COLLEGE OF HEALTH SCIENCE, SCHOOL OF MEDICINE,

DEPARTMENT OF PATHOLOGY

CYTOLOGICAL PATTERNS OF PATIENTS PRESENTING WITH LYMPHADENOPATHY IN TIKUR ANBESSA SPECIALIZED HOSPITAL RETROSPECTIVE CROSS-SECTIONAL STUDY

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ABBREVIATION AND ACRONYM

AAU	Addis Ababa University
ACD	Acid Fast Bacilli
ALCL	Anaplastic large cell lymphoma
AML	Acute myeloid leukemia
Ca	Carcinoma
DRPC	Department Research and Publication Committee
FNAC	Fine needle aspiration cytology
HG	High grade
HL	Hodgkin lymphoma
LCH	Langerhans cell histiocytosis
LG	Low grade
MEC	Mucoepidermoid carcinoma
NHL	non-Hodgkin's lymphoma
NL	Necrotizing Lymphadenitis
NPC	Nasopharyngeal carcinoma
RDD	Rosai-Dorfman disease
SCC	Squamous cell carcinoma
SLL	Small lymphocytic lymphoma
SRBCT	Small round blue cell tumor
TB	Tuberculosis
TASH	Tikur Anbesa Specialized Hospital
Undiff.	Undifferentiated

SUMMARY

Background: - From benign infections to rare malignancies, lymph node enlargement, or lymphadenopathy, presents a diagnostic challenge. Children often experience harmless or infectious causes, while adults face a spectrum from benign to cancerous origins. Acute or chronic, unexplained cases emerge in 0.6% of the population yearly. Though only 1.1% link to cancer, this risk increases with age. Understanding these patterns aids in the proper evaluation and management of lymphadenopathy across different patient groups.

Objective – This study was intended to examine the clinicopathological characteristics and Cytological patterns in patients presenting with lymphadenopathy in Tikur Anbesa Specialized Hospital (TASH), from 2019-2023.

Methods: A hospital-based retrospective cross-sectional analysis of all the cases of lymphadenopathy from January 2019 to December 2023 was conducted at the (TASH) department of pathology. The study population was all patients who had lymph node aspiration done in the pathology department at TASH during the study period. Data was collected from the registries and digital sources, imported into a computer, and analyzed using SPSS version 27. Ethical clearance was obtained from the Department Research and Publication Committee (DRPC) of pathology. Continuous data was summarized and described as a function of their statistical distribution, using means or medians, standard deviation and interquartile range. Categorical data was summarized as frequencies and proportions. Data was presented and visualized using tables and graphical charts.

Result: A total of 840 cases were evaluated out of which, 508 (60.5%) were females and 332 (39.5%) were males making the F: M ratio of 1.53:1. The patients were between the ages of 6 months and 85 years with a mean of 35.7 years. The majority of lymphadenopathies were localized (91%) and involved the cervical lymph nodes (51.4%). Significant portion of the patients presented with metastatic lesions (46.19%) followed by reactive lymphadenopathy (21%), lymphoma (17%) and tuberculous lymphadenitis (10.4%).

Metastatic lesions were most frequently encountered in female patients between the ages of 31-50 years and commonly involved the axillary lymph nodes. Carcinomas comprise the majority of

metastatic lesions (93.04%). Reactive lymphadenitis was most commonly seen under the age of 10 years and involved the cervical lymph nodes. Non-Hodgkin lymphoma made up 79% of lymphoma cases and had the highest number of cases with generalized lymphadenopathy.

Conclusion: Fine needle aspiration cytology (FNAC) is a simple, safe and rapid diagnostic tool in the assessment of patients with enlarged lymph nodes. It is important to know the patterns of diagnosis in a particular geographic area for accurate patient assessment. In our current study, metastatic lesions are the most common causes of lymph node enlargement in TASH.

Keywords: Cytological pattern, Clinicopathological Characteristics, lymphadenopathy, pathology.

1. INTRODUCTION

1.1 BACKGROUND

Lymph nodes make up an important part of the defense system of the human body, as they filter or trap any foreign particles. They are small, oval, or kidney-shaped structures measuring 0.1 to 1.5 cm, lying along the course of lymphatic vessels. Lymph nodes develop from the lateral part of the mesoderm during embryonic developmental stages (1-2). The main function of a lymph node includes lymphocyte production, biological filtration of lymphatic fluid, processing of antigen, and presenting it to the receptor through antigen-presenting cells (3). By doing so, they protect the human body from any foreign attack and are vital to the immune system. The human body consists of more than 1000 lymph nodes and most of them are usually non-palpable in healthy individuals (4). Lymph nodes are mainly found in the cervical, axillary, inguinal, iliac, mediastinal, and retroperitoneal regions. Lymphadenopathy refers to an abnormal increase in the size, number, or consistency of lymph nodes. This enlargement can be either generalized or localized (5). **(**Localized lymphadenopathy affects a single area of the body, whereas generalized lymphadenopathy impacts multiple regions**).** Inflammation of a lymph node is called lymphadenitis (6). The causes of lymphadenitis may span from an infectious process to a malignant disease (7-8). Determining the cause of lymphadenopathy solely through history and physical examination can be challenging. Various investigative techniques are employed to assess lymphadenopathy, including fine needle aspiration cytology (FNAC), core needle biopsy, flow cytometry, and open biopsy (9-12).

Lymphadenopathy has become a prevalent pathological condition globally, prompting numerous studies to evaluate its scope. It represents a clinical manifestation of either regional or systemic disease and often provides valuable insight into the underlying condition(13). Lymphadenopathy is frequently encountered in clinical practice, manifesting as either an acute or chronic condition.

Palpable lymph nodes larger than 5 mm are deemed abnormal. The annual occurrence of unexplained lymphadenopathy is 0.6%, with only 1.1% of cases being linked to malignancy-a proportion that rises with advancing age. (14). Approximately 50% of otherwise healthy children have detectable lymph nodes at any given time (15). In children, lymphadenopathy is predominantly benign or results from an infectious cause. For both adults and children, lymphadenopathy that persists for less than two weeks or remains unchanged for over 12 months is generally unlikely to have a neoplastic origin (16-17). Hodgkin lymphoma and low-grade non-Hodgkin lymphoma are notable exceptions, as they are commonly accompanied by systemic symptoms (18).

Aspirates from lymph nodes are typically highly cellular, and their interpretation can range from providing a clear diagnosis to necessitating a request for histopathology. Understanding the patterns of lymphadenopathy in a specific geographical area is crucial for making a confident and accurate diagnosis or suspecting a particular disease. Due to the quick results and minimal trauma, complications, or discomfort, aspiration cytology is now regarded as a valuable diagnostic method (19). Most studies have focused solely on the cytomorphological patterns of lymph node lesions, either in pediatric or adult populations. Therefore, the present study was conducted to investigate the clinicopathological features and cytomorphological patterns of lymph node lesions in both pediatric and adult groups.

1.1 Statement of the Problem

Lymphadenopathy can occur in different age groups at any site of the body. Studies in various countries on peripheral lymphadenopathy have shown that cervical lymph nodes are the most frequently enlarged and biopsied nodes of all peripheral lymph nodes (20). Lymphadenopathy is frequently due to a local or systemic, benign, self-limited, infectious disease. The cause of lymphadenopathy depends on its location. Viral and bacterial infections cause cervical lymphadenopathy. Mycobacterium and metastasis cause supraclavicular lymphadenopathy. Axillary lymphadenopathy is due to Staphylococcus, streptococcus, and cat scratch disease. Inguinal lymphadenopathy is due to sexually transmitted diseases (21).

