



**RESEARCH ARTICLE**

**FINE NEEDLE ASPIRATION CYTOLOGY OF PEDIATRIC CERVICAL LYMPHADENOPATHY**

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**ARTICLE INFO**

**Article History:**

Received 27<sup>th</sup> April, 2018

Received in revised form

19<sup>th</sup> May, 2018

Accepted 20<sup>th</sup> June, 2018

Published online 31<sup>st</sup> July, 2018

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**Key words:**

FNAC,  
Cervical,  
Lymphadenopathy,  
Children.

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**ABSTRACT**

**Background:** Cervical lymphadenopathy is a very common problem encountered in hospital settings, particularly in children. Underlying cause can be evaluated by using various diagnostic modalities. FNAC is a simple, quick and inexpensive method for evaluation of enlarged cervical lymph nodes. FNAC in children is less popular as compared to its use in adults.

**Objective:** To determine the utility of FNAC in diagnosing pediatric cervical lymphadenopathy.

**Methods:** The study was conducted at Northern Railway Central Hospital, New Delhi, from January 2015 to December 2016. 115 patients presenting with cervical lymphadenopathy, up to the age of 10, were included in the study. FNAC was used for making diagnosis.

**Results:** Cervical lymphadenopathy was quite common in children, with most common cytomorphological finding being reactive hyperplasia. Most of the etiologies were benign.

**Conclusion:** Different etiologies play role in development of cervical lymphadenopathy. FNAC is a safe and reliable diagnostic method in children obviating the need for excision biopsy.

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**Citation:** Dr. Namita Pandey and Dr. Seema Chadhha, 2018. "Fine needle aspiration cytology of pediatric cervical lymphadenopathy", *International Journal of Current Research*, 10, (07), 71835-71839.

**INTRODUCTION**

Lymphadenopathy is defined as enlargement of lymph nodes. This process is often secondary to infection and is frequently benign and self limited. Viral or bacterial infections lead to localized responses from lymphocytes and macrophages, leading to enlargement of nodes. There may also be localized infiltration by inflammatory cells in response to an infection of the nodes themselves. This is known as lymphadenitis. Finally, it is crucial to rule out rarer, more serious causes such as lymphomas or leukemias, which are due to proliferation of neoplastic lymphocytes or macrophages. Cervical lymphadenopathy is common in childhood. The incidence is difficult to ascertain because it is usually caused by viral upper respiratory tract infection and is self-limited. Causes of cervical lymphadenopathy in children are listed as under:

**Infectious:** Most common cause in children.

Viral upper respiratory infection, infectious mononucleosis (EBV, CMV), group A Streptococcal pharyngitis, acute bacterial lymphadenitis (e.g staphylococcus aureus), rubella, cat-scratch disease, toxoplasmosis, tuberculosis, atypical mycobacteria.

**Noninfectious:** Noninfectious causes of cervical lymphadenopathy in children are less common, but always should be considered in the differential diagnosis. Connective tissue disorders, kawasaki disease (unilateral cervical lymph node > 1.5 cm), periodic fever, aphthous stomatitis, pharyngitis, adenitis (PFAPA), kikuchi disease, medications.

**Neoplastic:** Malignant childhood tumours develop in the head and neck in  $\frac{1}{4}$  of cases. Neuroblastoma, leukemia, non-Hodgkins, and rhabdomyosarcoma are most common in those < 6 years old. In older children, Hodgkin's and non-Hodgkin's lymphoma are more common. Evaluation of cervical lymphadenopathy in children begins with thorough history and physical examination, which are crucial in narrowing the differential diagnoses. Diagnostic tests and imaging play an important role as well. Histopathology is considered the gold standard for pathological diagnosis. Though FNAC is not considered diagnostic, but it is a safe, minimally invasive and rapid procedure with good patient acceptance and low morbidity. FNAC is a popular initial investigation method in adults since long, but there are limited studies in the past regarding its utility in pediatric population. In our study, we used FNAC to assess the cyto-morphological spectrum of enlarged cervical lymph nodes in 115 children upto age of 10 years, in our set up.

