**BACKGROUND**

Lymphadenopathy is one of the commonest clinical presentations among the paediatric age group. Evaluation of a child with lymphadenopathy is a common clinical scenario for the paediatricians and poses a diagnostic challenge. Fine needle aspiration cytology (FNAC) is the first line of investigation for any individual with significant lymphadenopathy. To evaluate the role of FNAC in establishing the aetiology of lymphadenopathy in children. To study the different cytomorphological patterns associated with various lymphadenopathies.

**MATERIALS AND METHODS**

This study was carried out on paediatric patients (infants and children aged 1 year to 18 years) presented with significant peripheral lymphadenopathy referred for FNAC to the Department of Pathology, at Government Medical College, Jammu, for a period of three years. This includes a retrospective study conducted from November 1, 2014 to October 31, 2016 and prospective study from November 1, 2016 to October 31, 2017. FNAC was carried out in all cases on significant lymph nodes and aspirated materials was smeared and sent to laboratory, various stains were used for staining cytolological smears.

**RESULTS**

Fine needle aspiration cytology results, in 465 cases of lymphadenopathies, have been collected over a period of three years. The spectrum of cytomorphological diagnosis consisted of reactive hyperplasia (69.46%), tuberculosis lymphadenitis (24.73%), acute suppurative lymphadenitis (2.58%), non-Hodgkin's lymphoma (2.37%), Hodgkin's lymphoma (0.22%), Rosai-Dorfman Disease (0.43%), and Langerhans cell histiocytosis (0.22%). Reactive lymphadenitis was found to be the most common cause of lymphadenopathy in 6 to 10 years of age group and tuberculous lymphadenitis was most common in 11 to 18 years of age group. Males show preponderance of reactive hyperplasia (78.65%), while tuberculosis lymphadenitis showed a female preponderance (39.67%). Males and females were equally involved in Rosai-Dorfman disease.

**CONCLUSION**

FNAC is a very useful diagnostic tool in diagnosis of enlarged lymph nodes. Tuberculous lymphadenitis can be easily diagnosed by FNAC based on cytomorphology and ZN stain. However, limitations of FNAC should be kept in mind and histopathologic examination should be used in doubtful cases.

**KEYWORDS**

FNAC, Significant Lymphadenopathy, Paediatric Age ≤18 years.

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The exact incidence of lymphadenopathy is unknown, but the number varies from 38-45%. Lymph nodes are not considered significantly enlarged until their diameter exceeds 1cm for cervical and axillary nodes and more than 1.5cm for inguinal nodes. However, palpable supraclavicular nodes are always considered abnormal. Tubercular involvement of lymph node is the most common form of extra-pulmonary tuberculosis, responsible for 30-40% of cases in India. In rural India, the prevalence of tuberculous lymphadenitis in children up to 14 years of age is 4.4 per 1000. With estimated 80,000 deaths among children in 2013, tuberculosis continues to be major infectious disease among children. FNAC was first utilized in clinical medicine in early decades of twentieth century; however its status as a reasonably reliable diagnostic tool became established during last 30 to 40 years. It avoids the physical and psychological trauma occasionally encountered after surgical biopsy. It has been proven to be a simple, rapid, minimal invasive, cost effective and reliable diagnostic tool with low morbidity and does not require General anaesthesia, can be performed in outpatient department. Although FNAC is a useful technique, still there are some diagnostic pitfalls and limitations. The failure to establish a diagnosis may be due to faulty technique, sampling error, insufficient material.

**Aims and Objectives**
1. To evaluate the role of FNAC in establishing the aetiology of lymphadenopathy in children.
2. To study the different cytomorphological patterns associated with various lymphadenopathies.