In children and young adults, lymphadenopathy is typically caused by viral or bacterial infections, while malignant disorders are the primary cause of lymphadenopathy in individuals over 50 years of age. Localized or regional lymphadenopathy is commonly linked to viral infections, toxoplasmosis, connective tissue disorders, systemic lupus erythematosus, acute lymphoblastic leukemia, chronic lymphocytic leukemia, and lymphomas (22-23). The present study was undertaken to study the etiopathology of non-neoplastic and neoplastic lesions of enlarged lymph nodes by FNAC along with the study of their cytological patterns in patients presenting with lymphadenopathy in the Department of Pathology of Addis Ababa University.

1.2 Significance of the Study

The significance of studying cytological patterns in patients presenting with lymphadenopathy has clinical, diagnostic, and therapeutic implications. So, the finding helps in the early detection of various conditions, including infections, inflammatory diseases, and malignancies. Lymphadenopathy can be a sign of cancers such as lymphoma, leukemia, or metastatic carcinoma. Thus, cytological analysis provides critical information for the early identification of malignancies. So, accurate cytological diagnosis can prevent unnecessary surgeries or biopsies, reducing patient discomfort and healthcare costs. Studying cytological patterns helps in understanding the prevalence and distribution of different diseases causing lymphadenopathy in specific areas. Cytological patterns can provide insight into the prognosis of patients and this information can guide public health strategies and resource allocation.

Cytological studies contribute to the growing body of knowledge in pathology and oncology, aiding the development of new diagnostic markers and treatment protocols. Such studies provide important material for training healthcare providers, especially pathologists and oncologists, in the accurate interpretation of cytological results. This will in turn result in improved outcomes for neoplastic and nonneoplastic entities with characteristic presentation of lymphadenopathy.

2. Literature Review

Lymph node lesions at a Nepalese hospital revealed diverse findings. Of 144 FNACs, 109 were non-neoplastic, with tubercular cases dominating at 39%. Reactive features followed at 31%. Malignant lymphadenopathy comprised 35 cases, mostly metastatic (20.5%). Gender distribution was nearly equal, with a slight female majority. The 21-30 age group showed peak incidence. Cervical nodes were most commonly aspirated (69.4%), followed by supraclavicular and axillary. Tubercular lymphadenitis favored females 2:1. Reactive lymphadenitis, the second most common, showed male prevalence, especially in older age groups. Cervical and supraclavicular nodes were frequent sites. Metastatic deposits primarily originated from SCC (42%) and adenocarcinomas (34%). This study highlights the varied nature of lymph node lesions across demographics and anatomical sites (24).

A study conducted at a tertiary hospital in India found that out of 125 cases, cervical lymph nodes were the most commonly involved, with 87 cases (69.6%). Tuberculosis lymphadenitis was the most frequently diagnosed condition (24%), followed closely by reactive lymphadenitis (23.2%). Most lymphadenopathy cases (89.6%) were benign, while metastatic lymphadenitis was found in 8.8% of cases and lymphoma in 1.6%. (25)

A study at Government Medical College, Jammu, India, on the pattern of lymphadenopathy using fine needle aspiration cytology reviewed 960 cases. Of these, 830 (86%) were non-neoplastic, and 118 (12%) were neoplastic. Seven (0.7%) cases were atypical, leading to a recommendation for excision biopsy, while five cases (0.5%) were inconclusive due to unsatisfactory smears. Lymphadenopathy was observed across all age groups, from 1.5 years to 80 years, with a mean age of 44. The peak incidence for non-neoplastic lesions was 10 to 20 years, while for neoplastic

lesions, it was over 60 years. Out of the above 960 cases, 534 (59%) were males and 414 (43%) were females. (26).

A study at Hazrat Bari Imam Sarkar, Islamabad, Pakistan, found that 632 patients underwent FNAC. Tuberculous lymphadenitis was the most common diagnosis (56.1%), followed by reactive hyperplasia (28.29%). Metastatic malignancy appeared in 3.36% of cases, and lymphoma in 2.05%. Cervical lymphadenopathy was the most frequent site for TB (49.36%). Cervical lymph nodes showed metastatic cancer in 3.16% of cases and lymphoma in 1.74%. (27).

A separate study conducted in India found that the most commonly affected site was the cervical region, accounting for 897 cases (93.73%). Overall, benign lesions comprised 853 cases (89.13%), while malignant lesions accounted for 104 cases (10.87%). Among the benign lesions, tubercular lymphadenitis was the most frequently observed, with 501 cases (52.35%) (28).

A study in Imphal, Manipur, India, found a male-to-female ratio of 1:1.03 among patients aged 10 to 82 years, with the highest incidence in the 10-20 age range. The most commonly aspirated lymph nodes were, in decreasing order, cervical, inguinal, supraclavicular, submandibular, axillary, submental, postauricular, and preauricular. Of 1,000 cases, 403 were diagnosed with reactive hyperplasia, 293 with tubercular lymphadenitis, 264 with metastatic malignancy, 19 with acute suppurative lymphadenitis, and 13 with lymphomas (9 non-Hodgkin's and 4 Hodgkin's). Fungal bodies were detected in 8 cases. Among 293 tuberculosis cases, 131 showed caseation necrosis and were AFB-positive, while 172 showed granuloma without caseation necrosis and were AFB-negative. Metastatic deposits were found in 264 cases, with a slight male preponderance. Most metastatic deposits were squamous cell carcinoma, followed by adenocarcinomas, anaplastic large cell carcinoma, small cell carcinoma of the lungs, breast carcinoma deposits, undifferentiated metastatic deposits, and malignant melanoma. (29).

A study from a tertiary care center in south India on the cytological patterns of tubercular lymphadenitis and its histopathological correlation found that 200 cases (39.7%) exhibited features of tuberculous lymphadenitis. The majority (72.2%) were in their second to fourth decades of life, with a male-to-female ratio of 1:2. The cervical region was the most commonly affected site. Smears showed epithelioid granulomas with caseous necrosis in most cases (55%). AFB positivity was highest in smears showing necrosis alone, with or without epithelioid cell granulomas (76.3%). (30).

A study done at Hawassa University on the cytological patterns of lymphadenopathies revealed interesting findings. During the study period, 1,067 lymph nodes were aspirated. Cervical lymphadenopathy was most common (48.82%), followed by submandibular lymph nodes (22.77%). The 11-20 age group was the most affected, while those above 60 were less frequently affected. Tuberculous lymphadenitis was the most prevalent diagnosis (48.82%), followed by chronic non-specific lymphadenitis (20.33%), reactive lymphadenitis (16.21%), and pyogenic abscess (5.99%). The remaining cases were malignancies. (31)

A study conducted in Pakistan found that out of 632 patients who underwent FNAC, tuberculous lymphadenitis was the most frequent diagnosis, accounting for 56.1% of cases. This was followed by reactive hyperplasia at 28.29%. The sample also showed metastatic malignancy in 3.36% of cases and lymphoma in 2.05%. Cervical lymphadenopathy was the most common site for TB, observed in 49.36% of cases. Additionally, metastatic cancer in cervical lymph nodes was found in 3.16% of patients, and lymphoma in 1.74%. (32)

A study conducted in Kigali University Teaching Hospital showed out of 205 cases, 157 (76.6%) had cervical lymphadenopathy. Reactive lymphoid hyperplasia was the most encountered diagnosis (41 %) followed by tuberculous lymphadenitis (28.3%). Lymphoma was diagnosed in 12.2% of cases and metastatic lymphadenitis was seen in 6.3% of cases. (33)

3.OBJECTIVES OF THE STUDY

3.1 General Objective

The global objective of this study was to assess the cytological patterns in patients presenting with lymphadenopathy to the department of Pathology, Tikur Anbessa Specialized Hospital.

