Research Article

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Abstract

The goal of this study to detect prevalence of different causes of persistent cervical lymphadenopathy in Beni-Suef localities. This study had been conducted at Otorhinolaryngology department and radiology department, Beni-Suef University Hospital on 100 patients suffering from cervical lymphadenopathy not responding to medical treatment for 1month or progressively increasing size of lymph node within 2 weeks in spite of medical treatment. The patients (of 1- 78 years old) have done ultrasound guided tru-cut needle biopsy (89% of cases) and surgical excisional biopsy (11%). The results were 55% malignancy, 28% reactive cause, 8% TB, 3% granuloma and 6% other causes as SLE and pleomorphic adenoma.

Keyword : Cervical lymphadenopathy; tru-cut needle biopsy; surgical excisional biopsy.

Introduction

Cervical lymphadenopathy means enlargement of nodes more than 1cm in its short diameter. ^[1]. It is the commonest cause of swelling in the neck ^[2]. It commonly represents a transient response to benign local or generalized infection, but it may be due to serious cause as malignancy ^[3].

Reactive hyperplasia may be due to viral upper respiratory tract infection as rhinovirus, adenovirusor bacterial cervical infection by group (A) streptococci or staphylococcus aureus ^[4]. Anaerobic bacteria usually associated with dental caries may cause cervical lymphadenopathy ^[5].TB is an important cause of subacute and chronic cervical lymphadenopathy. It affects mainly posterior cervical and supraclavicular region. The nodes are early discrete, painless, and rubbery the become adherent to each other (matted) ^[6].

Lymphadenopathy occurs in >80% of cases of cat scratch disease and the most common affected site is the neck (43%)^[7]. Cervical lymphadenopathy may occur due to infection by toxoplasma gondii (Toxoplasmosis) and is the most common affected followed by axillary lymph nodes^[8]. Reactive lymph nodes may occur after immunization with vaccines and

usually painful ^[5], it may occur due to hypersensitivity reaction to drugs as pencillins, cephalosporins and others ^{[3].} It may occur in kawasaki disease in children below 5 years associated with fever, erythema of mucosa, skin rash and exudative bulbar conjunctivitis ^{[9].} Rosai Dorfman disease is benign disease known as sinus histiocytosis with massive lymphadenopathy, manifested by painless bilateral cervical lymphadenopathy, fever and extranodal manifestation in skin, orbit and central nervous system ^[10].

In Kimura disease, lymphadenopathy is painless and unilateral and affects Asian males ^{[11].} Kikuchi-fujimoto disease is a benign cause of lymphadenopathy which is painless associated with fever, night sweat, weight loss, arthralgia and hepatosplenomegaly ^{[12].} Lymphadenopathy may occur in autoimmune diseases as systemic lupus and suspected as lymphoma ^{[13],} in rheumatoid arthritis 82% of patients may have lymphadenopathy especially axillary and supraclavicular ^[14].

Lymphadenopathy may be due to malignant cause as lymphoma (Hodgkin and Non -Hodgkin), HL mainly affects neck and mediastinum and may have extranodal manifestations in tonsils while NHLaffects more abdominal

adenopathy with extanodal in major salivary gland, paranasal sinuses, maxilla, mandible and waldeyer's ring^[15]. Squamous cell carcinoma is one of malignant cause of lymphadenopathy especially with silent areas as tongue base, the patients may have the symptoms of primary origin as dysphagia more than 3weeks, hoarseness of voice, oral swelling or ulcerative mucosa of mouth^{[16].}

Surgical excisional biopsy is the gold standard for diagnosis, but postoperative complications may occur as wound infection, scarring, nerve injury, thrombophlebitis and patient needs to be placed in waiting list for surgery, hosted in hospital and operating room condition ^{[17].} Core needle biopsy is a viable alternative to surgical excisional biopsy with minor complications, it is cheap, feasible, fast and simple method ^{[18].}

Patients and Methods

This study was done in the Otorhinolaryngology department and radiology department, Beni-Suef University hospital from Jun 2018 to Jun 2019 on 100 patients with cervical lymphadenopathy not responding to medical treatment for more than 1 month.

