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Etiology of Cervical lymphadenopathy: A study in a tertiary care hospital, Dhaka, Bangladesh

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Abstract
This cross sectional observational study was carried out with an aim to assess the etiological pattern of patient having cervical lymphadenopathy. A total of 115 patients presented with cervical lymphadenopathy both inpatient and outpatient department of Medicine in Dhaka Medical College Hospital, during March 2014 to December 2014, were included in this study. A total of 115 consecutive patients having cervical lymphadenopathy both inpatient and outpatient department in the above mentioned hospitals were enrolled in this study to assess the etiological pattern of patient having cervical lymphadenopathy. Almost one third (29.6%) patients belonged to age 21-30 years and the mean age was found 42.1±15.6 years. The association between age with histological findings it was observed that lymphoma was found 27.6% in patients belonged to age 41-50 years, tuberculosis 14(43.8%) patients belonged to age 21-30 years, metastatic carcinoma was 10(41.7%) patients belonged to age 51-60 years, nonspecific lymphadenopathy 11(45.8%) patients belonged to age 21-30 years. Male to female ratio was 2.6:1. More than three fourth patients were married. More than one fourth, patients were laborer, one third were businessman, and others were housewives, student, and unemployed. More than half of the patients came from lower class and others from middle class family.

Keywords: etiology, cervical lymphadenopathy, Clinic opathological findings

1. Introduction
In everyday practice cervical lymphadenopathy is a common finding in a large proportion of patients. Most patients can be diagnosed on the basis of careful history, physical examination and investigations. Considering the previous studies done abroad among different ethnic area it can be said that there is great variation in etiology of cervical lymphadenopathy along with the clinical presentation. This study is intended to be performed to evaluate the common and uncommon etiology on the basis of histopathology as well as identify any non-specific cervical lymphadenopathy in Bangladeshi adult population. A BCPS dissertation shows out of 50 cases, biopsies were done in 31 cases which revealed lymphoma in 14, tuberculosis in 10, metastatic carcinoma in 5, and non-specific finding in 2 cases. FNAC were done in 7 cases out of which shows metastatic carcinoma in 4, non-specific findings 2, and tuberculosis in 1 case (Miah, 2007) [1]. Cervical lymph node enlargement is common clinical finding in medical practice[1]. Enlargement of lymph node may result from proliferation of lymphocytes intrinsic to the lymph node either due to infection or due to lymph proliferative disorder or from the migration & infiltration of nodal tissue by either extrinsic inflammatory cells or metastatic malignant cells (American Academy of Pediatrics, 2003) [2]. Cervical lymphadenopathy may be due to Infections, Malignancy, Autoimmune diseases, Miscellaneous/unusual conditions, and iatrogenic causes (Bazemore and Smucker, 2002) [3]. Any failure to decrease in size of lymph node within 10-14 days of treatment, a need for further evaluation is indicated (Buchino & Jones, 1994; Dajani *et al*. 1963) [4, 5]. The most common cause of cervical lymphadenopathy is reactive hyperplasia resulting from an infectious process, most commonly a viral upper respiratory tract infection (Peters & Edwards, 2000) [6]. Upper respiratory tract infection might be caused by rhinovirus, Parainfluenza virus, influenza virus, respiratory syncytial virus, coronavirus, adenovirus, or reovirus. Other viruses associated with cervical lymphadenopathy include Epstein-Barr virus (EBV), cytomegalovirus, rubella, rubeola, varicella-zoster virus, herpes simplex virus (HSV), coxsackievirus, and human immunodeficiency virus (HIV). Bacterial cervical lymphadenitis is usually caused by group A β-hemolytic streptococci or Staphylococcus aureus. Anaerobic bacteria can cause cervical lymphadenitis, usually in association with dental caries and periodontal disease. Group B streptococci and Haemophilus influenzae type b are less frequent causal organisms. Diphtheria is a rare cause. Bartonella henselae (cat scratch disease), atypical mycobacteria, and mycobacteria are important causes of subacute or chronic cervical lymphadenopathy (Spyridis, Maltezou, & Hantzakos, 2001) [7]. Chronic posterior cervical lymphadenitis is the most common form of acquired toxoplasmosis and is the sole presenting symptom in 50% of cases (Leung & Robson, 1991) [8]. In 2006 Yaris *et al*. performed a retrospective review of 126 patients in USA. Of the 126 patients 22.2% were found to have disease other than lymphadenopathy. Of those with lymphadenopathy, 76.6% had benign disease mostly belonging to acute lymphadenitis and 23.4% had malignancies. In a study performed by Ellison *et al*. [9]. in 1999 of 309 clavicular fine needle aspirations, they found