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DOI: <https://doi.org/10.24941/ijcr.30879.07.2018>

## MATERIALS AND METHODS

A total of 115 pediatric patients aged 0-10 years with palpable cervical lymphadenopathy were included in the study period, extending from January 2015 to December 2016. The cases included both inpatients and outpatients, referred to the cytology section at our hospital. Brief history was taken and clinical examination was done to note the site, number, size and consistency of enlarged lymph nodes, presence of tenderness or other signs of inflammation and other relevant findings, to provide diagnostic clues. Routine FNA procedure was done using 21-24 gauge needle, attached to 10 ml syringe. Wet fixed smears in absolute alcohol were stained by Hematoxylin and Eosin and examined microscopically. Special stains were used whenever required and histopathological correlation was done when possible.

## RESULTS

Out of 115 cases, 85 cases were in the age group of 6-10 years (73.9%), followed by 28 cases in the age group of 1-5 years (24.3%) and only 2 were infants (1.7%) (Table 1). Most cases (54.7%) presented with swelling in the neck region without any symptom. Symptomatic patients presented with throat pain (18.2%), painful neck swelling with fever (9.5%), fever and weight loss (7.8%), ear discharge (6.9%) and fever and loss of appetite (2.6%) (Table 2).

**Table 1 . Age-wise distribution of cases**

Age group	No. of cases	Percentage
Upto 1 year	02	1.7%
1-6 years	28	24.3%
6-10 years	85	73.9%
Total	115	

It was observed that most of the children with cervical lymphadenopathy were in the age range of 6-10 years.

**Table 2. Symptom-wise distribution of cases**

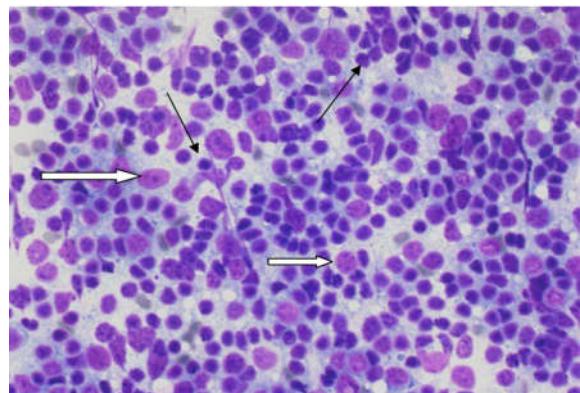
Symptoms	No. of cases	Percentage
Neck swelling only	63	54.7%
Throat pain	21	18.2%
Painful neck swelling with fever	11	9.5%
Fever and weight los	09	7.8%
Ear discharge	08	6.9%
Fever and loss of appetite	03	2.6%
Total	115	

It was observed that the most common presentation was asymptomatic neck swelling.

**Table 3. Sites of lymphadenopathy**

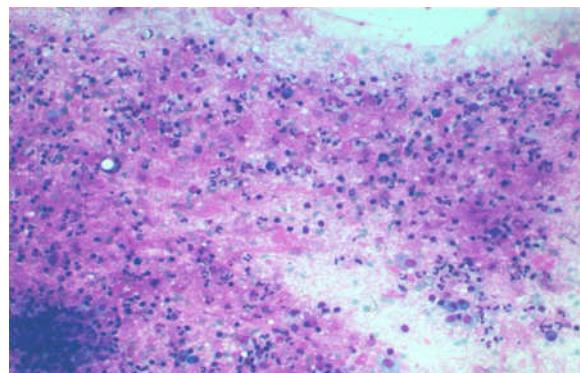
Site	No. of cases	Percentage
Lateral cervical	44	38.2%
Bilateral multiple	26	22.6%
Submental	13	11.3%
Submandibular	11	9.5%
Post- auricular	06	5.2%
Pre-auricular	04	3.4%
Occipital	02	1.7%
Part of generalised lymphadenopathy	09	7.8%
Total	115	

It was observed that the most common site of cervical lymphadenopathy was lateral cervical.