3.2 Specific Objective

The specific objectives of this study were to:

- Describe the cytological patterns in patients presenting with lymphadenopathy
- Describe sociodemographic characteristics of patients and the anatomical sites and side predilection of various lymph node lesions.

4. METHODS

4.1 STUDY DESIGN AND PERIOD

A hospital-based retrospective cross-sectional study was applied to obtain the clinicopathological and cytopathological data of patients attending the pathology department from January 2019 -December 2023.

4.2 Study Area

This study was done at the Department of Pathology, Tikur Anbessa Specialized Teaching Hospital (TASH). This is the largest referral and teaching university hospital in Addis Ababa, Ethiopia. TASH comprises one of the oldest pathology departments in Ethiopia.

4.3 Study Population

The study population comprised all the patients who had a lymph node result in pathology units of TASH, Addis Ababa, during the study period.

4.4 Eligibility Criteria

- **Inclusion criteria**
  - ✓ The inclusion criteria of the study were all patients taken a sample from the lymph node.
- **Exclusion criteria**
  - ✓ The study's exclusion criteria were patients whose sample was taken other than the lymph node.
  - ✓ Patients with two or more missing variables.

4.5 SAMPLING TECHNIQUE

Since this study is a retrospective facility-based cross-sectional study conducted with a very limited study period, all patients who had adequate information and samples taken from the lymph node during the study period and fulfilled the criteria were included.

4.6 Study Variables

4.6.1. Dependent variable:

- Pathological diagnosis
- Lymph node regions
- Lymph node number, site

4.6.2. Independent Variables:

- ✓ Age
- ✓ sex

4.7 Data Collection Tools and Procedures

Data was collected from the registry books and electronic device database in the pathology department, from the pathology department at Tikur Anbessa Specialized Hospital.

4.8 Data Processing And Analysis

After data collection, each variable was assessed for completeness based on the assigned coding. The data were then entered into SPSS version 27. Prior to data entry, the coding of individual variables was verified. Additionally, data cleaning was conducted to identify outliers, missing values, and inconsistencies before proceeding with analysis. Descriptive statistics, including frequency tables, graphs, and summaries, were used to characterize the independent variables. If outliers or missing values were detected during exploration, their causes were investigated, and if unresolved, the affected variables were excluded from the analysis. Continuous data were summarized according to their statistical distribution using measures such as mean or median, standard deviation, and interquartile range. Categorical data were reported as frequencies and proportions. Data presentation and visualization were carried out using tables and graphical charts.

4.9 Data Quality Assurance

The data collection was done by the principal investigator through a structured data collection protocol, and supervision was done for completeness and keeping it for analysis.

4.10 Operational Definitions

Lymphadenopathy: - refers to the abnormal enlargement of lymph nodes. It is a common clinical finding that can be localized (involving a specific group of lymph nodes) or generalized (involving multiple lymph node groups throughout the body).

Generalized lymphadenopathy- A lymphadenopathy involving more than two non- contiguous lymph node groups

Cytological pattern: - refers to the microscopic characteristics and arrangement of cells observed during cytological examination, particularly from tissue or fluid samples.

In the context of lymphadenopathy, cytological patterns help in diagnosing the underlying cause of lymph node enlargement, including infections, malignancies, or inflammatory conditions.

4.11 ETHICAL CONSIDERATIONS

Following the presentation of the proposal to the Department of Pathology, approval was obtained from the department's research and ethics committee. A letter of cooperation was then submitted to the relevant units, including the Head of the Pathology Department. As a retrospective study, all data were extracted from logbooks or electronic records. All information obtained from the charts will remain confidential and will not be disclosed to any third party.

5. RESULTS

Sociodemographic characteristics of the study population

A total of 840 cases were selected for analysis having met the inclusion criteria and having complete demographic and clinical data. Of the total 840 cases, 508 (60.5%) were females and 332 (39.5%) were males making the F: M ratio of 1.53:1. The mean, standard deviation, lowest and highest age limits were 35.7 yrs, 19.6, 6 month and 85 years respectively.

Most patients were 31-40 years old, accounting for 172(20.5%) cases, followed by 41-50 (18.5%) and 50-65 (15%). (Figure 1)

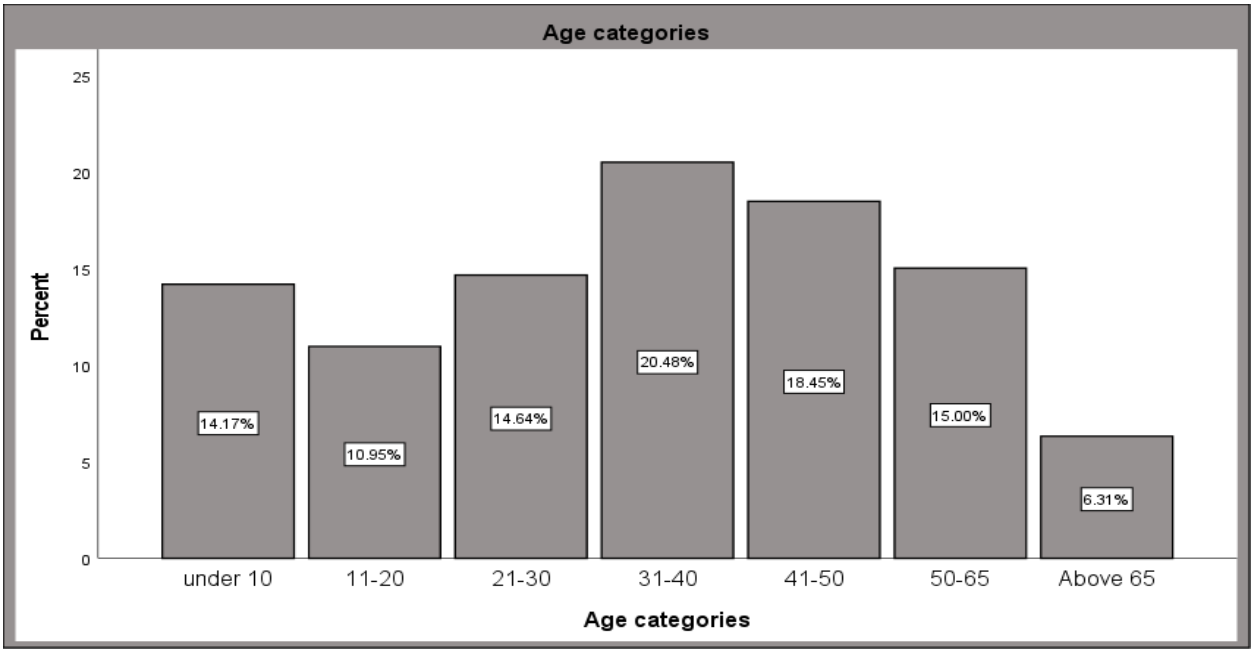

Figure 1- Age groups all cases.

Cytomorphological patterns

The majority of the lymphadenopathies were localized (91 %) and involved the left side of the body (40.5%). The most commonly involved lymph node group was cervical (51.4%), followed by axillary (25.4%).

