groups.

**Table (18): Results of investigations among the studied patients with lymphadenopathy according to the etiology**

Investigations	Non-neoplastic (n=126)				Neoplastic (n=44)		Test of sig.
	Infectious (n= 86)		non-infectious (n=40)		No.	%	
	No.	%	No.	%			
<b>Hematologic parameters</b>							
<b>Anemia</b>							$\chi^2=21.031^*$ $p=0.001$
Absent	59	68.6	28	70.0	13	29.5	
Present	27	31.4	12	30.0	31	70.5	
<b>WBCs</b>							$\chi^2=3.481$ $p=0.175$
Normal count	59	68.6	32	80.0	27	61.4	
Abnormal count	27	31.4	8	20.0	17	38.6	
<b>Platelets</b>							$\chi^2=11.996^*$ $p=0.002$
Normal count	72	83.7	32	80.0	25	56.8	
Abnormal count	14	16.3	8	20.0	19	43.2	
<b>Differential leucocytic count</b>							$\chi^2=12.241^*$ $p=0.002$
<b>Lymphocytes (n=35)</b>							
Normal count	61	70.9	30	75.0	19	43.1	
Abnormal count	25	29.1	10	25.0	25	56.8	
<b>Neutrophils</b>							$\chi^2=4.113$ $p=0.128$
Normal count	65	75.6	34	85.0	29	65.9	
Abnormal count	21	24.4	6	15.0	15	34.7	
<b>Blood film</b>							$^{MC}p = 0.002^*$ $^{MC}p < 0.001^*$ $^{MC}p = 0.001^*$ $\chi^2=14.671^*$ $p=0.001$
Activated lymphocytes	16	18.6	1	2.5	1	47.7	
Blast cells	0	0.0	0	0.0	16	36.4	
Toxic granules	14	16.3	1	2.5	0	0.0	
Normal	56	65.1	38	95.0	27	61.4	
<b>Laboratory investigations</b>							
<b>ESR</b>							$\chi^2=11.417^*$ $p=0.003$
Normal	37	43.0	30	75.0	25	56.9	
Elevated	49	57.0	10	25.0	19	43.2	
<b>CRP</b>							$\chi^2=13.720^*$ $p=0.001$
Normal	30	34.9	28	70.0	22	50.0	
Elevated	56	65.1	12	30.0	22	50.0	
<b>LDH level</b>							$\chi^2= 111.140^*$ $P<0.001$
Normal	86	0.0	40	0.0	11	25.0	
Elevated	0	0.0	0	0.0	33	75.0	