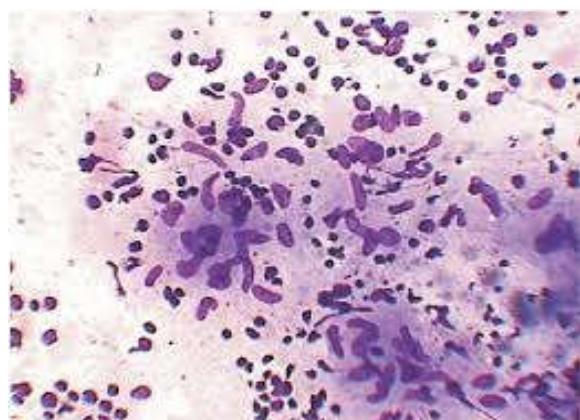
Here we see, polymorphous population of lymphocytes with small mature lymphocytes (black arrows) admixed with large reactive lymphocytes ( white block arrows). (H & E, 40x)

**Figure 1. Reactive hyperplasia lymph node.**



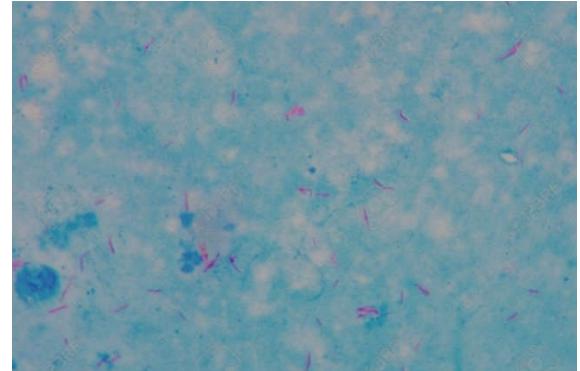
Here we see, polymorphs, lymphocytes and macrophages in a necrotic background with cellular debris. ( H & E, 40x).

**Figure 2. Acute suppurative lymphadenitis**



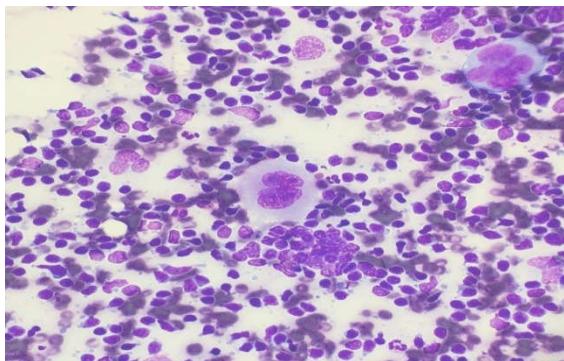
Here we see, well defined epithelioid granuloma. ( H & E, 40x)

**Figure 3. Tubercular lymphadenitis**



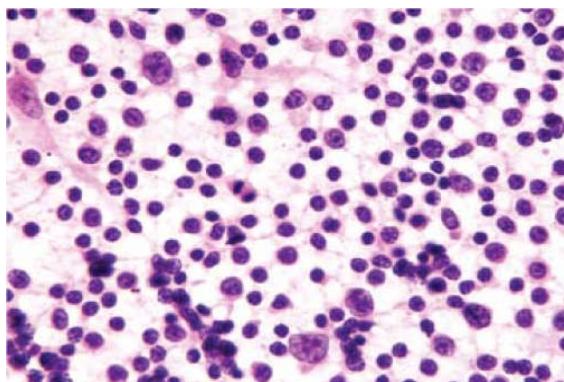
Here we see, pink rod like structures in a blue background. Slide positive for AFB.(ZN stain, 100x)