**MATERIALS AND METHODS**
This study was carried out on pediatric patients (Infants and children aged 1 year to 18 years) presented with significant peripheral lymphadenopathy referred for FNAC to the Department of Pathology, at Government Medical College Jammu for a period of three years. This study consisted of retrospective study w.e.f. November 1, 2014 to October 31, 2016 and prospective study from November 1, 2016 to October 31, 2017. In retrospective analysis, records of cases with lymph node aspirated in cytopathology section of Pathology department was examined with respect to age, sex, clinical diagnosis, site of lesion, local examination, any investigation done and cytological diagnosis. All available smears were reviewed. In prospective analysis, a brief clinical history, physical examination including local examination of palpable lymph nodes, available relevant investigations were noted. All the data was recorded in a pre-structured proforma.

**Inclusion Criteria**
- Age ≤ 18 years.
- Significant palpable peripheral lymph nodes i.e. >1cm for cervical and axillary nodes, > 1.5cm for inguinal nodes and >0.5cm for supraclavicular lymph nodes.

**Exclusion Criteria**
- Intra-abdominal and Intrathoracic lymph nodes.
- Un-cooperative child.
- Overlying skin showing acute inflammatory changes.

Written informed consent was obtained from the parents. Aspiration was conducted by the cytopathologist and both May-Grünwald Giemsa (MGG) and Papanicolaou (PAP) staining were performed on the smears obtained. Ziehl Neelsen (ZN) staining was done wherever tuberculosis was suspected.

**RESULTS**
The study comprises 465 patients presenting with significant peripheral lymphadenopathy which include 311 retrospective cases and 154 prospective cases.

<table>
<thead>
<tr>
<th>Lymph Node Group Affected</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>317</td>
<td>68.17</td>
</tr>
<tr>
<td>Submandibular</td>
<td>50</td>
<td>10.75</td>
</tr>
<tr>
<td>Generalised</td>
<td>41</td>
<td>8.82</td>
</tr>
<tr>
<td>Axillary</td>
<td>23</td>
<td>4.95</td>
</tr>
<tr>
<td>Submental</td>
<td>14</td>
<td>3.01</td>
</tr>
<tr>
<td>Supraclavicular</td>
<td>11</td>
<td>2.37</td>
</tr>
<tr>
<td>Inguinal</td>
<td>4</td>
<td>0.86</td>
</tr>
<tr>
<td>Occipital</td>
<td>3</td>
<td>0.65</td>
</tr>
<tr>
<td>Preauricular</td>
<td>2</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>465</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

*Table 1. Distribution of Patients According to Lymph Node Group Affected (n=465)*

Out of 465 case, cervical group of lymph nodes were most commonly involved (83.01%), followed by generalized (8.82%), axillary group (4.95%), supraclavicular group (2.37%) and least in inguinal group (0.86%). Thus, in the study 91.19% lymph nodes were localized, while 8.82% patients had generalized lymphadenopathy. Among the cases with localized lymph node involvement, anterior and posterior cervical group was involved in 317 cases (68.17%), submandibular in 50 cases (10.75%), axillary in 23 cases (4.95%), submental in 14 cases (3.01%), supraclavicular in 11 cases (2.37%), inguinal in 4 cases (0.86%), occipital in 3 cases (0.65) and preauricular in 2 cases (0.43%). Out of 41 generalised (if lymph nodes are enlarged in two or more non-contiguous areas) lymph nodes, FNAC of cervical was done in 23 (56.10%) patients, FNAC of submandibular was done in 7 (17.07%) patients, inguinal in 4 (9.76%) patients axillary in 3 (7.32%) patients, occipital in 2 (4.88%) patients, preauricular and supraclavicular in 1 (2.44%) patient each(Table 1).

<table>
<thead>
<tr>
<th>Size (cms)</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5-1.0</td>
<td>6</td>
<td>1.29</td>
</tr>
<tr>
<td>1.1-2.0</td>
<td>288</td>
<td>61.94</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>148</td>
<td>31.83</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>15</td>
<td>3.23</td>
</tr>
</tbody>
</table>
Table 2 shows the distribution of lymph nodes on the basis of size. The mean size of the lymph nodes was found to be 2.27 cm. Most of the patients (61.94%) showed significant enlargement of the lymph node in between 1.1 to 2 cm, followed by 2.1 to 3 cm (31.83%), 3.1 to 4 cm (3.23%), >4 cm (1.72%) and least in 0.5 to 1 cm (1.29%).

