



## Clinico-Pathological Profile of Peripheral Lymphadenopathy In Pediatric Age Group- Our Hospital Experience

<b>Dr.Radha.M</b>	Assistant Professor, Department of Pathology, KMCT medical college, Manassery, Kozhikode
<b>Dr V. Srinivasa Murthy</b>	Professor and Head, Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bangalore.
<b>Dr KGeethamala ,</b>	Assistant Professor, Department of Pathology, Belagavi Institute of Medical Sciences, Belagavi.

### ABSTRACT

**Background:** Peripheral lymphadenopathy (PL) is a common clinical entity in pediatric practice. Several studies have attempted to identify various characteristics, which may provide useful information to determine the etiology of lymphadenopathy in children. Still a significant number of patients remain with persistent lymphadenopathy, in which the etiology is unclear. Hence in this communication; the present study was taken up.

**Objective:** The present study was undertaken to completely evaluate the child with lymphadenopathy and arrive at etiological diagnosis with special emphasis on role of FNAC in categorizing different types of lymphadenopathy in children. **Materials and methods:** A two year prospective study was conducted in the dept. of pathology ESIC Medical College PGIMSR Rajajinagar, Bangalore. Totally hundred children ( $\leq 18$  years) with significant peripheral lymphadenopathy were studied with FNAC and subsequent biopsy wherever available. Relevant clinical data was analyzed.

**Results:** Mean age of the children with peripheral lymphadenopathy was 11 years (132 months).. Most common presenting complaint was swelling alone (46%). Cervical (77%) was commonest lymphnode group involved. FNAC in categorizing different types of lymphadenopathy in children revealed majority were non-neoplastic (95%), of which reactive lymphadenitis was the commonest (47.3%) followed by granulomatous lymphadenitis (23.1%), tubercular lymphadenitis (20%), suppurative (4.2%) and necrotizing lymphadenitis (1.05%). Rest 5% cases were neoplastic comprising of non-Hodgkin Lymphoma (60%) with high frequency followed by Hodgkin Lymphoma (20%) and metastasis (20%) from papillary carcinoma thyroid.

**Conclusion:** FNAC of lymph nodes is a first line method, for investigating the nature of the lesions, as it is economical and convenient alternative to open biopsy.

### KEYWORDS

Peripheral Lymphadenopathy, Children, FNAC.

### INTRODUCTION

Lymphadenopathy is one of the commonest clinical manifestation of patients, attending the outpatient department, including the pediatric population.<sup>(1,2)</sup> It may represent myriad of conditions from benign local or generalized infections to serious conditions like malignancies. In developing countries like India, acute respiratory tract infections, suppurative skin infections and tuberculosis are the major causes for lymphadenopathy.<sup>(1)</sup> With prevalence as high as 250 per 1,00,000 population,<sup>(2)</sup> tuberculosis is still rampant in this part of the world and the tuberculous involvement of lymph node is the most common form of extra-pulmonary tuberculosis, responsible for 30-40% of cases.<sup>(3)</sup>

Fine needle aspiration cytology (FNAC) is the first line of investigation for any individual with lymphadenopathy. It has been proven to be a rapid, minimal invasive, cost-effective and reliable diagnostic tool. However, FNAC has certain limitations in the diagnosis of malignancy as aspirated material is insufficient for marker studies and cytogenetics. So confirmation in such cases is done by open biopsy and histopathological examination (HPE).<sup>(3,4)</sup> A diagnostic work-up in children with persistent lymphadenopathy is difficult. Several studies have attempted to identify various characteristics, which may provide useful information to determine the etiology of lymphadenopathy in children. Still a significant number of patients remain with persistent lymphadenopathy, in which the etiology is unclear.<sup>(5-7)</sup> Hence in this communication; the present study was taken up to completely evaluate the children with lymphadenopathy and arrive at etiological diagnosis with special emphasis on role of FNAC in categorizing them.