that 55% of nodes sampled were malignant. Zeharia *et al*. (2008) [10] performed retrospectively on 92 children diagnosed with atypical mycobacterial lymphadenopathy. The parents of all 92 children in this study opted for non-surgical and non-medical conservative management, and patients were followed for a minimum of 2 years. Clinical profile includes 80% of patients were less than 4 years old, 80% of patients had lymphadenopathy greater than 3cm in size, 90% of patients had unifocal lymphadenopathy, Lymphadenopathy was most commonly found in Submandibular (50%), Cervical (25%), Pre-auricular (10%) regions, 85% of patients had a positive PPD (>10mm), 90% of cases were due to M. avium-intracellulare and M. haemophilum, 97.4% of patients had a dominant node with purulent drainage for 3-8 weeks.

2. Objectives

General Objective

- To assess the etiological pattern of cervical lymphadenopathy.

Specific Objectives

- To describe the types of variations in clinical presentation of cervical lymphadenopathy.
- To describe the demographic characteristics of patient having cervical lymphadenopathy.

3. Mrthodology and Materials

This cross sectional observational study was carried out with an aim to assess the etiological pattern of patients having cervical lymphadenopathy. A total of 115 patients presented with cervical lymphadenopathy both inpatient and outpatient department of Medicine in Dhaka Medical College Hospital, during March 2014 to December 2014, were included in this study. Patients aged ≥18 years, presented with cervical lymphadenopathy >1.0 cm in diameter, duration of cervical lymphadenopathy more than 7 days (subjective and objective) were enrolled in this study. Patients aged less than 18 years, extremely debilitated patient, patient with insignificant lymph node enlargement, e.g. <1.0 cm in cervical regions, patients who refuse to give consent, known case of lymphadenopathy and patients suggestive of haematologic malignancy were excluded from the study. The present study findings were discussed and compared with previously published relevant studies. The result of present study is as follows.

Inclusion criteria

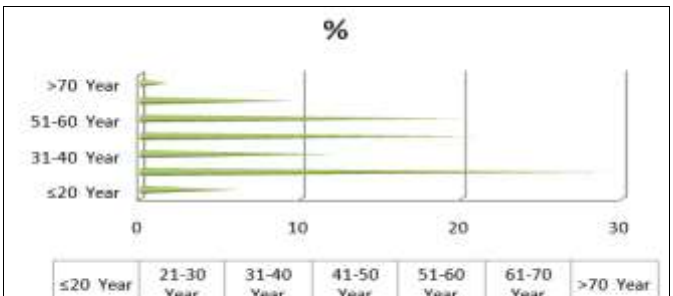
1. Patients aged 18 years and above.
2. Patients having cervical lymphadenopathy >1.0 cm in diameter.
3. Patients presented in outdoor and indoor, department of medicine, Dhaka Medical College and Hospital.
4. Duration of cervical lymphadenopathy ≥14 days (subjective and objective).

Exclusion criteria

1. Patient with insignificant lymph node enlargement, e.g. <1.0 cm in cervical regions.
2. The patients who refuse to give consent.
3. A diagnosed case of lymphadenopathy.
4. In those patient where FNAC/ biopsy is contraindicated, such as leukaemia.

