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ORIGINAL ARTICLE

Clinico-Pathological Correlates of Cervical Lymphadenopathy: A Hospital Based Study

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Abstract Neck is the most common site of peripheral lymph node enlargement and is very frequently encountered in oto-laryngological practice. This study was done to delineate distribution of clinico-demographic parameters in patients presenting with cervical lymphadenopathy in the otolaryngology out-patient department of a state hospital in India in a 1 year period and to correlate them with fine needle aspiration cytological diagnosis. Record-based cross sectional study in the department of Otolaryngology and department of Pathology, Calcutta National Medical College and Hospital, Kolkata. Case reports and cytological reports of 423 patients who underwent Fine Needle Aspiration Cytology (FNAC) of cervical lymph nodes between January 2009 and December 2009 were reviewed in relation to their demographic and clinical profiles. The cases were divided into three groups according to age and different parameters were described according to these groups. In the cyto-pathological diagnosis, tubercular lymph-adenitis was most prevalent diagnosis (45.4%). Among the metastatic secondaries, squamous cell carcinoma was most common (8.5%). Non-specific/reactive lymphadenitis was significantly more common in <14 years, TB lymph node in 15–59 years and malignancy among the ≥60 years age group. Jugulo-omohyoid (level III) and Supraclavicular (level VB) groups of Lymph nodes were found significantly more involved by malignancy whereas Jugulo-diagastric (level II), Post-auricular, Submandibular groups (level IB) were more commonly involved in TB. Malignancy patients presented late in respect to the tuberculosis patients. Knowledge about clinico-demographic perspectives of cervical lymphadenopathy in respect to their cytopathological diagnosis will help care giver practioners to detect/refer the respective cases early for investigations and treatment.

Keywords Cervical · Lymphadenopathy · Fine needle aspiration cytology · Clinicopathological

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Introduction

Cervical lymphadenopathy, a common presentation in otolaryngology out patient department, is frequently seen in children [1]. Lymph node enlargement may be due to

Malignancy, Infections, Autoimmune diseases, Miscellaneous/unusual conditions, and iatrogenic causes (pnemonic-MIAMI) [2]. Fine needle-aspiration cytology (FNAC) represents a cost-effective and rapid technique for the assessment of nodules and masses within the head and neck area [3]. In pediatric age group, sensitivity and specificity of FNAC as compared to gold standard of excision lymph node biopsy is found to be 94 and 100% respectively [4]. The success rate of FNAC in diagnosing metastatic carcinoma was found to be 100% in some studies [5, 6]. Although there are few studies depicting the clinicopathological presentation of cervical lymphadenopathy in children [1, 4, 7], same type of studies on general population are fewer [8–10]. The purpose of this study was to describe the pattern of lymphadenopathy with demographic and clinical profiles of the patients presenting in the out patient department of an Indian hospital. This would help the doctors attending patients in India to have a basic idea about prevalence of different clinical profiles of cervical lymphadenopathy for easier case detection and better therapeutic outcome.

Materials and Methods

A descriptive cross-sectional study was carried out for a period of 1 year in the otolaryngology department of Calcutta National Medical College and Hospital, a tertiary care government hospital and teaching Institution in Kolkata. All the patients, who attended to the Ear-Nose-Throat Out Patient Department with cervical lymph node enlargement and underwent Fine Needle Aspiration cytology as diagnostic investigation, were included in the study. With prior administrative approval, the data was collected by using a predesigned and pretested proforma. Thus information like age, sex, site of lymph node involvement, other clinical features with time interval between initiation of symptoms and care seeking etc., were gathered by reviewing the stored case sheets of 423 patients who underwent FNAC during the study period i.e., from January 2009 to December 2009.