Inclusion criteria:

1- Age: any age.

- 2- Sex: both genders.
- 3- Patients with cervical lymphadenopathy more than 1cm in its short diameter and not responding to medical treatment for 2 weeks
- 4- Patients have cervical lymphadenopathy progressively increasing in size in spite of medical treatment for 2 weeks.

Exclusion criteria:

1- Patients have systemic diseases explaining cervical lymphadenopathy as SLE.

2- Patients known to have any tumor which is the cause of cervical lymphadenopathy.

3- Patients with abnormal coagulation profile.

All patients were subjected to full history taking, complete otorhinolaryngeal examination, routine laboratory examination including CBC, ESR, CRP and LDH.

Persistent enlarged neck swellings not responding to medical treatment were subjected to ultrasound examination and nodal morphological features including size, shape, outline, cortex and hilum were evaluated.

Patients were subjected to ultrasound guided tru-cut needle biopsy or surgical excisional biopsy when the lymph nodes were small and needed total excisional or when the patients were uncooperative and refused tru-cut biopsy.

Ultrasound guided Tru-cut needle biopsy

- 1- All patients have done coagulation profile and biopsy was taken by tru-cut needle apparatus (16 GX10cm or 18GX10 cm) under ultrasound guidance using high linear probe.
- 2- Under local anesthesia, a small stab incision (2mm) was done in the skin with a scalpel then the apparatus was introduced into the swelling until taking biopsy tissue then the apparatus was withdrawn and a mild pressure was done for hemostasis and the incision site was covered by bandage.
- 3-The cores were placed into jars containing formaldehyde 10% and sent for histopathological examination.
- 4- Cores obtained from formalin fixed embedded tissue were stained with hematoxylineosin stain and Zeihl-Nelson stain in the case of suspicious of TB and used for conventional histology and immunohistochemistry was done to confirm the diagnosis of malignant lymphoma.

Surgical excisional biopsy:

Preoperatively all patients were subjected to routine laboratory investigations, the study was explained to all participants and a written informed consent was obtained from all patients or their relatives.

Surgical technique:

1- The procedure was done under general anesthesia.

2- Skin incision was done within neck creases, the subcutaneous tissue was dissected and the muscles were elevated taking care of great vessels as carotid arteries or nerves as spinal accessory nerve.

3- LNs were excised then suturing of subcutaneous tissue and skin was done and the incision was covered by bandage.

4- The biopsy was sent for histopathological examination as trucut biopsy.

Postoperative care and follow up:

- 1- Patients were discharged on the same day of the surgery, all patients received postoperative antibiotics for at least (7) days after surgery and instructed to avoid wetting of the wound.
- 2- Postoperative follow up was performed for 2 weeks, the sutures were removed within 7 days of operation and the patients were followed to notice any persistent significant or progressively increasing lymphadenopathy.

Statistical methodology:

Analysis of data was performed using SPSS v. 23 (Statistical Package for Social science) for Windows.

Description of variables was presented as follows:

• Description of quantitative variables was in the form of mean, standard deviation (SD), minimum and maximum.

- Description of qualitative variables was in the form of numbers (No.) and percent's (%).
- Association between categorical data was done using the Chi square test.
- Comparison between different categories regarding a scale variable was performed by ANOVA test.

The significance of the results was assessed in the form of P-value that was differentiated into:

- Non-significant when P-value > 0.05
- Significant when P-value ≤ 0.05
- Highly significant when P-value ≤ 0.001

Results

This cross sectional survey study was conducted to detect prevalence of different causes of persistent cervical lymphadenopathy in patients attended Beni-Suef University Hospital in the period from Jun 2018 to Jun 2019.