**Figure 4. AFB**



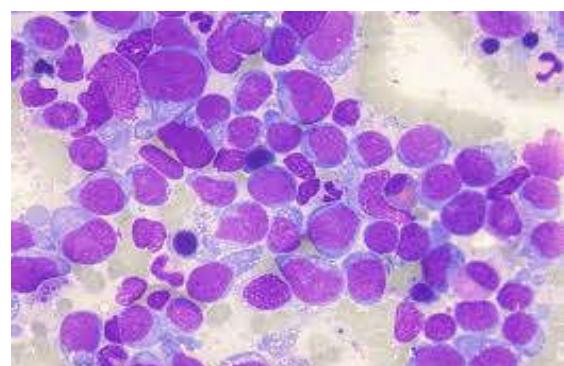
Here we see, classical RS cell (arrow) is visible in a background of lymphocytes, histiocytes and RBCs. ( H & E , 40 x)

**Figure 5. HL – MC type**



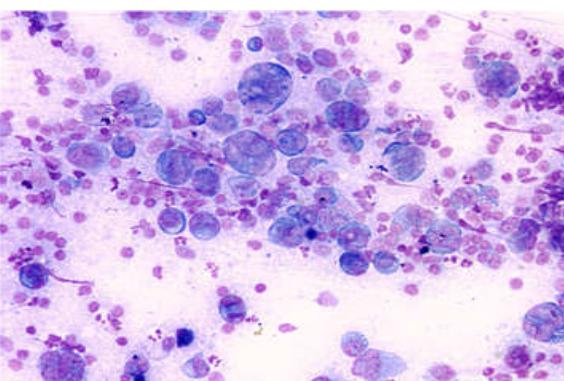
Here we see, Hodgkin cells/ popcorn cells (arrow), in a background of lymphocytes.(H & E,40x)

**Figure 6. HL – NLP type**



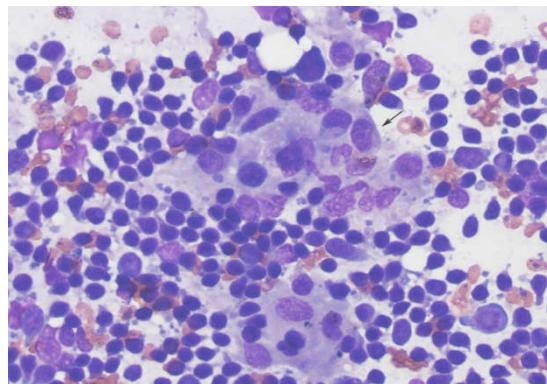
Here we see, atypical large lymphoid cells with high N/C ratio, scant cytoplasm, fine chromatin and inconspicuous nucleoli. Very few mature small lymphocytes and polymorphs seen admixed with the atypical cells.( H & E , 40x)

**Figure 7. NHL, of DLBCL subtype**



Here we see, large pleomorphic atypical lymphoid cells with irregular nuclei, moderate amount of basophilic cytoplasm, fine vesicular chromatin and inconspicuous nucleoli. Mature small lymphocytes and polymorphs are seen in the background. ( H & E, 40x)

**Figure 8. NHL, of ALCL subtype**



Here we see, clusters of histiocytes with spindled to oval nuclei, abundant pale basophilic cytoplasm and few with lipofuscin pigments ( arrow ), admixed with mature small lymphocytes. ( H & E, 40 x)

**Figure 9. Non-specific chronic lymphadenitis (sinus histiocytosis)**

Clinical examination revealed that out of 115, most of the patients 44 (38.2 %) had lateral cervical lymph node enlargement, followed by bilateral multiple enlarged nodes (mostly small and non tender) in 26 cases (22.6%), submental region in 13 cases (11.3%), submandibular region in 11 cases (09.5%), post auricular region in 6 cases (05.2%), pre-auricular region in 4 cases (3.4%) and occipital region in 2 cases (01.7%). 9 cases (7.8%) had cervical lymph node involvement as a part of generalised lymphadenopathy (Table 3). Out of 100 cases, FNAC results were inconclusive due to inadequate smear in 3 cases( 3% ). Reactive lymphadenitis (60%), acute suppurative lymphadenitis (20%) and tubercular lymphadenitis (8.6%) were the commonest lesions noted on FNAC findings (Table 4). Comparision of cytological and histological diagnosis was possible in only 3 cases of lymphomas (HL and NHL), the cytological diagnosis was concordant with the histopathological diagnosis in all 3 of them. AFB staining (ZN) was done in cases diagnosed as Tubercular lymphadenitis, and 4 out of 6 cases showed AFB positivity. Rest 2 cases were advised for excisional biopsy.