The cases were divided into pediatric (Age $\leq$14 years), adult (15–59 years) and elderly ($\geq$60 years). Patients' primary symptom was painless neck swelling subsequently found out to be of lymph nodal origin by fine needle aspiration cytology. Many pediatric patients had no additional symptom during presentation. Associated symptoms were mostly cough, weight loss (mostly in adult age group) and history of fever before 4 weeks. Sometimes, mostly in elderly, there was history of alteration of voice, pain during swallowing or blood tinged sputum. The patients were investigated by FNAC of neck swelling to get a cytological diagnosis in each case. The patients presenting with painful swelling or recent fever (within a month) with or without antibiotic therapy were not subjected to FNAC. This was done to avoid unnecessarily doing FNAC in acute infected or inflammed lesions, which may harm the prognosis of the patient.

FNAC was done by 10 cc disposable syringes with 18 G needle. Three or four punctures were done and ultrasonic guidance was sought where required. Smear was drawn in clean glass slides. Two slides were kept in 100% alcohol for fixation and used for hematoxylin-eosin and papanicolaou stain. Remaining slides were air dried for May-Grunwald Giemsa stain and Zeihl-Neelsen (ZN) stain. All the necrotic material suspected of tubercular origin were routinely subjected to cytological analysis after ZN staining. This method was similar to methods followed in different published studies in same type of urban Indian hospital setting with a primary objective of determining sensitivity and specificity of FNAC in cervical lymphadenopathy. Those studies depict the sensitivity of FNAC as 94% in pediatric age group [4], and 91.6–100% in general population [6]. The specificity was between 99 and 100% [4, 6].

Data pertaining to the FNAC report and other additional demographic and clinical attributes were assembled from the department of Pathology, Calcutta National Medical College and Hospital. Individual unique hospital registration number of the patient was used to correlate various information of a single patient in different registers. The collected data was analyzed using simple proportion, '*Z*' test, '*t*' test and χ^2 (Chi-square) tests. Epi info 3.4.3 version (CDC, Atlanta, retrieved from WHO website, on 01.11.09) and SPSS 17.0 were used for statistical calculations.

Results and Discussions

Analysis revealed that 23.4% (99), 65.2% (276) and 11.3% (48) of the study subjects were in the age group of <14, 15–59 and $\geq$60 years respectively, with an overall mean age of 29.04 $\pm$ 19.14 years, median of 22 years and a range of 3–85 years. Sex ratio (M: F) was 0.93:1, For the purpose of analysis, the lymph node diseases were clubbed broadly into three groups namely Non-specific inflammation/Reactive hyperplasia, Tubercular lymphadenitis and Cancers (malignancy).For better comparison with existing studies, the site of lymphadenopathy was described following the conventional system (jugulodigastric, submental etc.). Corresponding American Academy of Otolar yngology and Head Neck Surgery (AAO-HNS) classification (level-I to VI) is depicted alongside.

Analysis showed that the tubercular lymphadenitis ranked on the top (45.4%) followed by secondary metastasis from different other Primary malignancies (21.2%),

Reactive hyperplasia (19.9%), lymphoma (7.0%), chronic granuloma (3.5%) and Non-specific inflammatory involvement of lymph node (2.8%). Among the secondary deposits, Squamous cell carcinoma (8.5%) topped the list, closely followed by Adeno-carcinoma (7.8%) (Table 1).

Bhatt et al. [9] in their study observed 51.9, 27.6, 9, 6.4, 2 and 2.3% lymph node involvement by T.B, Reactive hyperplasia, Abscess, Metastatic deposit from other primary Carcinoma, cystic deformity of lymph node, and lymphoma respectively.

Shaik et al. [10] described that posterior group of lymph node was most commonly affected (in 150 out of 200 patients), submandibular was the 2nd most common affected site. Most common cause was TB lymphadenitis (49.5%), 2nd most common cause was reactive change (18.0%) followed by chronic non-specific lymphadenitis (12%), Non-Hodgkin's lymphoma (8%) and Hodgkin's lymphoma (5%). This study also highlighted that most common Cancers in younger than 40 years were lymphoma (55%) and thyroid Cancers (26%), whereas in patients older 40 years Squamous cell Carcinoma (67%) was more common. The most involved lymph nodes were Jugulo-diagastric chain.