Characteristics	Number N=100	Percent (100%)	
Sex		(
Female	49	49	
Male	51	51	
Age			
Mean ±SD	35.9±20.9		
Range(min-max)	(1-78)		
Median	34		

Table (1): Socio-demographic characteristics of the studied patients

Table (2): The lymph node characteristics in all patients under the study

Lymph node characteristics	Number	Percent
Gt	N=100	(100%)
Site		
Submandibular	12	12
Upper internal jugular	19	19
Middle internal jugular	26	26
Lower internal jugular	6	6
Posterior triangle and supraclavicular	32	32
Intra-parotid	4	4
Posterior auricular	1	1
Laterality		
Left	48	48
Right	48	48
Bilateral	4	4
Multiplicity		
Single	84	84
Multiple	14	14
Amalgamated	2	2

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Figure (1): Distribution of the site of the studied lymph nodes



Figure (2): Distribution of the diagnostic methods used to detect the causes of lymph nodes swelling.

Causes	Number	Percent
	N=100	(100%)
• <u>TB</u>	$\frac{\frac{8}{55}}{31}$	<u>8</u> <u>55</u>
• <u>Malignancy:</u>	<u>55</u>	<u>55</u>
* Lymphoma:		31
Unknown type of lymphoma	14	14
HL	9	9
B-cell lymphoma	4	4
T-cell lymphoma	1	1
Anaplastic	1	1
Plasmoplastic	1	1
Follicular	1	1
*Metastatic:	21	21
squamous	3	3
undifferentiated	6	6
adenocarcinoma	6	6
papillary thyroid carcinoma	33	3
undiagnosed		3 3 1
* Fibromatosis	1	1
* Round cell	2	2
• <u>Reactive</u>	<u>28</u>	<u>28</u>
Granuloma	$\begin{array}{c c} \underline{28} \\ \underline{3} \\ \underline{6} \\ 1 \end{array}$	$\frac{\underline{28}}{\underline{3}}$ $\underline{\underline{6}}$
• <u>Others</u>	<u>6</u>	<u>6</u>
SLE		
Sarcoidosis	1	1
Pleomorphic adenoma	2	2
Florid reaction with focal necrosis	2	2

There was a statistically significant relation between age of the patients and different categories of causes (P-value=0.005) as only the mean age of the patients with malignancy was significantly higher (old age 41.4 ± 19.5 years) than patients with reactive lymph nodes (young age 25.05 ± 19.9 years), but there was no significant difference between age of patients with TB and granuloma, TB and malignancy, TB and reactive, TB and others, malignancy and granuloma, reactive and granuloma (P-value > 0.05) (tab.4).

Causes	Ν	Mean of age ±SD	P-value
ТВ	8	28.8±19.5	
Malignancy	55	41.4±19.5	
Reactive	28	25.05±19.9	0.005*
Granuloma	3	49.5±13.4	
Others	6	37.4±20.1	

Table (4): Relation between the diagnosis (different causes) and the age of the patients

There was a statistically significant relation between sex of the patients and different categories of causes (P-value=0.011) as the malignant causes was more associated with males and reactive causes was more associated with females (**tab.5**).

Causes	S	Total	
	Females	Males	
ТВ	3	5	8
	6.1%	9.8%	8.0%
Malignancy	20	35	55
	40.8%	68.6%	55.0%
Reactive	19	9	28
	38.8%	17.6%	28.0%
Granuloma	2	1	3
	4.1%	1.8%	3.0%
Others	5	1	6
	10.2%	1.8%	6.0%
Total	49	51	100
	100.0%	100.0%	100.0%
P-value		0.011*	

 Table (5): Relation between the diagnosis (different causes) and the sex of the patients

There was a statistically significant relation between sex of the patients and different types of metastasis (P-value=0.048) as the undiagnosed primary site metastasis was more associated with females (**tab.6**).

Metastatic type	S	Sex		
	Females	Males		
Undiagnosed metastasis	3	0	3	
	50%	0%	14%	
Squamous	0	3	3	
	0%	20%	14%	
Undifferentiated	1	5	6	
	16.7%	33.3%	28%	
Adenocarcinoma	1	5	6	
	16.7%	33.3%	28%	
Papillary thyroid carcinoma	1	2	3	
	16.7%	13.3%	14.0%	
Total	6	15	21	
	100.0%	100.0%	100.0%	
P-value		0.048*		

Table (6): Relation between different types of metastatic tumors and sex of the patients

There was no statistically significant relation between age of the patients and different types of metastasis (P-value=0.607) (tab.7).