Regarding the cytomorphologic patterns observed, 534 (63.6%) cases were neoplastic, 293 (34.9%) cases were non-neoplastic and 13 (1.5%) cases were reported as ‘’see description”. Cases reported as “see description” were excluded from further evaluations. (Figure 2)

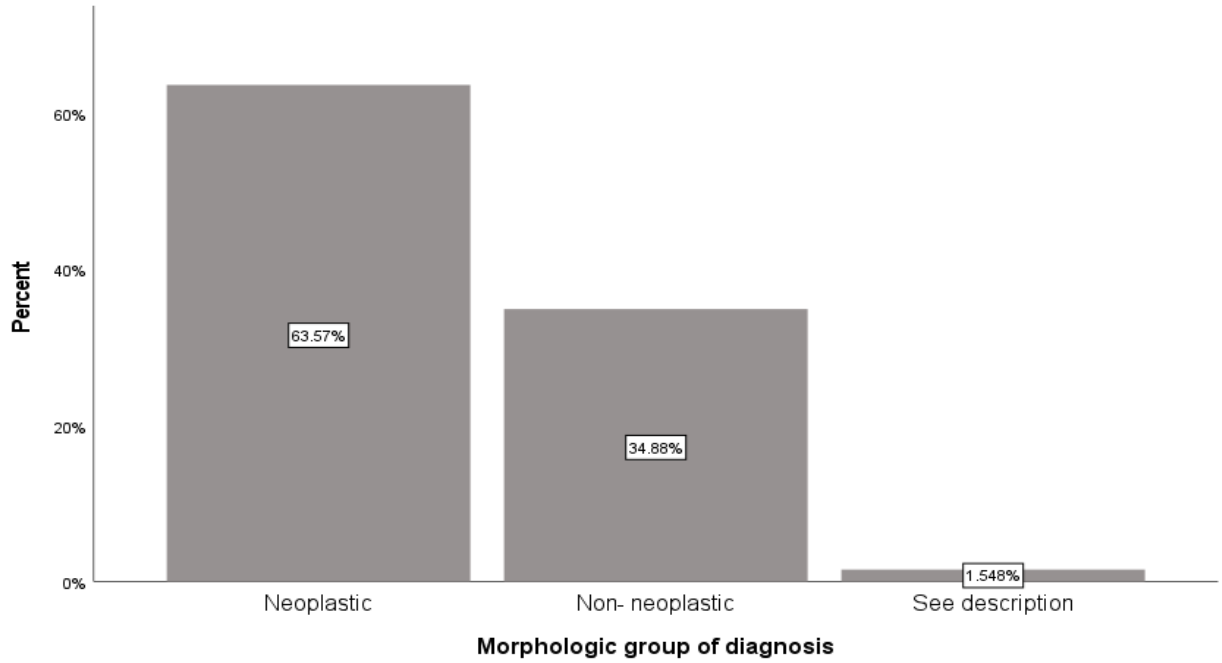

Figure 2- Morphologic groups of diagnoses.

Metastatic tumors were the most common cytological diagnosis, accounting for 388 cases (46.19%). This was followed by reactive lymphadenitis with 177 cases (21%), lymphoma with 143 cases (17%), and tuberculous lymphadenitis with 87 cases (10.4%). (Figure 3)

In patients under the age of 20 years, reactive lymphadenitis is the most common diagnosis (47.9%), followed by lymphoma (31.1%) and tuberculosis (10.1%). Metastatic lymphadenitis is the least reported diagnosis (2.5%).

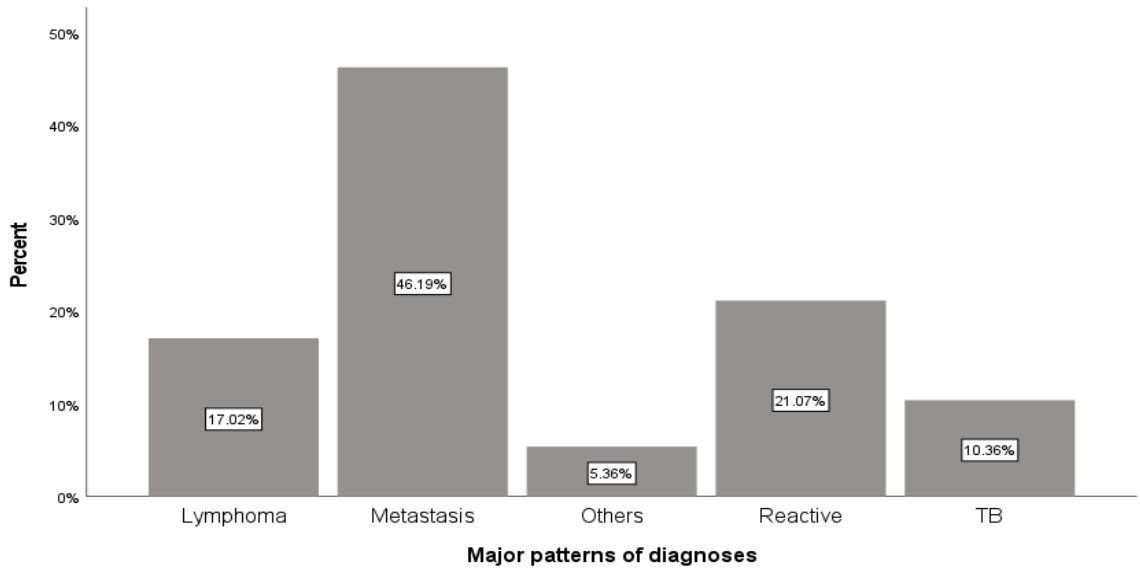

Figure 3- Major patterns of diagnoses

Non-neoplastic lesions

Among the non-neoplastic lesions, reactive lymphadenitis was the most frequently diagnosed, occurring in 177 cases (59.8%). This was followed by tuberculosis lymphadenitis, found in 87 cases (29.4%). There were also diagnoses of granulomatous inflammation in 12 cases (4.1%), pyogenic lymphadenitis in 13 cases (4.4%), Rosai-Dorfman disease in 3 cases (1%) and Langerhans Cell Histiocytosis* in 2 cases (0.7%). (Figure 4)