Naeimi Mohammad et al. [11] found that the male were predominantly (67%) involved in metastatic lymph node, mean age was 47.07 years with a range of (8–81 years). Squamous cell Carcinoma was the most common pathology regardless of age (45.9%), others were lymphomas (26%), thyroid (15%), salivary gland Cancers (5%). Jugulo-diagastric lymph nodes were most frequently involved.

Table 1 Distribution of different diseases causing cervical lymphadenopathy ($N = 423$)

Disease	Number	Percentage
Tubercular lymphadenopathy	192	45.4
Reactive hyperplasia	84	19.9
2ndary metastatic CA		
Squamous cell Ca	36	8.5
Adenocarcinoma	33	7.8
Poorly differentiated Ca	15	3.5
HCC	3	0.7
Malignant melanoma	3	0.7
Lymphoma		
Non-Hodgkin's disease	15	3.5
Hodgkin's disease	12	2.8
Lymphoproliferative disorder	3	0.7
Chronic granuloma	15	3.5
Non-specific inflammation	12	2.8
Total	423	100.0

Table 2 Distribution of lymph node diseases according to age group of patients ($N = 423$)

Age (in years) group (n)	Non-specific inflammation/ reactive hyperplasia n (%)	Tuberculosis n (%)	Cancer n (%)	X^2 of goodness of fit, df, P
<14 (99)				
Observed	51 (51.5)	36 (36.4)	12 (12.1)	23.5, 2, <0.001
Expected	33 (33.33)	33 (33.33)	33 (33.33)	
15–59 (276)				
Observed	60 (21.7)	156 (56.5)	60 (21.7)	66.8, 2, <0.001
Expected	92 (33.33)	92 (33.33)	92 (33.33)	
≥60 (48)				
Observed	0	0	48 (100.0)	96.0, 2, <0.001
Expected	16 (33.33)	16 (33.33)	16 (33.33)	

X^2 Chi square

df degree of freedom

Mansoor Ibrahim and Abdul-Aziz Sayed [12] also observed that TB lymphadenitis occurred most commonly in young female (65.2%).

Alam Kiran et al. [13] showed that overall frequency of malignancy was found to be higher in males (M: F = 2.4:1), may be due to less addiction by the females. 80% were metastatic lesion of lymph node while 15.3% were primary tumors i.e., Lymphomas. Among the metastatic tumors, Squamous Cell Carcinoma was the most common followed by Carcinoma breast and Adenocarcinoma.In the present study, the sex ratio of patients having lymph node cancers was revealed to be 2.33:1(M:F).

In this study, among children (up to 14 years), the non-specific lymphadenitis/reactive hyperplasia seemed to be the most frequent form of lymph node disease and it was revealed to be significant. On the other hand, in 15–59 years and ≥60 years age group Tubercular lymphadenitis and Carcinomatous involvement of lymph node respectively were found to be significantly more frequent (Table 2).

As per the findings of Khan et al. [7] reactive hyperplasia was the most frequent form of lymphadenitis in children followed by granulomatous involvement.

Shakya et al. [8] found that 50.4, 22.4, 4.8 and 10% diseased lymph node were involved in Reactive hyperplasia, TB, Malignancy and Granuloma respectively. Highest incidence of Cancer was seen in fifth decades (50.0%) whereas tubercular lymphadenopathy was found with increasing frequency through childhood (10.5%) and adolescence (21.7%) to young adulthood (30.4%).