Table (7): Relation between different types of metastatic tumors and sex of the patients

Type of metastasis	Ν	Mean age	Std. Deviation	Р-
				value
Undiagnosed	3(14%)	48.3	13.8	
Squamous	3(14%)	49	20.7	0.607
undifferentiated	6(28%)	57.8	6.7	
Adenocarcinoma	6(28%)	47	17.6	
Papillary thyroid carcinoma	3(14%)	43.6	9	

Table (7) shows that there was no statistically significant relation between age of the patients and different types of metastasis (P-value=0.607).

There was a statistically significant relation between the site of the lymph node and the cause of lymph node swelling (P-value < 0.001) as the TB was found more in the upper internal jugular, supraclavicular and posterior triangle, malignant lymph nodes were found more in the middle internal jugular, supraclavicular and posterior triangle and the reactive lymph nodes were found more in the middle internal jugular (tab. 8).

Site	Causes				Total	
	ТВ	Malignancy	Reactive	Granuloma	Others	
Submandibular	0	4	5	1	2	12
	0.0%	7.3%	17.9%	33.3%	33.3%	12.0%
Upper internal	4	6	8	0	1	19
jugular	50.0%	10.9%	28.6%	0.0%	16.7%	19.0%
Middle internal	0	17	9	0	0	26
jugular	0.0%	30.9%	32.1%	0.0%	0.0%	26.0%
Lower internal	0	4	2	0	0	6
jugular	0.0%	7.3%	7.1%	0.0%	0.0%	6.0%
Supraclavicular	4	23	2	1	2	32
and posterior	50%	41.8%	7.1%	33.3%	33.4%	32%
triangle	37.5%	18.2%	3.6%	33.3%	16.7%	16.0%
Intra parotid	0	1	2	1	0	4
	0.0%	1.8%	7.1%	33.3%	0.0%	4.0%
Posterior	0	0	0	0	1	1
auricular	0.0%	0.0%	0.0%	0.0%	16.7%	1.0%
Total	8	55	28	3	6	100
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
P-value	< 0.001**					

Table (8): Relation between different causes of lymph node swelling and their sites in all patients

There was no statistically significant relation between age of the patients and different types of lymphomas (P-value=0.618) (tab. 9).

Table (9): Relation between different types of lymphoma (Hodgkin and Non-Hodgkin) and the
age of the patients who diagnosed differentiated lymphoma

Type of lymphoma	Ν	Mean of age	Std. Deviation	P-value
HL	9(52.9%)	35.7	17.01	0.618
Non HL	8(47.1%)	40	17.07	

There was no statistically significant relation between sex of the patients and different types of lymphomas (P-value=0.457) (tab. 10).

 Table (10): Relation between different types of lymphoma (Hodgkin and Non-Hodgkin) and the sex of the patients who diagnosed differentiated lymphoma

Type of lymphoma	S	Sex Total		
	Females	Males		
HL	5	4	9	
	62.5%	44.4%	52.9%	
Non HL	3	5	8	
	37.5%	55.6%	47.1%	
Total	8	9	17	
	100.0%	100.0%	100.0%	
P-value		0.457		

There was no statistically significant relation between sex of the patients and different types of malignancy (P-value=0.451) (tab. 11).

ТҮРЕ	S	Sex		
	Females	Males		
Lymphoma	12	19	31	
	66.7%	55.9%	59.6%	
Metastatic	6	15	21	
	33.3%	44.1%	40.4%	
Total	18	34	52	
	100.0%	100.0%	100.0%	
P-value		0.451		

 Table (11): Relation between the type of malignancy (either lymphoma or metastatic) and the sex of the patients:

There was statistically significant relation between age of the patients and different types of malignancy (P-value=0.015) as the lymphoma was more prevalent in young age $(37.3\pm10.2 \text{ years})$, but the metastasis was more prevalent in old age $(50.1\pm13.6 \text{ years})$ (tab. 12).