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### MATERIALS AND METHODS

A two year prospective study from August 2012 to August 2014 conducted in the Department of Pathology, ESIC Medical College PGIMSR, Rajajinagar, Bangalore. Totally hundred children ( $\leq 18$  years) with significant peripheral lymphadenopathy (i.e., in cervical and axillary regions measuring more than 1cm, in inguinal region measuring more than 1.5cm and in other sites measuring more than 0.5 cm) were studied with FNAC and subsequent biopsy. Cases with repeated inadequate material and non- lymph node samples on FNAC were excluded from the study.

A detailed history was taken in all cases and a thorough general physical examination (including that of skin and tonsillopharyngeal region) and systemic examination was carried out. Investigations that were carried out in all cases were complete blood count (CBC), ESR, peripheral blood smear, FNAC, Ziehl Neelson (ZN) staining on FNAC smears. Aspiration of the selected lymph node was done using a sterile 22 or 23 gauge needle. The aspirate was examined for the nature of the material, and then several smears were prepared. Few of them air dried for Giemsa stain and few were fixed with 95% ethyl alcohol for staining with H&E. Z-N staining was done in all the cases. Corresponding biopsy samples of the same patients were studied with H&E stain and special stains performed appropriately. Immunohistochemistry was performed wherever

applicable.

### Statistical analysis

The data was analyzed using Statistical Package for the Social Sciences software version 18.0 (SPSS Inc, Chicago). Obtained parameters were evaluated using descriptive statistical analysis and presented in terms of percentage. Validation of FNAC was analyzed using sensitivity, specificity, positive predictive value & negative predictive value. Kappa statistics was used to find the agreements between FNAC and histopathological examination. p values were calculated to know the statistical significance.

### RESULTS

Total 108 patients of less than 18 years of age with lymphadenopathy were referred to pathology. Of these 8 were excluded from the study as 4 children were unco-operative, 2 were found to be non-lymph node lesions on FNAC (1 was salivary gland and another one lipoma), 2 smears were inadequate for evaluation due to hemorrhagic aspirates. Hence 100 cases were available for study. Histopathological correlation was available only in 30 cases.

Age of the patients varied between 4 months to 18 years, with mean age being 11 years(132 months).The youngest was four months diagnosed with reactive lymphadenitis and the oldest were 18 years (2 children) diagnosed with reactive lymphadenitis and Non-Hodgkin lymphoma(NHL) respectively.

Out of 100 patients 45 were male and 55 were female. There was female preponderance with male: female ratio being 0.8:1, though there are no etiological differences between them.

Most common clinical manifestation was swelling alone (46%). Other manifestations included fever, cough, cold, weight loss, sore throat, rash and discharge from the swelling in various combinations. The associated clinical features include thyroid gland swelling seen in one case of metastasis to lymphnode which on subsequent aspiration from thyroid showed features of papillary carcinoma. One case of NHL had abdominal pain and hepatosplenomegaly.

Past history of anti-tubercular treatment was noted in 2 cases, whereas history of contact with adult tuberculosis was present in 6 cases. All the children were immunized up to date. BCG scar was noted in all the children. One case was Human Immunodeficiency Virus (HIV) positive which was diagnosed with florid reactive hyperplasia of the lymphnode on FNAC.

Majority of the lymph nodes were localized(a single anatomic area involved) accounting to 90%, 4% had limited lymphadenopathy (two or three areas involved) and 6% had generalized lymphadenopathy (four or more anatomic areas involved). Among all localized sites, cervical (82.9%) was the most common site involved, of which anterior cervical group (65.3%) was more commonly affected. (Table 1)

On FNAC, reactive lymphadenitis (51.1%) was the commonest etiology in children presented with localized lymphadenopathy (90%). Among generalized lymphadenopathy (6%) cases, FNAC and corresponding excision and HPE diagnosed as 2 cases of lymphomas, 2 cases of reactive lymphadenitis, one of which was HIV Positive having florid reactive hyperplasia and one case was tubercular lymphadenitis.