4. Results

A total of 115 consecutive patients having cervical lymphadenopathy both inpatient and outpatient department in the above mentioned hospitals were enrolled in this study to assess the etiological pattern of patients having cervical lymphadenopathy. Almost one third (29.6%) patients belonged to age 21-30 years and the mean age was found 42.1±15.6 years. The association between age with histological findings it was observed that lymphoma was found 27.6% in patients belonged to age 41-50 years, tuberculosis 14(43.8%) patients belonged to age 21-30 years, metastatic carcinoma was 10(41.7%) patients belonged to age 51-60 years, nonspecific lymphadenopathy 11(45.8%) patients belonged to age 21-30 years. Male to female ratio was 2.59:1. More than three fourth patients were married. More than one fourth, patients were laborer, one third were businessman, and others were housewives, student, and unemployed. More than half of the patients came from lower class and others from middle class family. Regarding the clinical feature of the study patients, it was observed that majority patients had nonspecific symptom like generalized weakness, loss of appetite and weight loss, other features like fever, cough and headache also present in less number. Examination cervical lymph node observed that most of the lymph node was non tender, discreet in character, firm in consistency and mobile. On the other hand, lymph nodes fixed in metastatic carcinoma and matted in tuberculosis. On systemic examination, it was observed that splenomegaly and hepatomegaly were the common finding followed by ascites. Organomegaly was frequently seen lymphoma while ascites in metastatic cases. More than three fourth of the patients had normal findings in CXR P/A view followed by features of consolidation, features of effusion, bilateral hilar shadow and features of fibrosis. Hemoglobin level showed most patients were anaemic. Erythrocyte sedimentation rate were also high in most of the patients. Total count of WBC of the study patients were within normal limit. FNAC of lymph node was done in 45 cases and among them tuberculosis was found 21(46.7%), lymphoma 8(17.8%), metastatic carcinoma 8(17.8%), nonspecific lymphadenopathy 6(13.3%) and others were 2(4.4%). Biopsy of lymph node was done in 70 cases among them 21(30.0%) patients had lymphoma, 18(25.7%) had nonspecific lymphadenopathy, 16(22.9%) had metastatic carcinoma, 11(15.7%) had tuberculosis. Diagnosis of study patients by histopathology and other relevant investigations finally observed that 34(29.6%) patients had tuberculosis, 29(25.2%) had lymphoma, 24(20.9%) had metastatic carcinoma, 14(12.2%) had nonspecific lymphadenopathy.



	≤20 Year	21-30 Year	31-40 Year	41-50 Year	51-60 Year	61-70 Year	>70 Year
%	6.1	29.6	12.2	20.9	20	9.6	1.7

Mean± SD: 42.1±15.6, Range: 19-80

Fig 1: Distribution of study population by age (n=115)

Table 1: Distribution of study population by age (n=115)

Age (Years)	Number of patients	Percentage
≤20	7	6.1
21-30	34	29.6
31-40	14	12.2
41-50	24	20.9
51-60	23	20.0
61-70	11	9.6
>70	2	1.7
Mean±SD	42.1	±15.6
Range (Min, max)	19	,80

Table 2: Distribution of study population by age and histological findings (n=115)

Age (Years)	Histopathology report									
	Lymphoma (n=29)		Tuberculosis (n=32)		Metastatic Carcinoma (n=24)		Nonspecific lymphadenopathy(n=24)		Others (n=6)	
	n	%	n	%	n	%	n	%	n	%
≤20	2	6.9	2	6.3	0	0.0	2	8.3	1	16.7
21-30	4	13.8	14	43.8	3	12.5	11	45.8	2	33.3
31-40	5	17.2	6	18.8	0	0.0	1	4.2	2	33.3
41-50	8	27.6	4	12.5	6	25.0	6	25.0	0	0.0
51-60	6	20.7	3	9.4	10	41.7	4	16.7	0	0.0
61-70	4	13.8	2	6.3	4	16.7	0	0.0	1	16.7
>70	0	0.0	1	3.1	1	4.2	0	0.0	0	0.0

Table 3: Distribution of study population by sex with marital status (n=115)

Sex	n	Married		Unmarried	
		n	%	n	%
Male	83	65	78.3	18	21.7
Female	32	24	75.0	8	25.0
Total	115	89	77.4	26	22.6