Table (12) :Relation between the	type of malignancy	(either lymphoma o	r metastatic) and the
age of the patients:			

Туре	N	Mean age	Std. Deviation	P-value
Lymphoma	31	37.3	10.2	0.015*
Metastatic	21	50.1	13.6	

There was a statistically significant association between the elevated level of TLC and presence of TB (P-value=0.035) (**tab. 13**).

Table (13): Relation between differen	t causes of	lymphadenopathy	and th	ne total	leucocytic
count of the patients:					

TLC		Туре					
	ТВ	Malignancy	Reactive	granuloma	others		
Normal	5	37	28	4	4	78	
	62.5%	67.3%	100.0%	100.0%	80.0%	78.0%	
Elevated	3	12	0	0	1	16	
	37.5%	21.8%	0.0%	0.0%	20.0%	16.0%	
Lowered	0	6	0	0	0	6	
	0.0%	10.9%	0.0%	0.0%	0.0%	6.0%	
Total	8	55	28	4	5	100	
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
P-value		0.035*					

There was a statistically significant association between the elevated level of LDH and presence of malignancy (P-value < 0.001) (tab. 14).

LDH		Total					
	ТВ	Malignancy	Reactive	granuloma	others		
Normal	7	13	22	3	3	48	
	87.5%	23.6%	78.6%	75.0%	60.0%	48.0%	
Elevated	1	42	6	1	2	52	
	12.5%	76.4%	21.4%	25.0%	40.0%	52.0%	
Total	8	55	28	4	5	100	
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
P-value	< 0.001**						

Table (14): Relation between different causes of lymphadenopathy and the lactate dehydrogenase level of the patients:

There was a statistically significant association between the elevated level of ESR and presence of malignancy and TB (P-value < 0.001) (tab. 15).

ESR		Туре						
	ТВ	Malignancy	Reactive	Granuloma	Others			
Normal	0	6	16	2	4	28		
	0.0%	10.9%	57.1%	50.0%	80.0%	28.0%		
Elevated	8	49	12	2	1	72		
	100.0%	89.1%	42.9%	50.0%	20.0%	72.0%		
Total	8	55	28	4	5	100		
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%		
P-value		<	0.001**					

 Table (15): Relation between different causes of lymphadenopathy and the ESR of the patients:

There was no statistically significant association between the elevated level of CRP and different causes of lymphadenopathy (P-value > 0.05) (tab. 16).

CRP	Туре								
	TB Malignancy Reactive granuloma Others								
		50	21	4	4	86			
	87.5%	90.9%	75.0%	100.0%	80.0%	86.0%			
Elevated	1	5	7	0	1	14			
	12.5%	9.1%	25.0%	0.0%	20.0%	14.0%			
Total	8	55	28	4	5	100			
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%			
P-value		0.316							

Lymphadenopathy means abnormality in the size of lymph node more than 1cm in diameter, it may be a transient response to benign local or general infection, but the most serious is malignancy ^[3]. This study had been conducted at Otorhinolaryngology department and Radiology department, Beni-Suef University Hospital on patients with cervical lymphadenopathy not responding to medical treatment for

more than 1 month. The aim was to detect the prevalence of different causes of persistent cervical lymphadenopathy in Beni-Suef localities.

Our study was conducted on 100 patients suffering from cervical lymphadenopathy (not responding to medical treatment). The patients were conducted to CNB and surgical excisional

biopsy. The most common method used was tru-cut biopsy (89%) and (11%) of cases had surgical excisional biopsy when the lymph nodes were small and needed total removal or when the patients were uncooperative and refused tru-cut needle biopsy.

In the present study, the most prevalent site was posterior triangle and supraclavicular (level V) (32%) followed by the middle internal triangle (level III) (26%) and upper internal jugular (level II) (19%), ^[19], reported that the posterior group of lymph nodes was the most common affected LNs followed by submandibular LNs.

^{[20],} reported that level II was the most common affected LNs (26%) followed by level III (21%) and 7% of patients only had multiple levels affected, but in our study 14% of patients had multiple levels affected.