p: p value for comparing between the three studied groups

$\chi^2$ : Chi square test

MC: Monte Carlo test

\*: Statistically significant at  $p \leq 0.05$

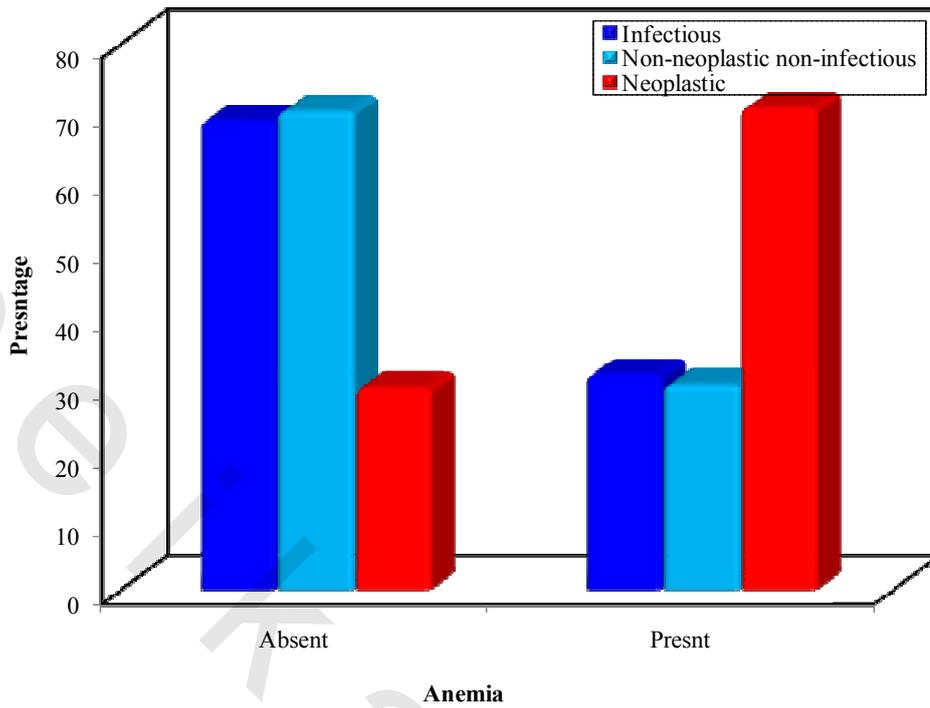


Figure (17): Comparison between the three studied groups as regards anemia

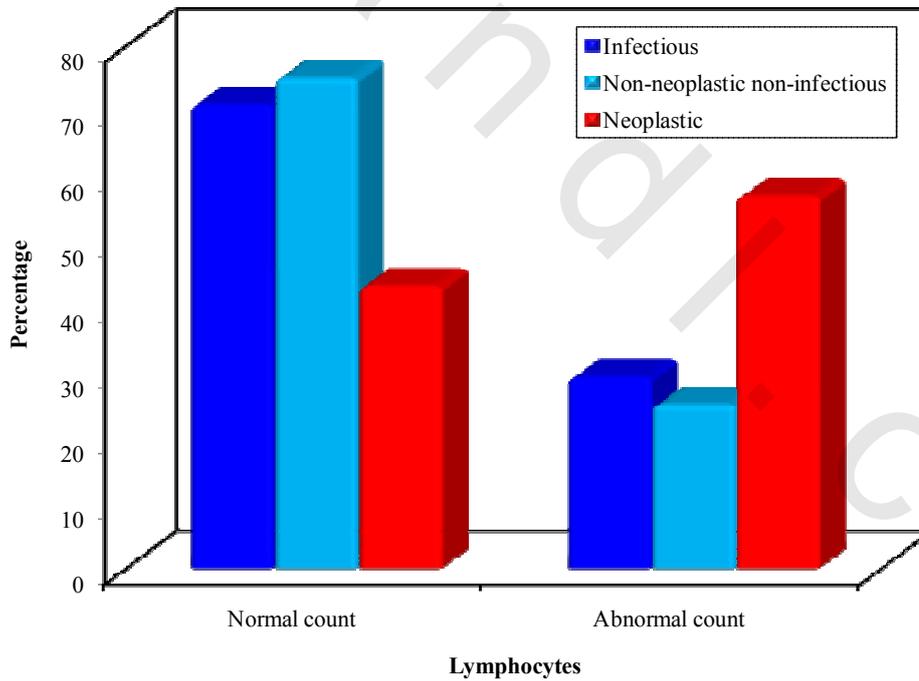


Figure (18): Comparison between the three studied groups as regards the lymphocyte count.