Khajuria Ruchi et al. [14] reported in their study that reactive hyperplasia was most common (74.5%) in 1st two decades of life and tuberculosis of lymph nodes in 2nd and 3rd decades (58.9%). 88% of metastasis lymph nodes were found

Table 3 Mode of presentation in different age group as per the sex of the study units ($N = 423$)

Mode of presentation	<14 (99)			15–59 (276)			≥60 (48)		
	Male no. (%)	Female no. (%)	X^2, *df*, *P*	Male no. (%)	Female no. (%)	X^2, *df*, *P*	Male no. (%)	Female no. (%)	X^2, *df*, *P*
Early	12 (23.5)	18 (37.5)	7.32, 2, 0.02578649	21 (17.9)	45 (28.3)	4.46, 2, 0.10757802	3 (8.33)	0	1.68, 2, 0.44932896
Intermediate	18 (35.3)	6 (12.5)		45 (38.5)	48 (30.2)		12 (33.33)	3 (25.0)	
Late	21 (41.2)	24 (50.0)		51 (43.6)	66 (41.5)		21 (58.33)	9 (75.0)	
Total	51 (100.0)	48 (100.0)	–	117 (100.0)	159 (100.0)	–	36 (100.0)	12 (100.0)	–

over 40 years of age. Cases of lymphoma were distributed in all age groups. The prevalence of malignancies causing metastatic cervical lymphadenopathy in decreasing order were Squamous Cell Carcinoma, Adenocarcinoma and undifferentiated Carcinoma. In the present study similar findings were revealed i.e., secondary cancers were 72.5% and among them 86.2% (75) were in more than 40 years of age whereas primary carcinoma of lymph node involved all age groups.

The average age of the patients having nonspecific lymphadenitis was shown to be significantly lower compared to other two groups. Median age for the patients having tubercular lymphadenitis was 20 years with a range of 4–55 years. Again lympho-proliferative disorders were found to have a predilection for the younger people i.e., mean age for this group was significantly lower than that for the group having secondary deposits (mean age 54.8 ± 14.7 vs. 34.6 ± 24.2, $t_{118} = 4.49$, $P < 0.001$).

Biswas [15] showed that peak TB lymphadenitis occurred in 2nd–3rd decades of life. Female was affected more (63.4%) than male.

According to the time interval between the initiation of symptoms and care seeking, the study participants were divided into three groups—early (presented within 2 weeks), intermediate (2–6 weeks) and late (>6 weeks) presenters.

Mode of presentation was found different between the sexes in the ≤14 years age group only. Intermediate presentation was comparatively more among the male in this group and the difference was significant (Table 3).

TB lymph node cases were found significantly high among female ($Z = 3.7$) but Cancer of lymph node was found significantly predominant among male ($Z = 5.76$). However, no significant sex difference was observed regarding non-specific inflammatory condition/reactive hyperplasia of lymph node ($Z = 0.6$) (Table 4). Again among the subgroups of malignancies clearly there was male preponderance. It was 72.41 and 60.6% in secondary metastasis and lymphoproliferative disorders respectively. Khajuria Ruchi et al. [14] reported in their study that males showed preponderance of reactive hyperplasia, lymphoma, and metastasis while TB lymph nodes had female preponderance.

Chhabra [16] found in her study that most common site of lymph node involvement was neck and TB was the most common infectious cause. Samar et al. [17] also reported TB as the common cause of peripheral lymphadenitis in developing world. Slight female preponderance was noted but it was seen in all ages and both sexes.

Table 4 Sex wise distribution of cervical lymph-adenopathy ($N = 423$)

Lymph node diseases (*n*)	Male no. (%)	Female no. (%)	*Z*, *P*
Non-specific inflammation (111)	51 (25.0)	60 (27.4)	0.6, 0.2743
Tuberculosis (192)	69 (33.8)	123 (56.2)	3.7, <0.0010
Cancers (120)	84 (41.2)	36 (16.4)	5.76, <0.0010
Total (423)	204 (48.2)	219 (51.8)	–

Jugulo-omohyoid (level III) and Supraclavicular (level VB) groups of lymph node were found to be involved mostly by malignancy and it was significant. In contrast Jugulo-diagastric (level II), Post-auricular, Submandibular (level IB) groups were found to be involved most commonly and significantly by T.B. However, involvement of the submental (level IA) group of lymph node was not significantly associated with any particular disease (Table 5).