## DISCUSSION

Cervical lymphadenopathy is a common problem in pediatric clinic. Park, in his study, found that around 90% of children aged 4-8 years old have cervical lymphadenopathy (Park, 1995). Cervical lymphadenopathy includes both inflamed (enlarged and tender) and non- inflamed (enlarged, non-tender) lymph nodes. It can be a part of more generalized lymphadenopathy, defined as enlargement of two or more non-contiguous lymph node regions.

### **Definition (Pediatric Cervical Lymphadenopathy, 2009)**

Pathologic Lymph Node - > 2 cm in pediatric patients is considered abnormal

Acute Lymphadenopathy - < 2 weeks' in duration.

Sub -acute Lymphadenopathy - 2-6 weeks' in duration.

Chronic Lymphadenopathy - > 6 weeks' in duration.

### **Classification of Cervical Lymphadenopathy Based on Clinical Presentation**

**1. Acute Unilateral:** This is the most common type of cervical lymphadenopathy. This is usually reactive and secondary to upper respiratory tract infection (URTI), skin infection, or dental infection.

**Table 4. Cytological diagnosis of 115 cases of cervical lymphadenopathy**

Diagnosis	No. of cases ( N/115)	Percentage	Further investigation
Reactive hyperplasia	69	60 %	No further investigation
Acute suppurative lymphadenitis	23	20%	No further investigation
Tubercular lymphadenitis	10	8.6%	cases confirmed by AFB positivity.
Granulomatous lymphadenitis	02	1.7%	Negative for AFB
Non-specific chronic lymphadenitis	03	2.6%	No further investigation
Hodgkin lymphoma	03	2.6%	2 cases confirmed by HPE 1 lost to follow up
Non-hodgkin lymphoma	02	1.7%	Confirmed on HPE
Unsatisfactory smears	03	2.6%	
<b>TOTAL</b>	<b>115</b>		

It was observed that most common cause of cervical lymphadenopathy in children, in our study, was reactive hyperplasia. Acute suppurative and tubercular lymphadenitis were other common causes.

Other rare causes are Kawasaki, cat scratch disease (Bartonella) and Kikuchi-Fujimoto disease (histolytic necrotising lymphadenitis).

**2. Acute Bilateral:** This type of lymphadenitis occurs secondary to viral URTI, Epstein-Barr virus (EBV), and cytomegalovirus (CMV).

**3. Sub-acute:** The common cause for this is Mycobacterium tuberculosis.

**4. Chronic:** This can be reactive in process secondary to neoplasia, lymphoma, leukemia, or soft tissue tumours.

Cervical lymph nodes include preauricular, parotid, jugulo-digastric, submental, submandibular, posterior cervical, superficial cervical, deep cervical, occipital and posterior auricular (mastoid) lymph nodes.

In our study, out of 115 children, most of them had enlarged lateral cervical lymph nodes (38.2%). Most of these cases were incidentally discovered by the parents and the children had no symptoms related to the lymphadenopathy. Other common sites were bilateral multiple (22.6%) and submental (11.3%). Generally, the cause of lymph node swelling in young patients – from babies to infants and adolescents – is benign in over 80% of cases. This figure decreases considerably with age, to the extent that a malignant cause is found in over 60% of patients age 50 and above (Isselbacher *et al.*, 1995). However, if there is a suspicion of malignancy in a young patient, the most frequent causes in children under 6 years of age are acute leukemia, neuroblastoma, rhabdomyosarcoma and non-Hodgkin lymphoma.

