

## Comparative study of fine-needle aspiration cytology and biopsy in diagnosis of lymphadenopathy in pediatric age group

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### ABSTRACT

**Background:** Excision biopsy and its histopathological examination have for many years been the final diagnostic procedure in diagnosis of lymphadenopathy. However, it is troublesome, expensive, and delays in treatment. **Objective:** The objective of the study was to find the association between fine-needle aspiration cytology (FNAC) and histopathology in diagnosing children with lymphadenopathy. **Materials and Methods:** This observational analytical cross-sectional study was conducted in the department of pediatrics of a teaching institution of Odisha, India. Fifty children attending our outpatient department and/or inpatient department for any cause, clinically diagnosed as local or general lymphadenopathy under 14 years of age were included in the study. Proportion of lymphadenopathies detected by FNAC, histopathology, and biopsy was calculated. We also calculate the proportion of lymphadenopathy detected by FNAC in three different types of scenarios, that is, definite diagnosis, diagnosis suspected and undiagnosed cases. **Results:** The median age was 7 years (2–14 years) and male-to-female ratio was 1.4:1. The most common symptom was fever (98%) and the most common physical finding was painless enlargement of lymph nodes (90%). There was statistically significant association between FNAC and definite diagnosis, diagnosis suspected and undiagnosed cases of tuberculosis by FNAC (Chi-square value=11.37,  $p<0.05$ ), for Hodgkin's lymphoma (Chi-square value=17.64,  $p<0.01$ ). FNAC has significant association in detecting tuberculosis, Hodgkin's, and non-Hodgkin's diseases of childhood ( $p<0.05$ ). **Conclusion:** FNAC can be used as a first-line diagnostic test for tuberculosis, Hodgkin's disease, and non-Hodgkin's lymphoma in the pediatrics age group in view of its availability.


**Key words:** Children, Excision biopsy, Fine-needle aspiration cytology, Lymphadenopathy, Treatment

In infancy and childhood, lymph nodes (LNs) play an important role in putting up defense against the infection and also in the antibody formation, T-cell activation, and cytokine secretion besides their function in removal of noxious substances both from lymph and blood. They react to a wide variety of etiological factors and manifest clinically by enlargement, which is termed as lymphadenopathy. It may be due to proliferation of normal lymphoid elements or infiltration by malignant or phagocytic cells. Solitary and generalized lymphadenopathies are not uncommonly met within pediatric age group. Normally, size of LN in cervical group is <1.5 cm, axillary group <1 cm, and among inguinal group, it is <1.5 cm. Any LN, bigger than this size, is considered as significant.

Locoregional lymphadenopathy always points towards the focus in the drainage area. Most common groups are cervical groups draining tonsil and mouth cavity; and inguinal group draining perineum and lower limbs. Tuberculosis commonly presents as posterior cervical lymphadenopathy. Generalized lymphadenopathy

commonly seen as a part of viremia, rickettsial infection. Sometimes BCG vaccination can present as left sided axillary adenitis (BCGadenitis). Besides clinical diagnosis, fine-needle aspiration cytology (FNAC) and biopsy of lymphnode is being done to arrive at diagnosis like TB, Chronic granuloma, leukemia, lymphoma etc.

Fine-needle aspiration cytology (FNAC) has been studied by various authors with convincing results and has been described as a simple, inexpensive, rapid, less traumatic, and effective procedure in the diagnosis of lymphadenopathies in children [1]. It is free from risk of infection or dissemination of tumor mass by the technique. Several nodes can be examined by this technique and in case of doubtful diagnosis, further specimens can be obtained. Indirect methods such as hematological or serological examination and skin tests, do not give a stamp of real diagnosis except in few cases such as leukemia and infectious mononucleosis. The excision biopsy and its histopathological examination have for many years been the final diagnostic procedure in diagnosis of lymphadenopathy. However, it is troublesome, expensive and there is delay in treatment because of time taken procedure. Apart from this, general anesthesia and hospitalization may be required,

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and it may cause complications such as hemorrhage and infection. In view of the high incidence of lymphadenopathy in children in Odisha, we planned to study FNAC and to compare its result with the excisional biopsy and histopathology in the diagnosis of lymphadenopathy in the pediatric age group.

## MATERIALS AND METHODS

The present cross-sectional analytical study was conducted in the department of pediatrics of a tertiary care teaching institution of Odisha, India, from April 2018 to April 2020. Prior approval was obtained from the Institutional Ethics Committee. All cases of lymphadenopathy (localized or generalized in children <14 years of age) were selected for the study after receiving written informed consent in local language from parents or legal heir. Critically ill children were excluded from the study. Sample size of the study was taken as 50 with convenient sampling method.