In the present study, the results were divided into 5 main categories: malignancy, reactive, TB, granuloma and others. The most prevalent cause of the studied lymph node swelling is malignancy (55%) followed by reactive causes (28%) then TB (8%) and granuloma (3%).

This study is similar to the study of ^[21], which reported more malignant cases and less TB, ^[21] reported that (35%) of adult cases were malignant followed by benign mass (21%), reactive (6%),TB (5%), non TB infection (14%) and non- diagnostic cases were (11%) and in children, malignancy and benign masses were the most common followed by reactive nodes (9%) and TB was diagnosed in 7% of cases.

^[22], reported that 59.13% of patients had malignancy and 40.87% had benign causes, ^[23], reported that 59% of cases were malignant and 34% were benign while ^[24], reported that only 22.38% of patients had malignancy and 77.6% had benign causes and ^[20], reported that only 19 % of cases had malignancy, 25% had TB and reactive causes were 46%.

^{[25],} reported that TB was the most prevalent cause 45.4% followed by secondary metastasis 21.2%, reactive causes 19.9%, lymphoma 7% and chronic granuloma 3.5%, ^[26], also reported that TB was the most common cause by (51.9%) followed by reactive cause (27.6%), metastasis (6.4%) and lymphoma (2.3%).

 $^{[27]}$, reported that reactive cause was the most prevalent cause of LNs by (50.4%) followed by TB (22.4%) then malignancy (4.8%) and granuloma (10%).

In this study, malignant lymph nodes were divided into: lymphoma (31%) of cases followed by secondary cancers (21%), round cell tumor (2%) and fibromatosis (1%), it is similar to the study of ^[21], which reported that the most common type of malignant lymph nodes was lymphoma.

In the present study, there were 9 cases of Hodgkin lymphoma and 8 cases of Non-Hodgkin lymphoma (4 B-cell lymphoma, 1 T-cell lymphoma, anaplastic, plasmoplastic and follicular lymphoma), ^[20], reported that both Hodgkin and Non-Hodgkin were equal in incidence (15.79%, n= 19) while ^[24], reported that NHL was 33.33% of total malignancy and HL was of 13.33% of total malignancy.

In this study, the second malignant type was metastasis (21%), adenocarcinoma and undifferentiated carcinoma were the most common type (each is 6%) followed by squamous cell carcinoma and papillary thyroid carcinoma (each is 3%) and 3% of cases of undiagnosed metastatic type, ^[21], also reported that metastasis was the second common type of malignancy in adult and squamous cell carcinoma was (24%) of malignant lymph nodes.^[20], reported that secondary cancers were the most malignant type (68.42%) of total malignancy, ^[24],

reported that secondary cancers were 53.3% of all malignant lymph nodes and ^[25], reported that secondary metastasis were 21.2 % of all lymph nodes and squamous cell carcinoma was the most metastatic type (8.5%) followed by adenocarcinoma (7.8%) while lymphoma was 7% of all nodes.^[28], reported that 80% 0f malignant nodes were metastatic, 15.3% were primary tumors and among the metastatic tumors squamous cell carcinoma was the most common followed by carcinoma of the breast and adenocarcinoma.^[29], reported that the

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prevalence of malignancy causing metastatic lymph nodes was squamous cell carcinoma, adenocarcinoma and undifferentiated carcinoma.

In the present study, others causes of cervical lymph nodes were 6% of all lymph nodes including: SLE, sarcoidosis, florid inflammatory reaction with focal necrosis and pleomorphic adenoma.

In this study there was a statistically significant relation between age of patient and different causes of cervical lymphadenopathy (P-value= (0.005) as the mean age of the patients with malignancy was higher (old age 41.4±19.5) than patients with reactive lymph nodes (young age 25.05± 19.9), ^[27], reported highest incidence of cancers was in the fifth decade, ^[25], also reported that reactive cause was the most prevalent cause in children up to 14 years old and TB and malignancy were in higher age.^[30], reported that reactive cause was the most common cause in children and ^[29], reported that reactive hyperplasia was the most common cause in the first two decade of life and TB in the second and third decade (58,9%) and (88%)of metastasis were over 40 years age.