Table 4: Distribution of positive clinical symptoms by histopathological findings (n=115)

Positive clinical symptoms	Histopathological findings										P value
	Lymphoma (n=29)		Tuberculosis (n=32)		Metastatic carcinoma (n=24)		Nonspecific Lymphadenopathy (n=24)		*Other (n=6)		
	n	%	n	%	n	%	n	%	n	%	
Generalized weakness											
Present	28	96.6	31	96.9	23	95.8	21	87.5	2	33.3	0.001^{s}
Absent	1	3.4	1	3.1	1	4.2	3	12.5	4	66.7	
Appetite											
Present	1	3.4	0	0.0	0	0.0	15	62.5	1	16.7	0.001^{s}
Lost	28	96.6	32	100.0	24	100.0	9	37.5	5	83.3	
Weight loss											
Present	29	100.0	30	93.8	22	91.7	19	79.2	2	33.3	0.001^{s}
Absent	0	0.0	2	6.3	2	8.3	5	20.8	4	66.7	
Cough											
Present	8	27.6	14	43.8	9	37.5	5	20.8	1	16.7	0.327^{ns}
Absent	21	72.4	18	56.3	15	62.5	19	79.2	5	83.3	
Sputum											
Present	3	37.5	13	92.9	6	66.7	4	80.0	0	0.0	0.037^{s}
Absent	5	62.5	1	7.1	3	33.3	1	20.0	1	100.0	
Alteration of bowel habit											
Present	0	0.0	0	0.0	9	37.5	2	8.3	0	0.0	0.001^{s}
Absent	29	100.0	32	100.0	15	62.5	22	91.7	6	100.0	
Haemoptysis											
Present	0	0.0	3	9.4	2	8.3	0	0.0	0	0.0	0.235^{ns}
Absent	29	100.0	29	90.6	22	91.7	24	100.0	6	100.0	

s= significant, ns= not significant, P value reached from chi square test

Table 5: Distribution character of fever by histopathological findings (n=115)

Character of fever	Histopathological findings										P value
	Lymphoma (n=29)		Tuberculosis (n=32)		Metastatic carcinoma (n=24)		Nonspecific lymphadenopathy (n=24)		Other (n=6)		
	n	%	n	%	n	%	n	%	n	%	
Presence of fever											
Present	26	89.7	32	100.0	8	33.3	19	79.2	5	83.3	0.001[s]
Absent	3	10.3	0	0.0	16	66.7	5	20.8	1	16.7	
Grade of fever	(n=26)		(n=32)		(n=8)		(n=19)		(n=5)		
High grade	7	26.9	5	15.6	7	87.5	5	26.3	3	60.0	0.001[s]
Low grade	19	73.1	27	84.4	1	12.5	14	73.7	2	40.0	
Associated with sweating											
Present	18	69.2	31	96.9	4	50.0	7	36.8	1	20.0	0.001[s]
Absent	8	30.8	1	3.1	4	50.0	12	63.2	4	80.0	

s= significant, P value reached from chi square test.

Table 6: Distribution of fever by histopathological findings (n=90)

Duration of fever (day)	Histopathological findings										P value
	Lymphoma (n=26)		Tuberculosis (n=32)		Metastatic carcinoma (n=8)		Nonspecific lymphadenopathy (n=19)		Other (n=5)		
	n	%	n	%	n	%	n	%	n	%	
<30	1	3.9	2	6.3	4	50.0	1	5.2	4	80.0	0.001[s]
30-60	22	84.6	25	78.1	4	50.0	9	47.4	0	0.0	
>60	3	11.5	5	15.6	0	0.0	9	47.4	1	20.0	
Mean± SD	53.3	±21.4	52.8	±27.3	26.4	±9.6	81.3	±54.9	32.8	±32.3	
Range (min, max)	20-120		20-150		14-45		14-180		14-90		

s= significant, P value reached from ANOVA test.