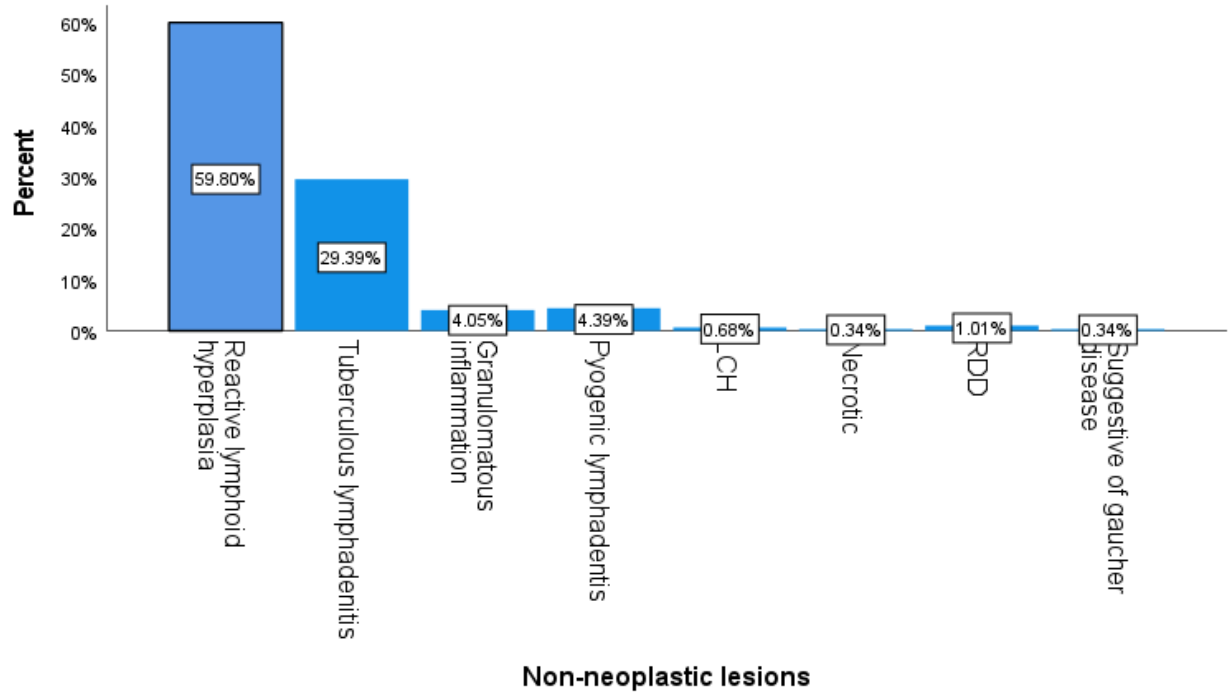

Figure 4- Frequency distribution of non-neoplastic lesions

Within non-neoplastic lesions, reactive lymphadenitis was seen mostly in the first three age groups [(57(32.2%) in ≤ 10 yrs; 28(15.8%) in 11-20 yrs and 26 (14.7%) in 21-30yrs] followed by tuberculosis [16.1% in 11-20 yrs, 25.2% in 21-30 yrs and 21.8% in 31-40 yrs]. Granulomatous inflammation has the highest frequency among 21-30 and 30-40 years (both 25%). Pyogenic lymphadenitis showed the highest among patients below 10 years and 11-20 years (23.1%). (Table S-1)

*Current opinion and evidences (of clonality and BRAF driver mutation) favor LCH is a neoplastic entity.

Most benign lesions occurred in the cervical lymph node groups 196 (66.2%) followed by inguinal lymph node 41(13.8%) and axillary lymph node 36 (12.1%) (Table S-2). Localized lymphadenopathy was observed in 286 patients (98%) with non-neoplastic lesions while generalized lymphadenopathy occurred in 7 patients (2%).

Neoplastic lesions

Among the neoplastic lesions secondaries of ductal carcinoma was most prevalent (147 cases, 24.7%), followed by secondaries of carcinoma (96 cases, 18.1%) and high- grade non-Hodgkin lymphoma (48 cases, 9.1%). (Figure 5)

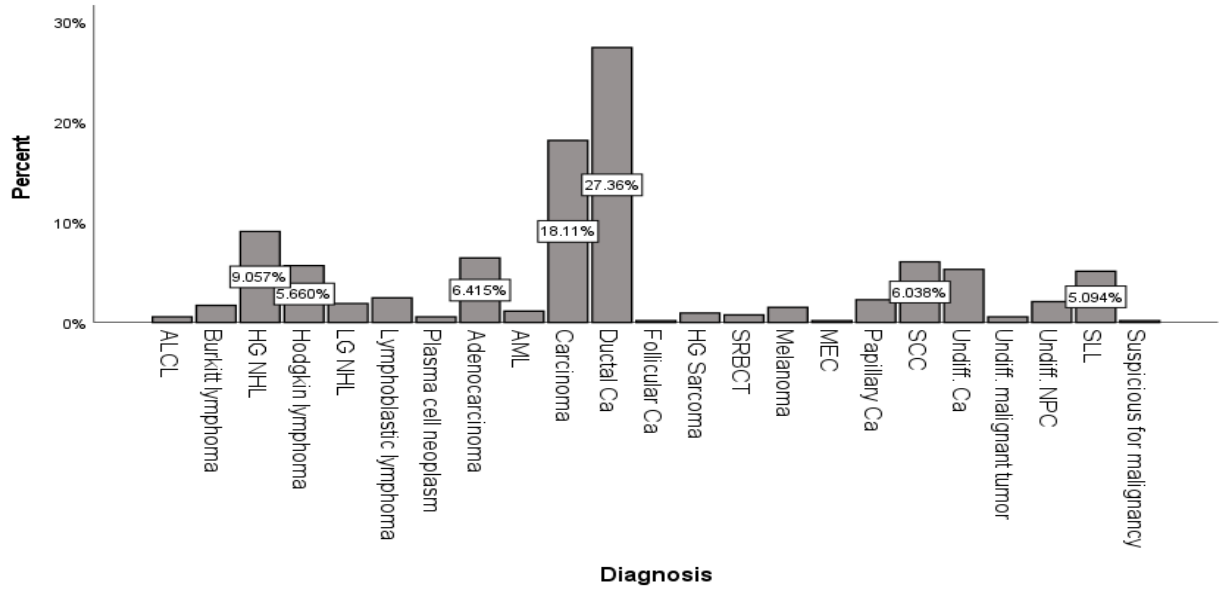

Figure 5- Frequency distribution of neoplastic lesions

Comparison between lymphoma and metastatic lymphadenopathies

Among the neoplastic lesions metastasis to lymph nodes accounted for 73% of cases and primary neoplastic lymphoid lesions accounted for 27% of cases (Figure 6). The highest number of cases of lymph node metastasis were recorded in the age groups 41-50 (109 cases), 31-40 (104 cases) and 50-65 (66 cases) respectively. While lymphomas where more prevalent below age 10 (37 cases), 50-65 (29 cases) and 11-20 (22 cases). Axillary, cervical, and inguinal lymph node groups were involved in 162, 161 and 42 cases of lymph node metastasis respectively. On the other hand, lymphomas more commonly involved the cervical group of lymph nodes either alone (65 cases) or as part of a generalized lymphadenopathy (37 cases). (Table S-3)