Between the ages of 7 and 13, non-Hodgkin lymphoma and Hodgkin's lymphoma are roughly equal, with rhabdomyosarcoma and thyroid cancer occurring more rarely. From the age of 13, Hodgkin's disease is the leading malignant cause of neck masses during childhood and adolescence (Brown and Azizkhan, 1998). In our study, reactive lymphadenopathy (60%) was the most common cytological diagnosis followed by acute suppurative lymphadenopathy (20%) and tubercular lymphadenopathy (8.6%). Malignancy was not a common underlying cause in this age group (5.2%). Malignant enlarged cervical lymph nodes showed HL (2.6%) and NHL (1.7%). Our findings were consistent with the above studies. Reactive hyperplasia is diagnosed on FNAC by a polymorphous population of lymphocytes and tingible body macrophages. Tubercular lymphadenitis are diagnosed on smears by presence of epitheloid granulomas, in a background of necrosis, lymphocytes and presence of acid fast bacilli on Ziehl Nelson (ZN) stain. Cytology of acute suppurative lymphadenitis consists of acute inflammatory infiltrate in a necrotic background.

Chronic non specific lymphadenitis includes follicular hyperplasia or sinus histiocytosis, which on FNA smears shows aggregates of macrophages/histiocytes, sdmixed with lymphocytes. In our study, the diagnoses were made based on these cytomorphological criteria (Figure 1-9). In 6 cases showing granulomatous lymphadenitis, ZN stain was used for confirming tubercular etiology, which showed AFB positivity in 4/6 cases (3.4%) and negative in 2/6 cases (1.7%). The latter were given the diagnosis of granulomatous lymphadenitis and were advised for excisional biopsy for further confirmation. NHLs in children are almost always one of the three types: lymphoblastic, small non- cleaved type (Burkitt and non- Burkitt) and large cell type (ALCL and DLBCL ). These are high grade lymphomas. In our study, we diagnosed 2 cases of NHL, both as high grade, large cell type (Figure 7 & 8). Histopathological examination confirmed the findings. In children diagnosed with HL, MC, NLPHL, and NS are the subtypes more commonly seen (Thomas *et al.*, 2002). In our study, we diagnosed 03 cases of HL, 2 MC and 1 NLPHL subtype (Figure 5 & 6). 2 cases were confirmed by HPE. 1 case was lost to follow-up. Primary diagnostic evaluation of childhood peripheral lymphadenopathy is mainly based on group of lymph nodes involved and FNA. A careful history and thorough physical examination are the first steps in establishing the cause of a neck mass. Location, size, consistency, and mobility of the mass provide clues and are useful for comparison during follow-up. Amongst diagnostic modalities, FNA is a rapid, simple, accurate diagnostic procedure and important initial step in the evaluation and management of enlarged cervical lymph nodes in children. It is very well tolerated by children, and there were no complications.

## Conclusion

Cervical lymph node enlargement is a common clinical problem in the pediatric population, reactive, pyogenic and granulomatous enlargement being important causes. Since the diagnosis varies from a simple infection to malignancy, this can be a matter of anxiety for both the family as well as the treating doctor. FNAC can be recommended as a first line of investigation in the diagnosis of cervical lymphadenopathy in paediatric age group.

## Abbreviations

AFB – Acid fast bacilli.

ALCL – Anaplastic large cell lymphoma.

CMV – Cytomegalovirus.

DLBCL – Diffuse large B cell lymphoma.

EBV – Ebstein Bar Virus.

FNAC – Fine needle aspiration cytology.

HL – Hodgkins Lymphoma.  
HPE – Histopathological examination.  
NHL – Non-Hodgkins Lymphoma.  
NS – Nodular sclerosis.  
ZN – Ziehl Neelsen.

**Acknowledgement:** I am sincerely grateful to Dr. Seema Chaddha (Incharge Histopathology, Sr. DMO, NRCH, New Delhi ) for her constant support and encouragement.

**Conflict of interest statement:** No conflict of interest.

**Funding statement:** Self

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