54 patients had a maximum lymph node diameter of 2.5-3 cm. Benign etiologies of reactive, granulomatous and tubercular lymphadenitis were found in these patients.2 cases of this category also were malignant. 2 other cases of malignant had size more than 3 cm. In 93% of cases, nodes were firm in consistency, majority of them were benign; soft in 5 % of cases, hard in 2% of cases which turned to be malignant. 98% of cases had mobile lymphnodes. Rests 2% of cases were immobile which later were diagnosed as NHL cases.

The nature of aspirate was sanguineous fluid in 75 cases, 16 cases were caseous material, 4 cases purulent material and grey white material in 5 cases.

Out of 100 cases, majority were non-neoplastic (95%).In non-neoplastic, reactive lymphadenitis was the commonest (51.1%) followed by granulomatous lymphadenitis (23.1%), Tubercular etiology (20%), Suppurative lymphadenitis (4.2%) and necrotizing lymphadenitis (1.05%). Among 19 cases of tubercular etiology, 10 cases were AFB positive and all 19 cases had caseous necrosis and granulomas.

3 cases of Non-Hodgkin lymphoma were seen with high frequency among neoplastic lesions followed by each case of Hodgkin lymphoma (HL) and Metastasis to lymphnode from papillary carcinoma thyroid.

Only 30 corresponding lymph node excision biopsy were available for correlative histopathological study. The overall diagnostic accuracy of FNAC when compared to gold standard Histopathology was 73.3%. The sensitivity and negative predictive value of 100% was seen in case of Granulomatous lymphadenitis. Similarly specificity and positive predictive value of 100% was seen cases of necrotizing lymphadenitis and malignancies. The sensitivity of FNAC in diagnosing commonest lesions in our study like reactive lymphadenitis, Granulomatous lymphadenitis and tubercular lymphadenitis were 90.9%, 100% and 75% respectively and specificity for these lesions were 78.9%, 92.3% and 96.5% respectively. (Table 2)

Granulomatous lymphadenitis and malignancy are in good agreement whereas agreements were lesser in reactive and tubercular lymphadenitis. Both suppurative and necrotizing lymphadenitis was also not in good agreement. (Table 2)

### DISCUSSION

FNAC is one of the routinely used diagnostic procedures on patients presenting with lymphadenopathy. Out of 108 cases referred to pathology, 2 (1.2%) excluded cases were mimicking lymphadenopathy in the present study. In a study conducted by Yaris et al<sup>(5)</sup>, out of 126 referred, 28 cases were mimicking lymphadenopathy. 2 smears(1.2%) were excluded because of inadequacy of the smear in the present study, similar to the studies done by Dhingra V et al<sup>(6)</sup> and Annam V et al<sup>(7)</sup> where inadequacy rate was 6.25% and 3.57% respectively attributable to small lesion size.

In the present study age of the children was in a range from 4 months- 18 years with mean age being 11 years (132 months) which is higher when compared to studies done by Tanteo et al<sup>(8)</sup>(108 months), Yaris et al(86 months)<sup>(5)</sup> and Karadeniz et al(84 months)<sup>(9)</sup>.The demographics of the study showed a female preponderance (55%)which is in contrast to other studies<sup>(5,8)</sup> where there is male predominance, further authors concluded stating that there is no predilection for lymphadenopathy with regards to gender.

Swelling alone(46%) was the predominant clinical manifestation in the present study which correlated well with the studies done by Tanteo et al (82%)<sup>(8)</sup> and Reddy MP et al (52%).<sup>(10)</sup> 90% of cases in the present study presented with localized lymphadenopathy (single site) similar to the studies by Yaris et al<sup>(5)</sup>- 52%, and Karadeniz et al<sup>(9)</sup>- 36.1%.

In the present study, no relationship was established between the number of lymph nodes involved and malignancy, but the studies done by Dhingra V et al<sup>(6)</sup>,Oguz et al<sup>(11)</sup> and Soldes OS et al<sup>(12)</sup> showed that the risk of malignancy increases with more the number of lymph nodes involved.