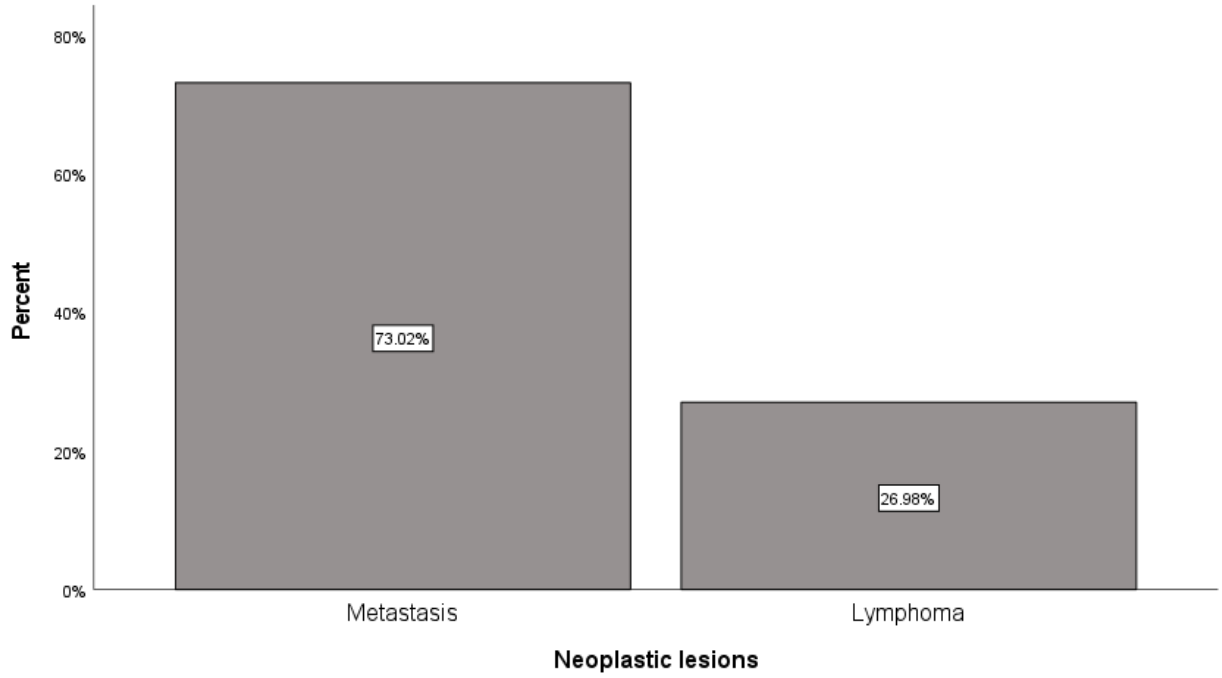

Figure 6- frequency distribution of metastatic lymphadenopathies and lymphoma

Lymphoma

By traditional broad classification of lymphoid lesions in the current study, non-Hodgkin lymphomas make up the majority (79.02%) and Hodgkin lymphoma constitutes the rest (20.08%).

In turn high grade NHL constitute the highest number of cases among NHL (42.5%), followed by SLL (23.9%) and lymphoblastic lymphoma (11.5%) (Figure 7). Majority of the patients with non-Hodgkin lymphoma were male (61.1%) and were in the age group of below 10 (24.8%), 50-65 (23.9%) and 31-40 (14.2%) (Table 7). The most commonly involved lymph node group is cervical, either alone (40.71%) or in conjunction with axillary and inguinal lymph nodes (30.97%)(Figure S-1). Most patients had localized lymphadenopathy (58.65%).

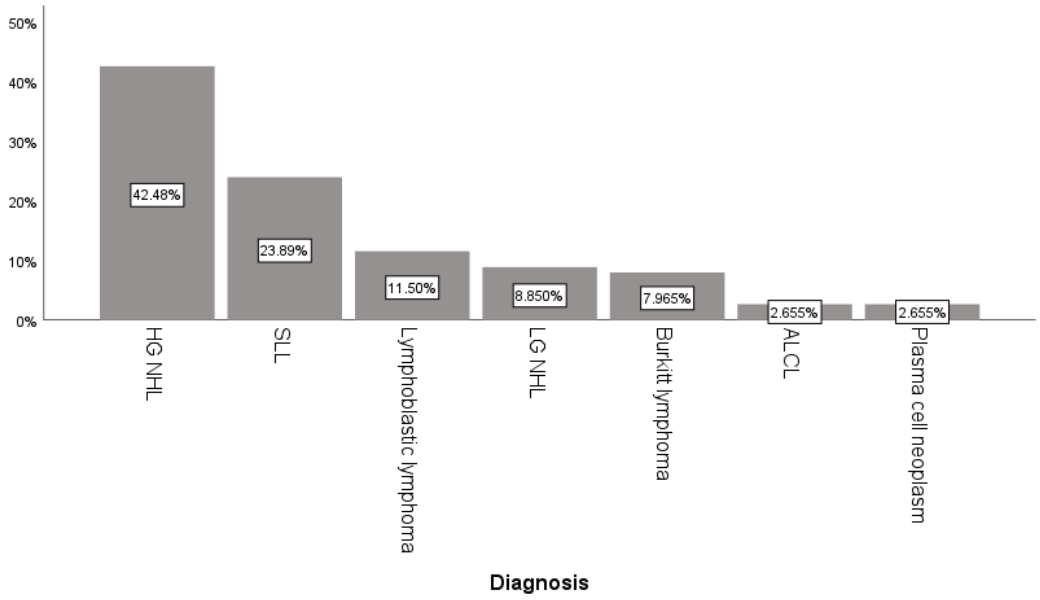

Figure 7- Frequency distribution of diagnosis of non-Hodgkin lymphoma

Looking at Hodgkin lymphoma, the peak age groups are 11-20 (33.3%), under the age of 10 (30%) and 21-30 (16.7%). There is a slight male preponderance (56.7%) and cervical (63.3%) and axillary (20%) lymph nodes are most commonly involved. (Table 1)

Age categories	N	%
under 10	9	30.0%
11-20	10	33.3%
21-30	5	16.7%
31-40	1	3.3%
41-50	1	3.3%
50-65	2	6.7%
Above 65	2	6.7%

Lymph node group	N	%
Axillary	6	20.0%
Cervical and axillary	2	6.7%
Cervical	19	63.3%
Inguinal	1	3.3%
Intraabdominal	2	6.7%

Sex	N	%
Female	13	43.3%
Male	17	56.7%

Table 1- Frequency distribution of Hodgkin lymphoma based on sex, age groups and lymph node groups

Metastatic lymphadenopathies

Regarding metastatic lymphadenopathies, carcinomas are by far the leading diagnoses (93%) followed by Melanoma (2%) and AML (1.5%) (Figure 8). The majority of patients were female (68.8%) and presented with localized lymphadenopathy (97.4%).

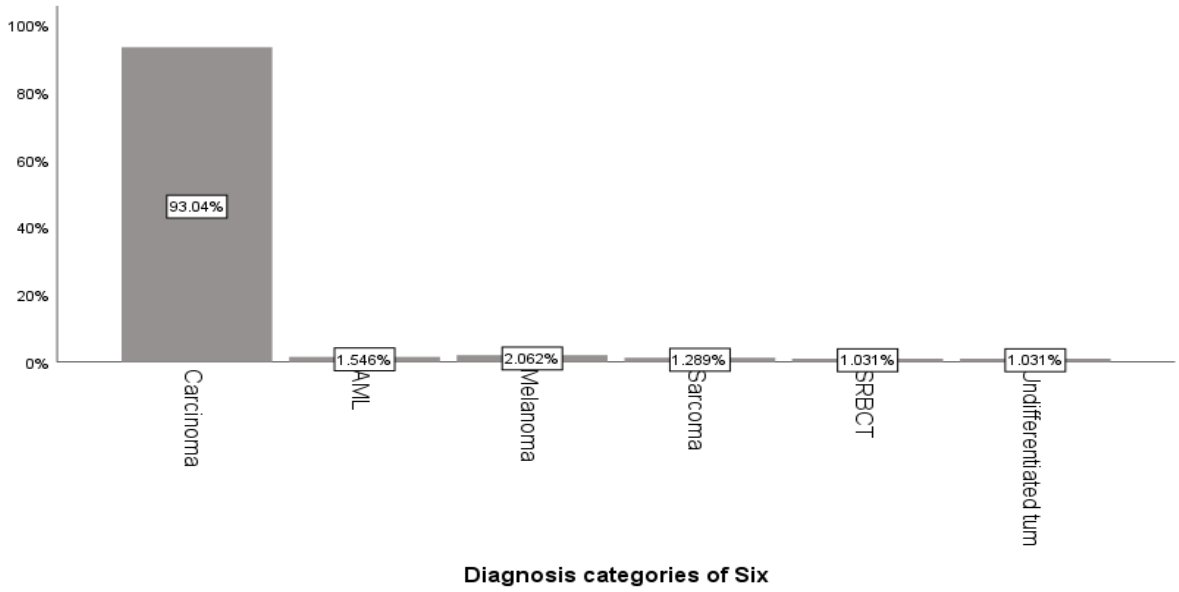

Figure 8- Frequency distribution of metastatic lymphadenopathies

Looking at carcinomas in particular, ductal carcinomas were most prevalent (40.4%), followed by carcinoma (27%), and adenocarcinoma (9.4%) (Figure 9). Most patients were female (70.9%) in the age group of 31-65 (74.9%). Ductal carcinoma involved predominantly the axillary group of lymph nodes (108 cases), while carcinoma involved cervical lymph nodes (41 cases), and squamous cell carcinoma involved inguinal lymph nodes (15 cases). (Table S-6)