FNAC was done in all cases. The material in the needle was collected in three slides. Two were fixed immediately in alcohol and stained with Papanicolaou stain. The third smear was dried and stained with Ziehl–Neelsen staining to search for AFB in case of suspected tubercular lymphadenitis. The smears were immediately fixed in a mixture of equal amount of ether and 95% ethyl alcohol, contained in a Kapolin jar which could contain 10 slides back to back before drying. Minimum 15 min were allowed for the purpose of the smear to get adherent to the slide. Smears were stained by Papanicolaou cytological staining technique. It is then observed under high-power field for comment.

LN biopsy was undertaken by local anesthesia in most cases and under general anesthesia in few cases of non-cooperative young children. Excision of gland was done in toto under strict aseptic conditions. A longitudinal section was made in the gland and it was preserved in 10% normal saline. After processing and block making of the tissue, serial histologic sections of 4–5 micron thickness were cut with microtome and were stained with hematoxylin and eosin. The stained slides were examined under microscope.

Definite diagnosis was defined as cases diagnosed by biopsy and histopathology. Suspected diagnosis was defined as cases diagnosed history and physical examinations. Undiagnosed cases were defined as cases could not be diagnosed either by FNAC and/or histopathology. In all cases, complete history is taken with history, family history, and socioeconomic condition. Any history of contact with tuberculosis was searched in all cases. Thorough physical examination was done including the systemic examination related to lymphadenopathy. Hematological, stool and urine examination, chest X-ray, and Mantoux test were done in all cases. In cases of lymphoma and leukemia, bone marrow examination was done.

All the relevant data were recorded in a predesigned case report format. Data validation was done manually by two separate persons not involved in the study. Continuous data were expressed in mean (standard deviation) and categorical data were expressed in proportions (percentages). All the descriptive and inferential statistics were done by SPSS v 25.0 (IBM, NY, USA). Pearson's Chi-square test was applied to calculate the strength of association. For all statistical purposes,  $p < 0.05$  was considered statistically significant.

## RESULTS

The following observations were made among the 50 children with lymphadenopathy after being studied. Out of total 50 study participants, male outnumbered the female (M:F=1.4:1), with mean age of the study population was  $7.6 \pm 3.1$  years. The age group distributions revealed that only 6% were <2 years. The maximum number of cases belonged to the age group of 5–14 years (66%) followed by 14 cases (28%) belonging to age group of 2–5 years.

Various etiological groups of lymphadenopathies include tuberculous (30%), Hodgkin's lymphoma (24%), non-Hodgkin's lymphoma (16%), leukemia (10%), pyogenic (4%), metastasis (2%), histiocytosis (2%), and non-specific causes (12%). The most common symptom was fever in 98% of cases. The most common (90%) physical finding was painless enlargement of LNs. Table 1 describes the findings of FNAC in different etiological groups. There was statistically significant association between FNAC and definite diagnosis, diagnosis suspected and undiagnosed cases of tuberculosis by FNAC (Chi-square value=11.37,  $p < 0.05$ ; Cramer's V: 0.783) similarly also with Hodgkin's lymphoma (Chi-square value=17.64,  $p < 0.01$ ; Cramer's V: 0.821). Comparing with the histopathology and biopsy, FNAC has significant association in detecting tuberculosis, Hodgkin's, and non-Hodgkin's diseases of childhood ( $p < 0.05$ ). Among other diseases, FNAC failed to detect them.

## DISCUSSION

In this present study of 50 participants, males were predominating as compared to female. Most of the children presented with lymphadenopathy of any cause were between 5 and 14 years of age group. The most common symptom was fever and the most common physical finding was painless enlargement of LNs. Strength of association between FNAC and diagnosed cases, clinically suspected cases and undiagnosed cases of tuberculosis and Hodgkin's lymphoma was strong. FNAC has significant association in detecting tuberculosis, Hodgkin's, and non-Hodgkin's diseases of childhood as compared with histopathology and biopsy. However, FNAC failed to make a confirmatory diagnosis of leukemia, pyogenic, secondary metastasis, non-specific lesions, and histiocytosis when compared with biopsy and histopathology.