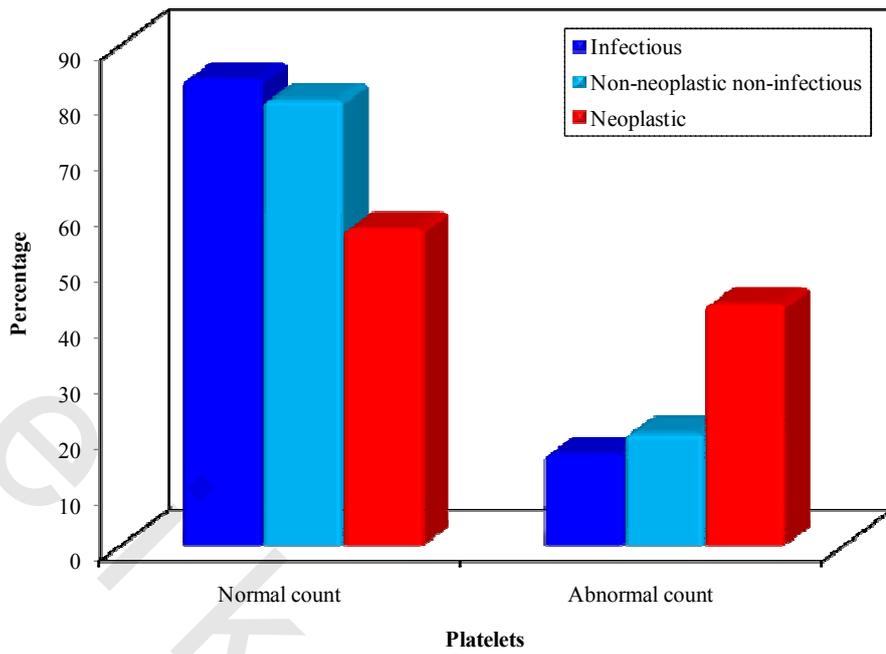


Figure (19): Comparison between the three studied groups as regards the platelet count.

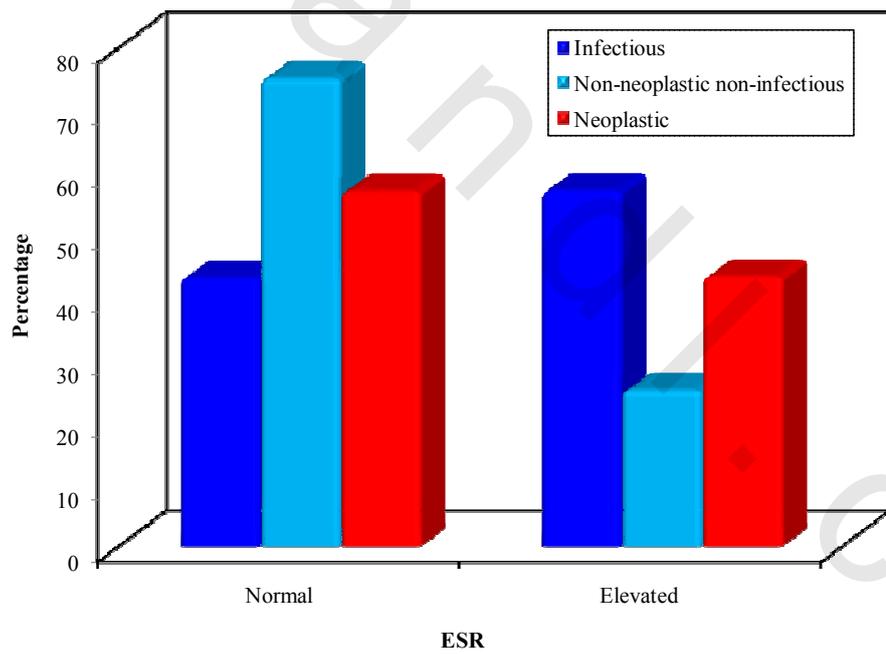


Figure (20): Comparison between the three studied groups as regards ESR results.