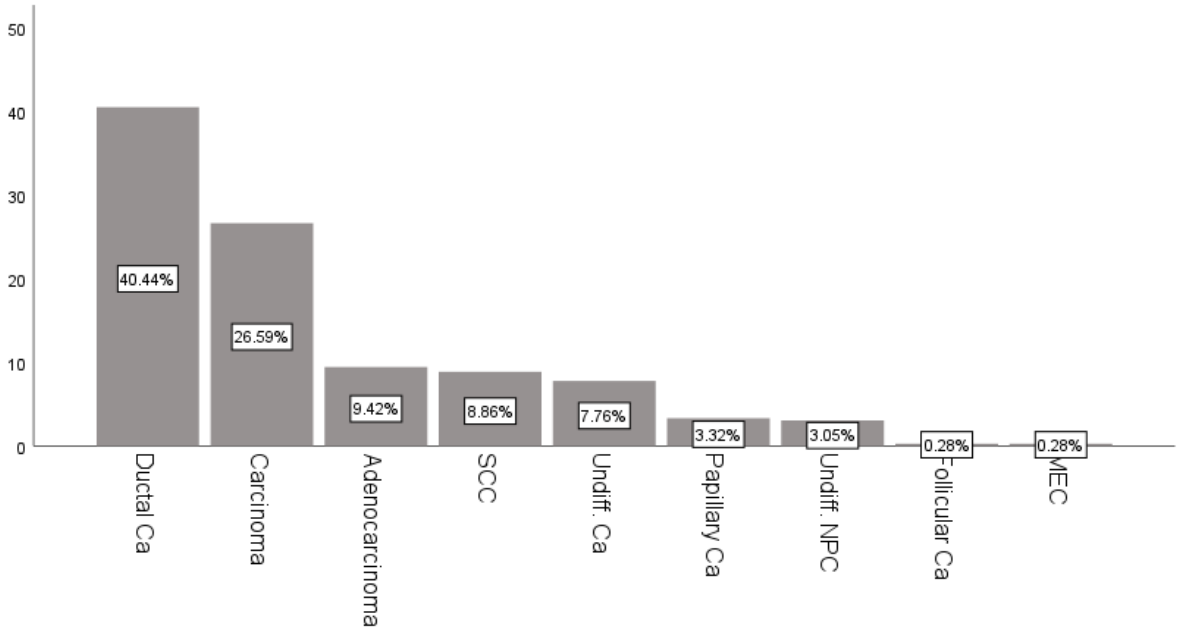

Figure 9- Frequency distribution of metastatic carcinomas

6. DISCUSSION

Fine needle aspiration of lymph nodes is a relatively simple, safe, cost effective and rapid procedure most suited for low- income countries like Ethiopia. It continues to play a pivotal role in the work up of patients with non- specific lymphadenopathies. It is used to guide the management of patients with lymphadenopathies and decreases the need for expensive and invasive procedures such as open biopsies.

In our current study, out of 840 cases evaluated 508 (60.5%) were females and 332 (39.5%) were males making the F: M ratio of 1.53:1. This is in contrast to studies done in Hawassa, Ethiopia and Manipur, India which showed slight male preponderance (31,29). The highest number of cases were recorded in the age group 31-40 ,172(20.5%). This is also different from studies done in several places including India (25,26), Pakistan (32) and Hawassa, Ethiopia (31), which reported 11-20 and 21-30 as the most prevalent age group. This difference could be attributed to the difference in the frequency of benign and malignant lesions in the current study as compared to the previous studies.

Cervical lymph nodes are the most commonly involved group of lymph nodes (51.4%) which is similar to studies from Hawassa, Ethiopia (31), Nepal (24), and Jammu, India (26).

Metastatic Lesions are the most frequent diagnoses accounting for 46.2% of cases followed by reactive lymphadenitis (21.02%) and lymphoma (17.02%). This pattern of distribution of diagnoses is different from all the studies included in the literature review which showed higher prevalences of reactive lymphadenitis and tuberculosis (24,25,26,27,28,29,31,32). This difference can be explained by the nature of the patient population of Tikur Anbessa Hospital which is predominated by oncologic patients (a significant proportion of patients present with an already diagnosed tumor which required evaluation of lymph nodes for metastasis). Carcinomas make up the bulk of metastatic lesions (93.04%) which in turn is predominated by ductal carcinoma (40.44%). Most patients were female (70.9%), between the ages of 31-65 (74.9%) and had involvement of the axillary lymph nodes (160/388 cases). These findings could be due to the high number of breast carcinoma cases evaluated for lymph node metastasis.

Lymphomas make up the second largest group of neoplastic lesions (26.96%) in the current study. Among lymphomas, non-Hodgkin lymphomas (79.02%) are more common than Hodgkin lymphoma (20.98%). Similar findings have been reported by a group from Jammu, India (26) and Hawassa, Ethiopia (31).

Hodgkin lymphoma is more common below the age of 30 (80%) and majorly involves the cervical lymph nodes (63.3%). Males are the slight majority (56.7%). Similar results are reported from a study done in Hawassa, Ethiopia, who found that Hodgkin lymphoma is more common in the first three decades (85.7%) and also reported a male majority (71.4%) (31). A study from Karachi Pakistan found cervical group of lymph nodes were most commonly enlarged in cases of Hodgkin lymphoma (90% of cases of HL). (32)

Among the non-neoplastic conditions, reactive lymphoid hyperplasia comprise the overwhelming majority (59.8%). It is most commonly reported in patients under the age of 10 (32%), while it is least reported in patients aged above 65 years (5.6%). Cervical group of lymph node involvement is most commonly seen (59.8%). Similar findings were reported by studies from Hawassa, Ethiopia, which stated the most commonly affected age group was <10 years (31.2%) (31). A study from Karachi, Pakistan also found similar findings; 50% of patients were below 20 years old and 31% had cervical lymphadenopathy (32). A study from Jamu, India had also similar findings; 58.7% of patients were below 20 years old and 86.7% of patients had cervical lymphadenopathy (26).

Tuberculous lymphadenitis comprises 29.4% of the non-neoplastic lesions. It most commonly involved cervical group of lymph nodes (77%). The highest number of cases were seen in 21-40 age group (47%). Studies from Jammu, India and Karachi, Pakistan, showed similar findings regarding the most commonly involved lymph nodes group which is cervical (80% and 49.3% respectively) (26,32). However, the above studies found a slightly younger age group to be most affected by TB lymphadenitis; < 20 years old in Pakistan and 21-30 years old in Jammu, India. (26,32)

7. CONCLUSION

Lymphadenopathy is a common presentation of various clinical condition requiring prompt and accurate diagnosis to provide treatment as early as possible. FNAC is the first line valuable tool for the diagnosis of lymph node lesions.

In general, various lymph node lesions with different age, anatomic and sex distribution were observed.

Compared to multiple publications, in the current study, there is a significant burden of metastatic carcinoma, particularly ductal carcinoma.