Table 7: Distribution of lymph node character by histopathological findings (n=115)

Lymph node character	Histopathological findings										P value
	Lymphoma (n=29)		Tuberculosis (n=32)		Metastatic carcinoma (n=24)		Nonspecific lymphadenopathy (n=24)		Other (n=6)		
	n	%	n	%	n	%	n	%	n	%	
Tenderness											
Preset	1	3.4	2	6.3	2	8.3	0	0.0	5	83.3	0.001[s]
Absent	28	96.6	30	93.8	22	91.7	24	100.0	1	16.7	
Character											
Matted	1	3.4	11	34.4	1	4.2	1	4.2	0	0.0	0.001[s]
Discreet	28	96.6	21	65.6	23	95.8	23	95.8	6	100.0	
Consistency											
Hard	1	3.4	0	0.0	18	75.0	0	0.0	0	0.0	0.001[s]
Firm	28	96.6	32	100.0	6	25.0	24	100.0	6	100.0	
Fixity											
Mobile	28	96.6	32	100.0	7	29.2	24	100.0	5	83.3	0.001[s]
Fixed	1	3.4	0	0.0	17	70.8	0	0.0	1	16.7	

s= significant, P value reached from chi square test

Table 8: Distribution of positive sign by histopathological findings (n=115)

Positive sign	Histopathological findings										P value
	Lymphoma (n=29)		Tuberculosis (n=32)		Metastatic carcinoma (n=24)		Nonspecific lymphadenopathy (n=24)		Other (n=6)		
	n	%	n	%	n	%	n	%	n	%	
Liver											
Palpable	15	51.7	3	9.4	9	37.5	5	20.8	0	0.0	0.001[s]
Not palpable	14	48.3	29	90.6	15	62.5	19	79.2	6	100.0	
Spleen											
Palpable	23	79.3	8	25.0	0	0.0	7	29.2	0	0.0	0.001[s]
Not palpable	6	20.7	24	75.0	24	100.0	17	70.8	6	100.0	
Ascites											
Present	2	6.9	2	6.3	9	37.5	2	8.3	0	0.0	0.002[s]
Absent	27	93.1	30	93.8	15	62.5	22	91.7	6	100.0	