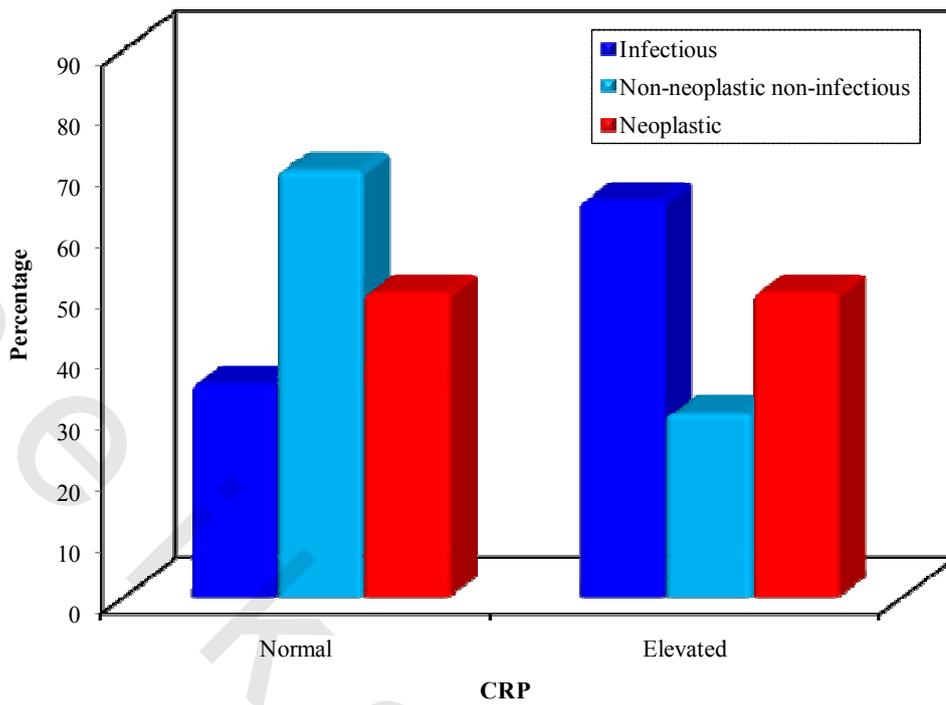


Figure (21): Comparison between the three studied groups as regards CRP results.

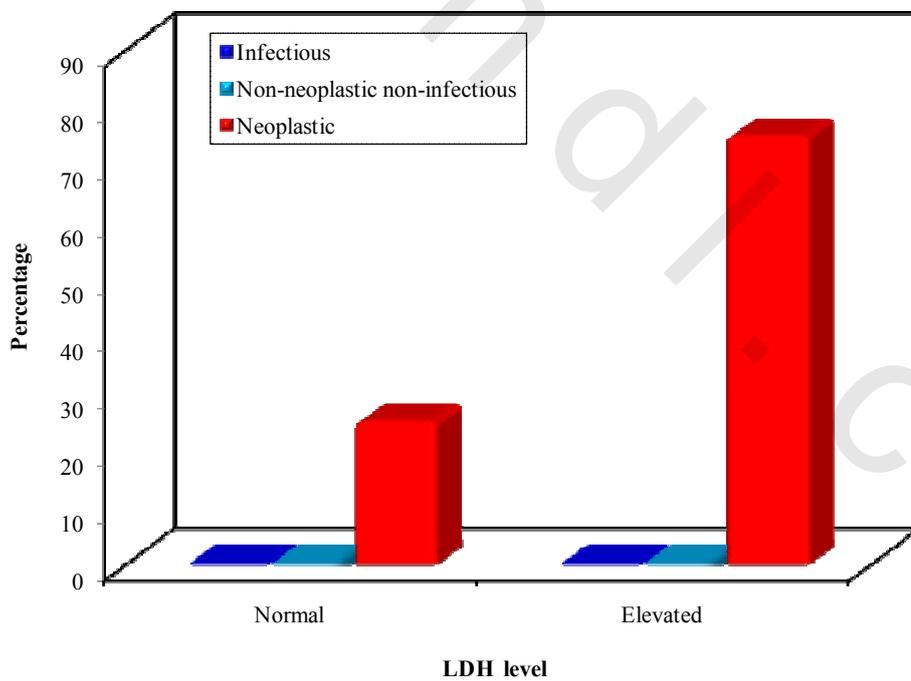


Figure (22): Comparison between the three studied groups as regards LDH results.

## Results

Table (19) and Figures (23-25) illustrate the difference in the radiologic results of the three studied groups.

No significance statistically regarding the ultrasound neck of each studied group (<sup>MC</sup>p=0.670).

In contrast, the abdominal ultrasound study including presence of LNs (p=0.001), hepatomegaly (p=0.004) or splenomegaly (p=0.001) was statistically significant.