<table>
<thead>
<tr>
<th>Cytomorphological Diagnosis</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive Lymphadenitis</td>
<td>323</td>
<td>69.46</td>
</tr>
<tr>
<td>Tuberculous Lymphadenitis</td>
<td>115</td>
<td>24.73</td>
</tr>
<tr>
<td>Acute suppurative Lymphadenitis</td>
<td>12</td>
<td>2.58</td>
</tr>
<tr>
<td>Lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>11</td>
<td>2.37</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>1</td>
<td>0.22</td>
</tr>
<tr>
<td>Rosai-Dorfman Disease</td>
<td>2</td>
<td>0.43</td>
</tr>
<tr>
<td>Langerhans Cell Histiocytosis</td>
<td>1</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>465</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table 3. Cytomorphological Diagnosis of FNA Report (n=465)

Out of 465 cases, 281 were males and 184 were females. Male patients dominated the study (60.43%), with male to female ratio of 1.53:1. Males showed preponderance of reactive hyperplasia, acute supportive lymphadenitis and lymphoma, while tuberculosis lymphadenitis showed a slight female preponderance.

<table>
<thead>
<tr>
<th>Group No.</th>
<th>Cytologic Picture on Aspirated Smear</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Epithelioid granuloma without necrosis</td>
<td>19</td>
<td>16.5</td>
</tr>
<tr>
<td>II</td>
<td>Epithelioid granuloma with necrosis</td>
<td>56</td>
<td>48.7</td>
</tr>
<tr>
<td>III</td>
<td>Necrotic material without epithelioid granuloma</td>
<td>40</td>
<td>34.8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>115</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table 6. Pattern of Various Types of Cytologic Picture on Aspirates in 115 Patients with Tubercular Lymphadenitis

The cytological features resulting from different combinations of above mentioned components are depicted in table 6. The most common combination was the epithelioid cells with necrosis (Group II) in 48.7%. In addition to clusters of epithelioid cells, amorphous cellular debris or necrotic material was present. Lymphocytes and Langshans' giant cells were seen.

The next most frequent cytological appearance was amorphous a cellular material without epithelioid granuloma (Group III) in 34.8%. Degenerating polymorphonuclear leucocytes and lymphoid cells were seen in the background. Epithelioid cells without necrosis (Group I) were seen in 16.5% cases. The background consisted of reactive lymphoid cells and giant cells.
Table 7 shows result of Acid Fast Bacilli (AFB) reaction. Acid Fast Bacilli (AFB) was positive in 50 patients with overall positivity of 43.48%. The high-test frequency of positivity 72.5% was seen in cases showing necrosis without epithelioid cells in Group. The positivity in cases showing most exact picture of tuberculosis in Group 2 that is granuloma with necrosis was 35.71% and in Group 1 with only granula, AFB positivity was 5.3%.

Table 8 shows the distribution of neoplastic lesions of lymph nodes. Among the lymphomas non- Hodgkin’s lymphoma was more common and was seen in 11 patients (91.66%). Hodgkin’s lymphoma was seen in 1 patient (8.33%). In non- Hodgkin’s lymphoma smears show predominance of monomorphic cells. In Hodgkin’s lymphoma aspirate show characteristic classic Reed-Sternberg cells and a polymorphous infiltrate. Scattered mononuclear variants of Reed- Sternberg cell with large nuclei and prominent nucleoli were also seen. The Reed-Sternberg cell appeared as a large cell, with two or more nuclei with prominent nucleoli. The cytoplasm was moderate in amount with pale blue colour. Background showed reactive lymphoid cells with eosinophils and plasma cells.