The cervical group of lymphnodes were the commonly involved (81.9%) in the present study, similar to studies done by Reddy MP et al<sup>(10)</sup>(85%), Dhingra V et al<sup>(6)</sup>(79%) and Puiu et al<sup>(13)</sup>(58.6%). The predominant involvement of cervical lymph nodes can be explained on the basis of prevalent population in our country that is from low socio-economic group. They

have high incidence of oropharyngeal, dental, and scalp infections which results in reactive hyperplasia of cervical lymph nodes.

Though there is no difference in the etiology with respect to size of the lymph nodes in the present study, Oguz et al<sup>(11)</sup> concluded saying, lymph node size <1 cm was in favour of benign etiology and size > 3cm was in favour of malignancy. Based on observation done by Karadeniz et al<sup>(9)</sup>, a maximum lymph node size of 2 cm was considered an appropriate limit to distinguish malignant disease from benign causes.

Benign(non-neoplastic) lesions were the majority(95%) in the present study which correlated well with the other similar studies<sup>(14,15)</sup>. Reactive lymphadenitis(51.1%) constituted the majority of the non-neoplastic lesions in the present study, which was in concordance with other studies by Reddy MP et al<sup>(10)</sup>(54%), Annam V et al<sup>(7)</sup>(58%) and Yaris et al<sup>(6)</sup>(60%).

In the present study, 23.1 % of cases were diagnosed as granulomatous lymphadenitis similar to studies done by Reddy MP et al<sup>(10)</sup>(23%) and Dhingra et al<sup>(6)</sup>(28.1%). Though granulomatous response is seen in a wide variety of infectious and noninfectious processes, as tuberculosis is so common in our country, every clinically relevant case of granulomatous lymphadenitis should be considered as tuberculous lymphadenitis, unless proved otherwise.<sup>(16)</sup> In the present study authors correlated all the cases of granulomatous lymphadenitis with the clinical presentation, Montoux test, AFB staining. Only after ruling out the specific causes for granulomatous lymphadenitis, the remaining cases where etiology could not be ascertained were considered as granulomatous lesions.

The present study showed tubercular adenitis to be a significant and prevalent cause of lymphadenopathy (19%). Out of 19 cases, 10 were found to be AFB positive. These findings are in agreement with those of Annam V et al<sup>(7)</sup>, who diagnosed tubercular lymphadenitis in 28.1% cases, of which 7% were AFB positive and Tanteo MCJB et al<sup>(8)</sup>, who diagnosed 32% of cases. Hemalatha et al<sup>(17)</sup> and Sen et al<sup>(18)</sup> showed a higher incidence of tuberculosis in the cervical group of lymph nodes, followed by the axillary group. Kumar et al<sup>(19)</sup> stated that the cervical group of lymph nodes were mainly involved in the cases of tuberculosis in children, whereas the cervical and the axillary types were both involved in adults. In the present study no such correlation was found.

According to studies conducted independently by Oguz A et al<sup>(11)</sup>, Soldes OS et al<sup>(12)</sup> and Kumral et al<sup>(20)</sup>, stated that the probability of a malignant disorder is directly related to group of lymph nodes involved (supraclavicular and posterior auricular), duration of the lymph node enlargement (>4 weeks), size of the lymph node (>3 cm), number of lymph nodes (generalized lymphadenopathy), abnormal complete blood cell findings, abnormalities in chest X-ray, and abdominal ultrasonography. In contrast, in the present study only variable to predict malignancy was duration of lymphadenopathy.

Overall, the diagnostic accuracy of the cyto-smears was 73.3% and the overall sensitivity and specificity were 73.3% and 88.5%, respectively. These findings are lower than the studies done by Reddy et al<sup>(10)</sup> – sensitivity 94% and specificity 100% and Dhingra V et al<sup>(6)</sup> – sensitivity 91.3%, specificity 99.1% and over all diagnostic accuracy of 98.89%. The lower values in the present study could be attributed to the lower sample size available for correlation.

The sensitivity of FNAC in detecting the most common lesion in our study i.e., Reactive lymphadenitis was 90.9% indicating that FNAC is a reliable method in diagnosing reactive lymphadenitis. We have also found FNAC a satisfactory tool in the diagnosis of granulomatous, tubercular, necrotizing, suppurative and malignant lymphadenopathy in terms of specificity. Though the sensitivity in diagnosing these lesions (except granulomatous) was less than 90%, the high specificity is regarded as an asset to rule out the pathological glands.