In the present study, there was a significant relation between sex of patients and different categories of causes (P-value=0.011) as the malignant causes were more associated with males, (68.6%) of males were malignant and there was a statistically relation between sex different types of metastasis (Pand value=0.048) as the undiagnosed metastasis was more associated with females, also ^[20], reported that malignancy was more in males, 28.3% of males have malignancy and only 11.1% of females have malignancy.^[31], reported male predominance of metastatic lymph nodes (67%), ^[28], also reported that malignancy was higher in males (M: F: 2.4:1), this may be due to less addiction by females, ^[25], reported that the sex ratio of patients with cancers was M: F: 2.33:1 and ^{[29],} reported male predominance of lymphoma and metastasis.

In this study reactive hyperplasia was more associated with females, (38.8%) of females have reactive cause,^{[29],} reported male predominance of reactive hyperplasia and there was

no significant sex difference observed regarding reactive hyperplasia as reported by ^{[25].}

In the present study there was statistically significant relation between the site of the lymph node and the cause of the cervical lymphadenopathy (P-value < 0.001) as TB is more found in the upper internal jugular (level II) and post triangle group, this result resembles the results reported by ^{[32],} that TB more in the Jugulodigastric group (33.3%) followed by posterior triangle group (20%) and ^{[33], [34], [31],} ^[19] and ^[25], which reported that TB was more in the Jugulodigastric LNs, then posterior auricular and submandibular LNs.

In this study, malignant lymph nodes were found more in the posterior triangle group (level V) followed by middle internal jugular group (level III) this results as ^[20], which reported highest incidence of malignancy in level V (36,8%) followed by level III (23,8%) and level I had least incidence of malignancy (10%) and ^[25], which reported that malignancy was found more in Juguloomhyoid (level III) and supraclavicular lymph nodes (level VB).

In the present study, reactive lymph nodes were found more in the middle internal Jugular lymph nodes.

In our study, there was a statistically significant relation between age of patients and different types of malignancy (P-value=0.015) as lymphoma was more prevalent in young age $(37.3\pm10.2 \text{ years})$, but metastasis was more prevalent in old age (50.1 ± 13.6) , ^[19], reported that the most common cancers in younger than 40 years were lymphoma (55%) and in older than 40 were metastasis (squamous cell carcinoma 67%)^[29] and ^{[25],} reported that secondary cancers were in more than 40 years as our study while lymphoma involved in all age groups.

In the present study there was a statistically significant relation between the elevated level of LDH and the presence of malignancy (p-value < 0.001), this resembles which reported by ^{[35],} that LDH catalyzes the conversion of pyruvate into lactate even under normal oxygen concentration in malignancy and the tumor microenvironment acidification can promote tumor progression and metastasis.

In this study there was a statistically significant association between elevated level of TLC and presence of TB (P-value=0.035), this results resemble the study of ^{[36],} which described changes in leucocytic count and lymphocytes during treatment, they noticed elevated total WBC in patients at diagnosis relative to control and returned to normal by the end of treatment. In the present there was a statistically significant association between elevated level of ESR and presence of TB (P-value < 0.001), this results resemble what was reported by ^[37], that high ESR above 100 was associated with active TB and without any underlying disease affecting the ESR level, ESR may be a valuable diagnostic test to suspect TB.

In this study there was a statistically significant association between elevated level of ESR and presence of malignancy (P-value < 0.001), this results resemble which was reported by ^[38], that ESR and CRP play important roles in cancer development and progression.

Our results not agree with ^[39], who reported that the prevalence of malignancy in patients with elevated ESR was low.

Conclusion

The present study was a cross sectional study to detect prevalence of different causes of persistent cervical lymphadenopathy in Benisuef localities.

True-cut needle biopsy and surgical excisional biopsy were done to patients with persistent cervical lymphadenopathy, the results illustrated that malignancy was the most common cause by (55%) followed by reactive cause (28%) with less TB cases (8%).

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