**DISCUSSION**

The study was undertaken to evaluate the role of FNAC in clinically significant lymphadenopathy in children. Symptoms and signs, although indicative of etiology, are no substitute for a morphological diagnosis. FNAC offers clear advantages. It is minimally invasive, produces a speedy result and is inexpensive. Enlarged lymph nodes are a prime target for fine needle aspiration. It is accepted by most patients as a non-invasive method of lymph node aspiration. In developing countries including India, where facilities for biopsy are not readily available, FNAC is useful in providing diagnosis. It also reduces pressure on financial resources necessary to perform a surgical biopsy.

We have presented our experience with 465 cases of lymphadenopathy over a period of 3 years. Our primary aim was to help clinician in arriving at an early diagnosis in cases presenting with lymphadenopathies. Hence diagnosis was based on definite cytomorphological findings with clinico-cytological correlation.

In our study ages of the children were in the range from 0 to ≤18 years with mean age being 9.17 years. Schoot LV et al.3 also showed the mean age of 9 years (range 15 months to 20 years). In our study patients were divided into three groups with maximum number of patients in the age group of 11 to 18 years (38.28%), followed by 6 to 10 years (34.19%) and ≤5 years (27.53%). This is comparable with the findings of Silas OA et al.10 where majority of patients (46.4%) belong to 10 to 14 years while age range 0 to 4 years had the least number of cases (8.9%).

In our study reactive lymphadenitis was more common in 6 to 10 year of age group 126 (79.2%) and tuberculosis lymphadenitis was more common in 11 to 18 years of age group 64 (36.2%). This is comparable with Singh N et al.11 where reactive lymphadenitis commonly seen in 5 to 10 years age group and tuberculosis lymphadenitis commonly seen in 10 to 16 years of age group.

In the present study, incidence in males (60.43%) was more than that in females (39.57%). The M:F (male:female) ratio was 1.53:1. Similar to our study Singh N et al.11 showed that the incidence in males (70.08%) was more than in females (29.92%) with male to female ratio is 2.34:1.

In the present study, cervical group of lymph nodes was most commonly involved (90.12%), followed by axillary group (5.59%), supraclavicular group (2.58%) and least in inguinal group (1.72%). Single lymph node involvement (55.5%) was more commonly seen as compared to multiple lymphadenopathy (44.5%). This was similar to the findings reported by Agarwal D, et al.12 who found cervical lymph node as the most common site of involvement. Other studies done by Dhinag V et al,13 Singh N et al,14 Haque MA et al.,14 Pandit AA et al,15 Steel BLS et al,16 Radha M et al,17 Reddy MP et al,18 Changty S et al.19 Reported an incidence of 79%, 96.79%, 87.18%, 65%, 47%, 81.9%, 85%, 90% for cervical lymph node respectively. Easy accessibility could be the most plausible explanation to this finding.

In our study maximum number of cases (61.94%) presented with the size of lymph node in between 1.1 to 2
cm. The mean size of the lymph node was 2.27 cm. The difference in the aetiology with respect to size of the lymph nodes was observed in the present study. All cases of lymphomas in our study presented with the size of ≥2 cm. Oguz A et al.\textsuperscript{20} concluded saying, lymph node size <1 cm was in favour of benign aetiology and size >3 cm was in favour of malignancy. Based on observation done by Karadeniz C et al.\textsuperscript{21} a maximum lymph node size of 2 cm was considered an appropriate limit to distinguish malignant disease from benign cause.

Cytomorphological patterns obtained in this study were predominantly non-neoplastic 453/465 cases (97.41%) as compared to neoplastic lesions 12/465 cases (2.58%). This is comparable with the findings of Singh N et al.\textsuperscript{11} where non-neoplastic lesions were 91.57% and neoplastic lesions were 1.61%.