As far as the diagnosis of tubercular lymphadenitis was concerned, the sensitivity of the cytosmears in the present study was 75%, which is lower as compared to the study by Dhingra V et al<sup>(6)</sup>(98.89%). However, specificity (96.5%) in the present study is at par with that of Dhingra et al<sup>(6)</sup>(98.4%). The positive predictive value of a cytologically malignant FNA sample in comparison with 'gold standard' histopathology was 100%, similar to study done by Annam V et al<sup>(7)</sup>(100%). The sensitivity(66.6%) and specificity(100%) of the cytosmears in the cases of neoplastic lesions of lymph node in the present study were in concordance with that of Dhingra V et al.<sup>(6)</sup>

**CONCLUSION**

The study highlights the fact that, FNAC is a rapid, simple, accurate diagnostic procedure and important initial step in the evaluation and management of lymphadenopathy in children. It is very well tolerated by children. By reducing the necessity to perform excision biopsy in many cases, saves children from surgical complications. Thus it can be recommended as a first line of investigation in the diagnosis of lymphadenopathy in the pediatric age group.

**TABLES**

**Table 1: Overall age-wise distribution of cases:**

Age (Years)	Number of cases	Sex		Lymphnode involvement		
		Male	Female	General-ized	Local-ized	Site
≤1	6	3	3	0	6	Cervical
1.1-10	47	24	23	4	43	Cervical
10.1-18	47	18	29	2	45	Cervical

**Table 2 : Validity of FNAC with respect to gold standard Histopathology.**

Diagnosis	Sensitiv-ity (%)	Spec-ificity (%)	Positive Pre-dictive value (%)	Nega-tive Pre-dictive value (%)	Kappa value (%)	p value
Reactive	90.9	78.9	71.4	93.75	66.1	0.000 <sup>s</sup>
Tubercular	75	96.5	75	96.5	60.9	0.001 <sup>s</sup>
Granu-lomatous	100	92.3	66.6	100	76.2	0.000 <sup>s</sup>
Suppurative	50	96.4	50	96.4	34	0.850 <sup>NS</sup>
Necrotizing	33.3	100	100	93.1	47.4	0.002 <sup>s</sup>
Malignancy	66.6	100	100	92.3	76.2	0.000 <sup>s</sup>

S:Significant, NS: Not Significant.

**LEGENDS**

**Figure 1: Distribution of cases: 1a- Non-neoplastic cases. 1b-Neoplastic cases.**

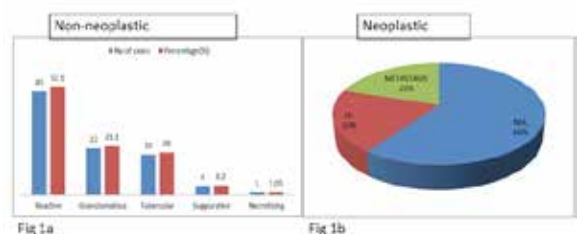
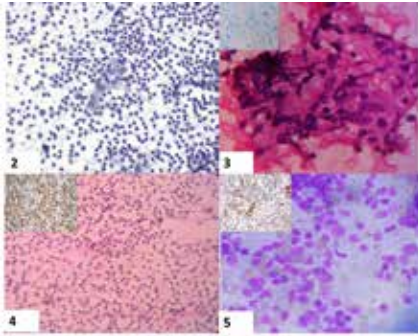


Figure 2: FNAC aspirate of Giemsa stain showing reactive lymphadenitis  
 Figure 3: FNAC aspirate of H& E stain showing tubercular lymphadenitis with epithelioid granulomas, caseous necrosis and inset showing ZN staining AFB positive bacilli  
 Figure 4: FNAC aspirate of Giemsa stain showing NHL inset showing IHC positive for CD 20 marker  
 Figure 5: FNAC aspirate of Giemsa stain showing HL inset showing IHC positive for CD 15 marker



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