The prevalence of lymphadenopathy was more between 2 and 10 years, similar to our present study. Murty *et al.* [2] were of opinion that increased prevalence of enlarged LNs in this age group may be due to they are frequently exposed to upper respiratory infection and due to immature immunological system. Our study revealed that tubercular lymphadenopathy is leading in the series. Similar results were observed by studies done earlier by Reddy *et al.* [3] and Sheikh *et al.* [4]. Among malignant conditions, Hodgkin's disease was observed in 24% of cases in the present study which was higher than the study done by Singh *et al.* [5] (16.7% cases). This higher prevalence in our study may be due to a smaller number of samples and type of sampling techniques.

Presenting symptoms were fever in 98%, loss of weight in 66%, and loss of appetite in 64%; similar symptoms were reported by Murty *et al.* [2]. According to a study done by Sheikh

**Table 1: Results of FNAC in different etiological groups (n=50)**

Etiology	Definite diagnosis no. (%)	Diagnosis suspected no. (%)	Undiagnosed no. (%)
Tuberculosis	12 (80)	01 (6.66)	02 (13.33)
Hodgkin's disease	09 (75)	01 (8.33)	02 (16.66)
Non-Hodgkin's lymphoma	05 (62.5)	0	03 (3.75)
Leukemia	05 (100)	0	0
Pyogenic	02 (100)	0	0
Secondary metastasis	0	0	01 (100)
Non-specific	04 (66)	0	02 (33.3)
Histiocytosis	0	0	01 (100)

FNAC: Fine-needle aspiration cytology

**Table 2: Histopathology versus FNAC in the diagnosis of lymphadenopathy (n=50)**

Etiology	Diagnosis by FNAC no. (%)	Diagnosis by histopathology no. (%)	p value
Tuberculosis	12 (80)	15 (100)	0.03*
Hodgkin's disease	09 (75)	12 (100)	0.02*
Non-Hodgkin's lymphoma	05 (62.5)	08 (100)	0.03*
Leukemia	05 (100)	05 (100)	> 0.05
Pyogenic	02 (100)	02 (100)	> 0.05
Secondary metastasis	0	01 (100)	-
Non-specific	04 (66.6)	06 (100)	>0.05
Histiocytosis	0	01 (100)	-

\*Statistically significant (p&lt;0.05). FNAC: Fine-needle aspiration cytology

*et al.* [4], the signs and symptoms in children were quite similar to our study and were non-specific. They observed fever, anorexia, and loss of weight in 86.57%, 82.1%, and 71% of their cases, respectively. Painless lymphadenopathy was the most common physical finding in our study similar to the previous study [4].

By FNAC, definite diagnosis was predicted in 37 cases (74%) and in 2 cases (4%) diagnosis was suspected and in 11 cases (22%) diagnosis could not be made. Table 2 denotes definite failure of diagnosis in 26% of cases was due to bizarre pattern of cellular material which could not predict the characteristic findings necessary for cytological diagnosis. The same type success rate in FNAC was found by Friedman *et al.* [6] (80%), Mahanta *et al.* [7] (76%), and Kline *et al.* [8] (94%). Bhandari *et al.* [9] put forth that FNAC is practicable at bedside and outpatient's department without any significant complication. This is a simple and safe and minimally traumatic diagnostic method in cases of lymphadenopathy. Chitale *et al.* [10] found that successful cytological diagnosis in 80% of cases found that FNAC is simple, speedy, and accurate. Steel *et al.* [11] confirmed that FNAC is simple safe and allows immediate diagnosis when patient is first examined. There are no previous studies delineating the role of FNAC in detecting tuberculosis, Hodgkin's, and non-Hodgkin's disease among childhood lymphadenopathies as compared to histopathology and biopsy.

However, the present study has certain limitations like cross-sectional study design, so causality could not be established. Sample size was too small to arrive at certain inference. Moreover, the sampling technique was of non-random type. This was due to our resource poor setting and time constrain of the study. The

majority of patients were belonging to southern part of Odisha, so the results could not be generalized due to varied climatic and geographical conditions. Confounders and effect modifiers could not be avoided due to the study design *per se*. Hence, in future, a diagnostic study Phase II with larger samples will definitely help in getting better results in assessing the diagnostic accuracy of FNAC as compared to biopsy-proven histopathology.

## CONCLUSION

FNAC can be used as a first-line diagnostic test for tuberculosis, Hodgkin's disease, and non-Hodgkin's lymphoma in the pediatric age group in view of its availability. Lymphadenopathy is commonly seen in Odisha due to various etiological factors and FNAC is a safe, easy, inexpensive, and less traumatic method and can be done bedside or at outpatient department. Hence, FNAC can be a useful and reliable screening test in diagnosis of lymphadenopathy in children.

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