Among the non-neoplastic lesions in this study, nonspecific reactive lymphadenitis was the most common pattern 323/465 cases (69.46%), followed by tuberculosis lymphadenitis 115/465 cases (24.73%), acute supportive lymphadenitis 12/465 cases (2.58%), Rosai-Dorfman disease 2/465 cases (0.43%) and Langerhans cell histiocytosis 1/465 cases (0.22%). Similar findings were reported by Radha M et al.\textsuperscript{17} who observed reactive lymphadenitis (51.1%) as the most common cause of lymphadenopathy, followed by tuberculous lymphadenitis (43.1%), acute supportive lymphadenitis (4.2%). Other studies showing similar results with nonspecific reactive hyperplasia as the predominant pattern, were done by Lake MA et al.\textsuperscript{22} Annam V et al.\textsuperscript{23} and Hag IA et al.\textsuperscript{24}

Tuberculosis lymphadenitis constituted the second largest group in the present study of 24.73%. Cytodiagnosis of tuberculosis depends on demonstration of epithelioid cells and Langhans giant cells with or without accompanying necrosis. However, epithelioid granulomas can be seen in non-tuberculous lesions such as sarcoidosis, brucellosis, cat scratch disease, leprosy, toxoplasmosis and occasionally malignancies such as Hodgkin’s disease and metastatic tumours (Christ M and Kennedy M, 1982;\textsuperscript{25} Kline TS, 1981).\textsuperscript{26}

In western countries, demonstration of epithelioid cells in lymph node aspirates may suggest sarcoidosis as the first possible diagnosis. But in India, findings would suggest tuberculosis unless proved otherwise.

Epithelioid cells have been considered most important for diagnosis of tuberculosis. These epithelioid cells were present in 65.2% of our cases of tuberculosis lymphadenitis. This is comparable with the findings of Annam V et al.\textsuperscript{23} and Ahmad S, et al.\textsuperscript{22} where the incidence of epithelioid cells in tuberculosis lymphadenitis was 74.46% and 74.7% respectively. Rajwanshi et al (1987) reported incidence of epithelioid cells of 87% of their cases which is much higher than in our study.

In our study, AFB positivity was 72.5% in smears containing cellular necrotic material without epithelioid granulomas whereas positivity was 35.71% in smears showing epithelioid granulomas with necrosis and 5.26% in smears showing epithelioid granulomas without necrosis. Our overall positivity for AFB was 43.5%. Similar patterns were seen in studies done by other authors (Agarwal R et al.;\textsuperscript{28} Nidhi P et al.;\textsuperscript{29} Masilamani S et al.\textsuperscript{30} who have reported. Lowest AFB positivity rate in smears showing epithelioid granuloma without necrosis and highest AFB positivity rate in smears showing necrotic material without epithelioid granuloma.

In the present study, diagnosis of Rosai-Dorfman disease was made in 2 patients (0.43%) and Langerhans cell histiocytosis in 1 patient (0.22%).

In our study only 12/465 cases (2.58%) were neoplastic out of which 11 cases were of non-Hodgkin’s lymphoma and 1 case of Hodgkin ‘lymphoma. Non-Hodgkin’s lymphoma (91.67%) was the commonest lymphoma diagnosed in our study as compare to Hodgkin’s lymphoma (8.33%). Similar findings were found in study done by Silas OA et al.\textsuperscript{10} where non-Hodgkin’s lymphoma was the commonest malignant lesion observed 76.9% followed by Hodgkin’s lymphoma 15.4%.

However, it must be realized that FNA not only offers tissue diagnosis but serves as a preliminary screening procedure for a number of clinical considerations e.g. lymphoma, leukemia, metastasis, tuberculosis and lymphadenopathy not otherwise specified. Following the cytodiagnostic decision regarding biopsy from appropriate sites, if necessary, other relevant investigations can be done.

The role of FNA is of immense value in patients who are not suitable candidates for excisional biopsies. As the confidence of clinicians increases, as indicated on cytology reports the excision biopsy is avoided, especially in cases of granulomatous lesions. The value of aspiration cytology lies in a positive diagnosis which should be correlated to clinical diagnosis. As is evident from the foregoing account, we could make definite diagnosis of tuberculosis based on cytomorphologic features and AFB positivity.