**Table (19): Results of radiologic investigations among the studied patients with lymphadenopathy according to the etiology**

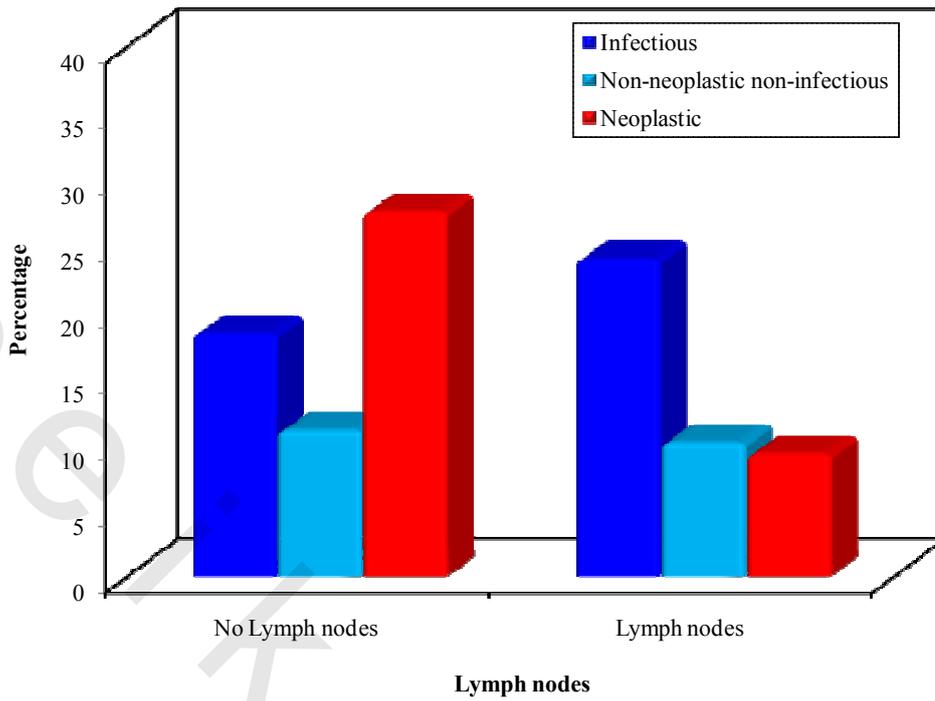
Radiologic Investigations	Non-neoplastic				Neoplastic		Test of sig.
	Infectious		non-infectious		No.	%	
	No.	%	No.	%			
<b>Ultrasound for neck LNs (n=76)</b>							<sup>MC</sup> p=0.670
Pathologic lymph nodes	2	2.6	3	3.9	2	2.6	
Non pathologic lymph nodes	30	39.5	29	38.2	10	13.2	
<b>Ultrasound abdomen Lymph nodes(n=109)</b>							$\chi^2=8.931^*$ p=0.001
No Lymph nodes	20	18.3	12	11.0	30	27.5	
Lymph nodes	26	23.9	11	10.1	10	9.2	
<b>Liver (n=109)</b>							$\chi^2=10.905^*$ p=0.004
Normal	45	41.3	17	16.0	30	27.5	
Enlarged	1	0.9	6	5.0	10	9.2	
<b>Spleen (n=109)</b>							$\chi^2=13.706^*$ p=0.001
Normal	46	42.2	17	15.6	30	27.5	
Enlarged	0	0.0	6	5.0	10	9.2	