Reactive lymphoid hyperplasia and tuberculous lymphadenitis are the most commonly encountered benign lesions.

Lymphomas are the second most common neoplastic condition after metastasis to lymph nodes.

Cervical lymph nodes are the most common anatomic site of lymphadenopathy.

8. LIMITATIONS OF THE STUDY

This study has not tried to evaluate the correlation between size of lymphadenopathy with diagnostic pattern. This is due to the lack of documentation of lymph node size in a significant proportion of the cases.

9. RECOMMENDATIONS

There are significant discrepancies in the reporting formats of cytology of lymph nodes. It will be better to devise a local reporting format or adopt standardized international reporting schemes.

There are gaps in patient data management with some missing and incomplete patient information. Better data management will be key for future studies.

There is lack of application of ancillary tests such as flow cytometry, IHC, cytogenetics and molecular tests which are important for proper classification of diagnostic entities. The application of these ancillary tests has to evaluated case by case whenever available (i.e. evaluation of cases suspicious for lymphoma or metastasis of unknown primary).

There is lack of application of special stain like Ziehl–Neelsen (ZN) stain for acid-fast bacilli (AFB) considering the high burden of tuberculous lymphadenitis in our part of the world. This will be instrumental to confirm the diagnosis of tuberculosis in typical cases as well as cases with granulomatous inflammation without caseous necrosis.

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11. SUPPLEMENTARY TABLES AND FIGURES

	Granulomatous inflammation	LCH	Necrotic	Pyogenic lymphadentis	Reactive lymphoid hyperplasia	RDD	Suggestive of gaucher disease	Tuberculous lymphadenitis
under 10	2	2	0	3	57	1	0	12
11-20	0	0	0	3	28	1	1	14
21-30	3	0	1	2	26	0	0	22
31-40	3	0	0	1	25	0	0	19
41-50	2	0	0	2	14	1	0	9
50-65	1	0	0	2	17	0	0	11
Above 65	1	0	0	0	10	0	0	0

Table S-1- Frequency distribution of non-neoplastic lesions based on age groups.

	Granulomatous inflammation	LCH	Necrotic	Pyogenic lymphadentis	Reactive lymphoid hyperplasia	RDD	Suggestive of gaucher disease	Tuberculous lymphadenitis
Axillary	0	0	0	2	26	0	0	8
Cervical and axillary	0	1	0	0	6	0	0	1
Cervical	9	1	0	9	106	3	1	67
Cervical and inguinal	0	0	0	0	1	0	0	0
Epicondyle	0	0	0	0	1	0	0	0
Inguinal	2	0	0	0	31	0	0	8
Intraabdominal	0	0	1	0	1	0	0	2
Periauricular	1	0	0	2	5	0	0	1

Table S-2- Frequency distribution of non-neoplastic lesions based on lymph node group involved.

	Lymphoma	Metastasis
Age categories		
	Count	Count
under 10	37	3
11-20	22	21
21-30	13	52
31-40	17	104
41-50	15	109
50-65	29	66
Above 65	10	32
Lymph node group		
Axillary	12	162
Axillary and Inguinal	3	2
Cervical and axillary	21	14
Cervical	65	161
Cervical and inguinal	6	1
Cervical, axillary and inguinal	16	0
Epicondyle	0	0
Inguinal	9	42
Intraabdominal	11	0
Periauricular	0	5

Table-S-3- Frequency distribution of neoplastic lesions (metastasis and lymphoma) based on age group and lymph node group

Sex	N	%	*Age categories*	N	%
Female	44	38.9%	under 10	28	24.8%
Male	69	61.1%	11-20	12	10.6%
			31-40	16	14.2%
			41-50	14	12.4%
			50-65	27	23.9%
			Above 65	8	7.1%

Table- S-4- Frequency distribution of non-Hodgkin lymphoma cases based on sex and age groups.

	Adenocarcinoma	Carcinoma	Ductal Ca	Follicular Ca	MEC	Papillary Ca	SCC	Undiff. Ca	Undiff. NPC
Axillary	4	41	108	0	0	0	4	3	0
Axillary and Inguinal	0	0	0	0	0	0	0	1	0
Cervical and axillary	2	4	7	0	0	0	0	0	1
Cervical	16	41	31	1	1	11	12	24	10
Cervical and inguinal	0	0	0	0	0	0	0	0	0
Cervical, axillary and inguinal	0	0	0	0	0	0	0	0	0
Epicondyle	0	0	0	0	0	0	0	0	0
Inguinal	12	7	0	0	0	0	15	0	0
Intraabdominal	0	0	0	0	0	0	0	0	0
Periauricular	0	3	0	0	0	1	1	0	0

Table S-6- Frequency distribution of metastatic carcinomas based on lymph node groups

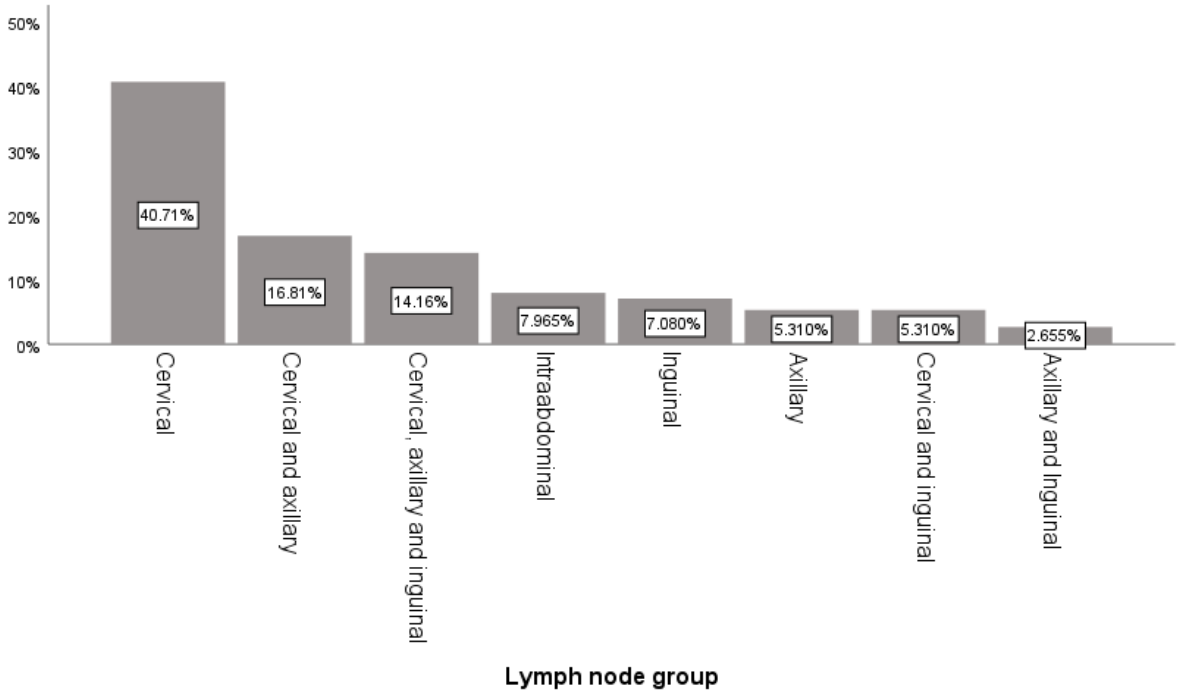

Fig- S-1- Frequency distribution of lymph nodes groups involved by non-Hodgkin lymphoma.