In the present study it is obvious that most of the causes of lymphadenopathy can be determined on basis of cytomorphological features of FNAC. Reactive lymphadenitis and tuberculosis lymphadenitis together constitute 94.19% of cases in our study. The diagnosis of tuberculosis could be easily made from presence of granulomas and necrosis and further confirmed by ZN positivity. The cases suspected to be lymphomas have to be always confirmed by histopathological examination. One case of Langerhans cell histiocytosis and two cases of Rosai-Dorfman disease were also diagnosed on characteristic cytomorphological features. Statistics from accumulated literature reveal that the overall diagnostic accuracy in cases of all types of lymphadenopathy varies from 86 to 98.89% (Mohan MS et al.;\textsuperscript{31} Dhingra V et al.;\textsuperscript{13} Schoot LV et al)\textsuperscript{3} For lymphomas the diagnostic accuracy varies between 88 to 96.5% (Singh A et al.;\textsuperscript{22} Carter TR et al.;\textsuperscript{33} Das DK et al.;\textsuperscript{34} Russel J et al.;\textsuperscript{25} Gupta SK et al.).\textsuperscript{36}

From the results of this study and those from the literature, FNAC is recommended as the initial diagnostic tool in children with persistent and suspicious peripheral lymphadenopathy. It has proven to be a rapid, simple, and accurate diagnostic tool with low morbidity. Keeping the limitations of FNAC in mind, a surgical biopsy is still obligatory in any doubtful case. Thus, FNAC may have a
triage function in the selection of those patients who can undergo clinical follow-up and those requiring a surgical biopsy.

CONCLUSION
1. Fine needle aspiration cytology results, in 465 cases of lymphadenopaties have been collected over a period of three years.
2. The spectrum of cytomorphological diagnosis consisted of reactive hyperplasia (69.46%), tuberculous lymphadenitis (24.73%), acute supplicative lymphadenitis (2.58%), non-Hodgkin’s lymphoma (2.37%), Hodgkin’s lymphoma (0.22%), Rosai-Dorfman Disease (0.43%), and Langerhans cell histiocytosis (0.22%).
3. Reactive lymphadenitis was found to be the most common cause of lymphadenopathy in 6 to 10 years of age group and tuberculous lymphadenitis was most common in 11 to 18 years of age group. Males show preponderance of reactive hyperplasia (78.65%), acute supplicative lymphadenitis (2.49%), non-Hodgkin’s lymphoma (2.49%), Hodgkin’s lymphoma (0.36%) and Langerhans cell histiocytosis (0.36%), while tuberculous lymphadenitis showed a female preponderance (39.67%). Males and females were equally involved in Rosai-Dorfman disease.
4. Males show preponderance of reactive lymphadenitis while tuberculous lymphadenitis showed a female preponderance.
5. Cervical lymph nodes were involved most often in all types of lymphadenopathies, while inguinal nodes were least involved.
6. In case of tuberculous lymphadenitis, epithelioid granuloma with necrosis was the most frequent cytomorphological pattern (48.7%), followed by necrotic material without granuloma (34.8%) and epithelioid granuloma without necrosis (16.5%). The AFB positivity rates were 35.71%, 72.5% and 5.26% respectively. Overall AFB positivity was 43.5%.
7. Rosai-Dorfman disease and Langerhans cell histiocytosis were noted as rare causes of lymphadenopathy.

FNAC is a very useful diagnostic tool in diagnosis of enlarged lymph nodes. Tuberculous lymphadenitis can be easily diagnosed by FNAC based on cytomorphology and ZN staining. Care must be taken in evaluating reactive lymphadenitis and lymphomas. FNAC as a diagnostic tool is an inexpensive outdoor procedure and suitable for developing countries like India. However, limitations of FNAC should be kept in mind and histopathologic examination should be used in doubtful cases.

REFERENCES