s= significant, P value reached from chi square test

5. Discussion

In our country a study done by Miah (2007) [1] to find out the variation in clinical presentation, aetiological pattern of Lymphadenopathy and to find out any variation of aetiological pattern of Lymphadenopathy in the northern part of Bangladesh in comparison to other parts of the country. Their observational study included 50 adult patients, admitted in medicine wards of Rangpur Medical college hospital. Aged >13 years, presented with generalized Lymphadenopathy or regional Lymphadenopathy and presented with enlarged lymph nodes > 2cm in inguinal region and > 1 cm in the cervical and other regions were enrolled in their study. Aged under 13 years, extremely debilitated patient and patient with insignificant lymph node enlargement, e.g. <1 cm in cervical regions and < 2 cm in inguinal regions were excluded from their study. Pandav *et al*. (2012) [12] described cytomorphological patterns of FNAC of cervical lymph nodes and its utility in establishing diagnosis. Biopsy and special stains were done in selected cases. Patients included in the present study were in the age group of 11 months to 80 years. Almost forty percent (38.0%) cases were of tubercular lymphadenitis, 24.0% cases show Metastatic tumors, 22.0% hyperplasic lymph nodes, 11.0% acute lymphadenitis, 3.7% Lymphoma and 1.4% were Leukemia Lymphadenopathy. Tubercular lymphadenopathy was found with increasing frequency through adolescence 43.30% to young adulthood 54.75% & 48.18% in adulthood. 30.59% cases of tuberculosis were in age group of 11-40 years. 17.8% cases of metastatic tumors were in the age group of 31- 60 years. Highest incidence of metastatic malignancy was seen in the fifth decade 35.0%. The most frequent causes of cervical lymphadenopathy are tuberculosis, metastatic malignancies and reactive lymphadenitis. Yaris *et al*. (2006) [13] study, the clinical and laboratory features of children with lymphadenopathy were evaluated. Over a 3-year period, 126 patients were referred to the clinic for lymphadenopathy. Twenty-eight of cases have diseases mimicking lymphadenopathy; 98 (mean age: 86±55 months) have lymphadenopathy. Localized, limited, and generalized involvement was found in 52%, 30%, and 18% of patients. The most common localization was the head and neck region. The causes of lymphadenopathy were benign diseases in 75 patients. Sixty percent were reactive lymphadenopathy, 39% were lymphadenitis. Lymphadenitis was more frequently localized and bigger than 3 cm compared with reactive adenopathy. Twenty-three patients have malignant diseases whose mean age was higher than others. The enlargement of supraclavicular nodes was more likely due to malignant disease. A total of 45 patients underwent FNAC in this study and it was observed that among them tuberculosis ranked on the top (46.7%). In our country Biswas *et al*. (2013) [14] study showed that the tubercular lymphadenitis was (45.4%), which is similar to our study. Another study done by Pandav *et al*. (2012) [12\ found that 38.0% cases were of tubercular lymphadenitis which also consistent with our study. In our FNAC series next common case was lymphoma in 17.8% patients. which is consistent (about 17% of lymphoma cases) with study done by Ageep (2012) [15] but it is not consistent with study done by Biswas *et al*. (2013) [14] where lymphoma case is 7%, which may be duo to common practice of biopsy in suspected case of lymphoma. Metastatic carcinoma 17.8%, was next to lymphoma, this finding is similar to Biswas *et al*. (2013) [14] 21.2% and also Pandav *et al*. (2012) [12] 24%. Nonspecific lymphadenopathy in our series was 13.3% that is also similar with Biswas *et al*. (2013) [14] 19.9% but more in Pandev *et al*. (2012) [12] 22%. It may be due to inclusion of only adult patient in our study. In this present series a total of 70 patient underwent lymph node Biopsy and it was observed that 30.0% patients had lymphoma, in our country Miah (2007) [1] showed lymphoma cases were (28%), another study done in Saudi Arabia by Albasri *et al*. (2014) [16] which shows number of lymphoma were 24.6% which is similar to our study and according to Olu-Eddo & Ohanaka (2006) [17] lymphoma cases were 23%. In this series the second leading cause of lymphadenopathy were nonspecific lymphadenopathy (25.7%), In India Mohan *et al*. (2007) [18] showed nonspecific lymphadenitis cases were 35.6%. In our country Rahman *et al*. (2013) [11] observed nonspecific cases were 31.8% in his study. In both this study number of nonspecific cases were little bit higher than our study.

Limitations of the Study

The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not be reflected the exact picture of the country.

7. Conclusion and Recommendations

From this study, it is concluded that cervical lymphadenopathy is a common clinical problem and the commonest cause was tuberculosis followed by lymphoma and metastatic carcinoma. There were sufficient etiopathological and clinical features that differentiate age groups with lymphadenopathy. For evaluation of etiology of lymphadenopathy, we should consider important signs and symptoms like “B” symptoms, consistency, fixity of lymph node and organomegaly. Lymph nodes were fixed in metastatic carcinoma and matted in case of tuberculosis. It will help the practitioner, especially at primary care level to think in a systematic way for detection of respective cases early and thereby avoiding the diagnostic delay in cases like Tuberculosis and Malignancy. It can be of very helpful of the urban and rural primary health care levels, where in places improved diagnostic facility to detect lymph node diseases is yet to be available due to scarcity of resources. In cases of fever with cervical lymphadenopathy, fever is an important finding for think about common diseases like Tuberculosis, Lymphoma and metastatic diseases. Low grade fever is common in Tuberculosis and Lymphoma while high grade fever is commonly seen in metastatic diseases. FNAC may be a handy tool for metastatic disorder and tuberculosis whereas biopsy is almost certain for metastatic disorder or lymphoma. A good number of lymphadenopathy patients were nonspecific which need further investigation workup for confirmatory diagnosis. Lymph nodes are usually hard in metastatic carcinoma and matted in case of tuberculosis. Further studies can be undertaken by including large number of patients.

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