Reactive hyperplasia/secondary metastasis of lymph node can be predicted to some extent as per the anatomical basis of lymphatic drainage of the primary sites but for the lymphoma and TB the above findings have more relevance.

Samar et al. [17] observed in their study that tubercular lymphadenitis involved mostly the Jugulo-diagastric group of lymph node (33.3%) followed by posterior triangle (20.0%) and multiple site. Dandapat et al. [18] in their study also revealed that highest TB lymph node was associated with Jugulo-diagastric chain. Dass [19] reported that upper jugular nodes were most commonly affected by TB.

Patients with enlarged cervical lymph nodes due to malignancy presented late i.e., after an interval of 6 weeks from the onset of symptoms. On the contrary, non-specific inflammation of lymph nodes/reactive hyperplasia presented early whereas tubercular lymphadenitis presented mostly after a lapse of intermediate interval form the onset (Table 6). This difference was statistically significant.

Table 5 Distribution of lymph nodes according to etiology ($N = 423$)

Lymph nodes (n)			Non-specific inflammation n (%)	Tuberculosis n (%)	Cancer n (%)	X^2 of goodness of fit, df, P
Group	Level (American Head Neck Society Classification)					
Jugulo-omohyoid (72)	III	Observed	6 (8.3)	27 (37.5)	39 (54.2)	23.2, 2, <0.001
		Expected	24 (33.33)	24 (33.33)	24 (33.33)	
Jugulo-diagastric (114)	II	Observed	39 (34.2)	60 (52.6)	15 (13.2)	26.9, 2, <0.001
		Expected	38 (33.33)	38 (33.33)	38 (33.33)	
Post-auricular (45)		Observed	18 (40.0)	27 (60.0)	0	25.2, 2, <0.001
		Expected	15 (33.33)	15 (33.33)	15 (33.33)	
Submandibular (81)	I B	Observed	27 (33.3)	45 (55.6)	9 (11.1)	24.0, 2, <0.001
		Expected	27 (33.33)	27 (33.33)	27 (33.33)	
Submental (36)	I A	Observed	15 (41.7)	15 (41.7)	6 (16.6)	4.5, 2, >0.10
		Expected	12 (33.33)	12 (33.33)	12 (33.33)	
Supraclavicular (75)	V B	Observed	6 (8.0)	18 (24.0)	51 (68.0)	43.4, 2, <0.001
		Expected	25 (33.33)	25 (33.33)	25 (33.33)	

Table 6 Distribution of cervical lymph-adenopathy according to their mode of presentation ($N = 423$)

Mode of presentation	Cancer lymph node			Tubercular lymphadenitis			Non-specific lymphadenitis/reactive hyperplasia		
	Present	Absent	X^2, df, P	Present	Absent	X^2, df, P	Present	Absent	X^2, df, P
Early (<2 weeks)	18 (18.2)	81	7.01, 2, 0.03002604	48 (48.5)	51	6.01, 2, 0.04962676	33 (33.3)	66	7.35, 2, 0.02529235
Intermediate (2–6 weeks)	39 (29.5)	93		69 (52.3)	63		24 (18.2)	108	
Late (>6 weeks)	63 (32.8)	129		75 (39.1)	117		54 (28.1)	138	

Key Message

The findings of the present study may act as first-hand knowledge regarding age-sex distribution of lymph node diseases, their mode of presentation and predilection for different lymph node groups. It will help the care giver doctors, especially at primary care level, to think in a systematic way for detection/referral of the respective cases early and thereby avoiding the diagnostic delay in cases like TB/Cancers of lymph nodes. It can be of very helpful for the urban or rural primary health care levels where, in many places, improved diagnostic facility to detect lymph node diseases is yet to be available due to scarcity of resources.

Conflict of interest The Authors declare presence of NO conflict of interest.

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