p: p value for comparing between the three studied groups

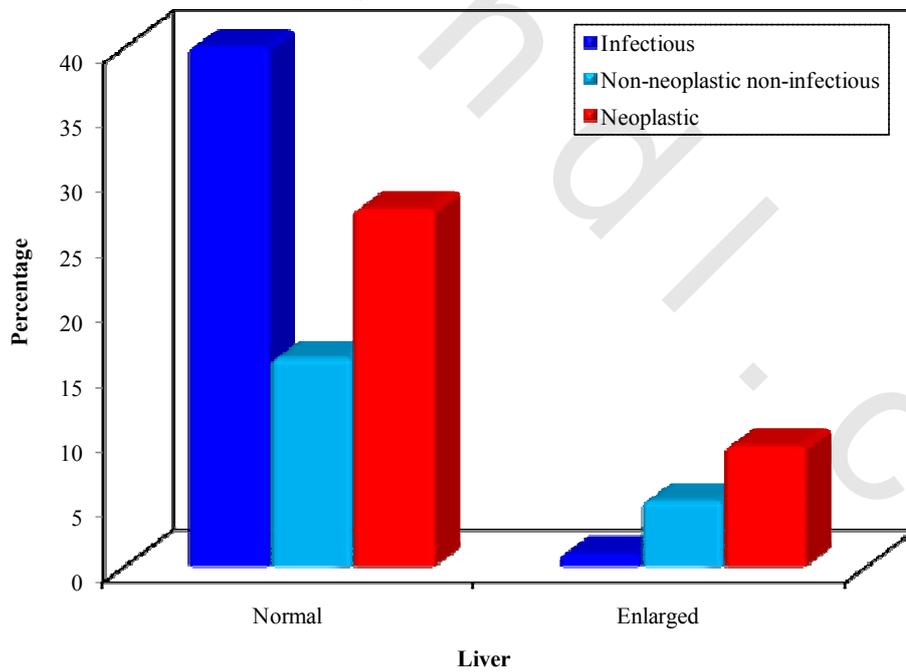
$\chi^2$ : Chi square test

MC: Monte Carlo test

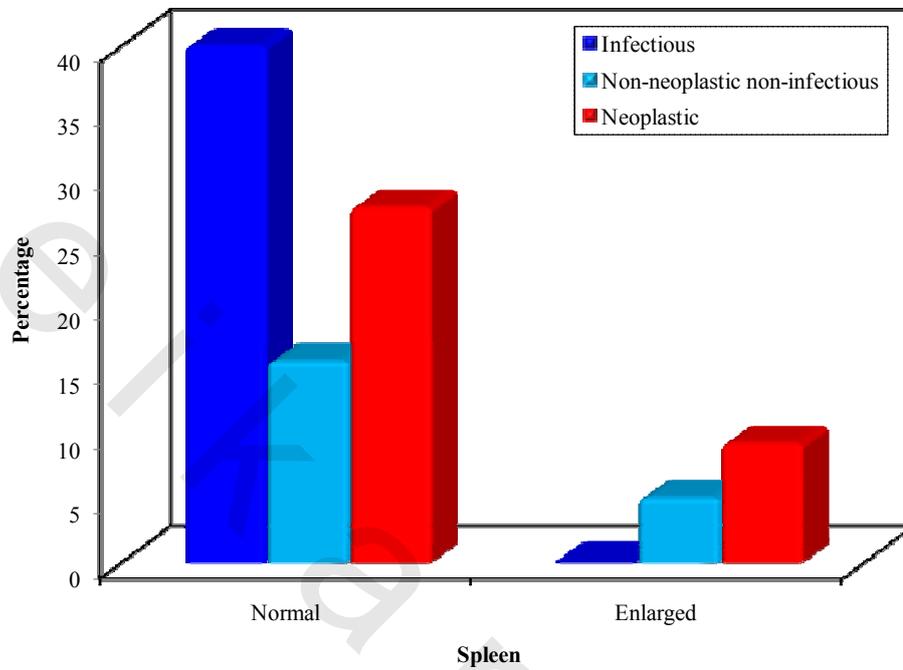
\*: Statistically significant at  $p \leq 0.05$



**Figure (23):** Comparison between the three studied groups as regards the presence or absence of lymph nodes in the abdominal US of the patients.



**Figure(24):** Comparison between the three studied groups as regards presence or absence of hepatomegaly in the US abdomen of the patients.



**Figure(25):** Comparison between the three studied groups as regards presence or absence of splenomegaly in the US abdomen of the patients.