

# Histopathologic Patterns of Lymph Node Diseases Among Patients Diagnosed in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia

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**Abstract:** Lymphadenopathy is one of the most typical clinical presentations in patients of all age groups. The causes are different based on age, sex, duration, and patterns of involvement. There is a lack of evidence on histopathologic patterns of lymph node diseases. This study aims to determine the histopathologic pattern of lymph node diseases diagnosed in Hawassa university's comprehensive specialized hospital. An institution-based cross-sectional study was conducted among 188 histopathologically diagnosed lymph node biopsies received from September 2014 to August 2020 at Hawassa university's comprehensive specialized hospital (HUCSH). All the samples collected for the diagnoses at a given period were included in the study. The collected data was cleaned and entered into open Epi- version 3 and exported to SPSS version 20 statistical software for analysis. Descriptive analyses like frequency distribution, proportion and dispersion were calculated. The finding was presented using frequency tables, graphs, and charts. Both univariate and multivariate analyses were done. The Adjusted Odd Ratio (AOR with 95% CI) was used to show the strength of the association, and a P-value of  $\leq 0.05$  was considered statistically significant. Of the 188 lymph node biopsies, 119 (63.3%) were male cases, and 69 (36.7%) were female cases. The age range of the study subjects is 1 to 84 years, with a mean of  $31.28 \pm 18.64$  years. Localized lymphadenopathy (LAP) was found in 168 (89.4%) of the patients, and the remaining 20 (10.6%) were generalized. Among localized LN groups, cervical, mesenteric, and inguinal LN groups are the most commonly biopsied groups accounting for 66 (35.1%), 55 (29.3%) and 14 (7.4%), respectively. Regarding the size, 72.2% of benign reactive conditions were less than 2cm, whereas 74.5% of lymphomas have a size of at least 2cm. 86.9% of nonspecific reactive conditions have a duration of less than one month, whereas 89% of malignant conditions collectively presented with LAP of more than 1-month duration. A third of 61 (32.4%) were identified as histopathologically reactive nonspecific conditions and lymphomas consist 44 (23.4%) and metastatic lesions (40, 21.3%) and tuberculosis lymphadenitis (36, 19.1%). This study's histopathologic pattern of Lymph Node (LN) disease was comparable with other developing countries. Reactive nonspecific conditions and tuberculous lymphadenitis are more common before the age of 45 years. Metastatic lesions were found more common after the age of 45 years.

**Keywords:** Reactive Nonspecific Conditions, Localized LAP, Histopathologic Pattern

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## 1. Background

Lymph nodes are one of the components of the lymphoreticular system, which play a vital role in filtering and trapping viruses, bacteria, and other pathogens. Under normal circumstances, they tend to be less than one centimetre, but they can be as large as 1.5 cm in inguinal and submandibular areas, particularly in adolescents and young adults, due to repeated infections of the lower extremities and oral cavity [1].

Lymphadenopathy is one of the common clinical problems and based on the age and sites of involvement, and the causes can be broadly classified as inflammatory (including infectious and autoimmune causes), metastatic lesion and lymphoma [2-4].

The specific disease process classifying as localized when it involves a single region, such as cervical or inguinal, and generalized when it involves more than one region is paramount for a clinician. Head and neck infections like Epstein-var virus and Cytomegalovirus can manifest by anterior cervical lymphadenopathy. In contrast, the usual presentation for malignancies like lymphoma and metastatic carcinoma from the head and neck region is challenging posterior cervical lymphadenopathy, particularly in the elderly [1, 5].

Supraclavicular lymphadenopathy carries the highest risk for harboring malignant conditions as evidenced by two studies with an estimated risk of 34 and 50 percent, particularly in patients above 40 [6, 7]. Malignant neoplasms involving the lungs, mediastinum, and esophagus drain to right supraclavicular lymph nodes, as left supraclavicular lymph nodes (Virchow's node) usually harbour metastatic lesions from abdominal and pelvic organs, stomach, gallbladder, ovaries, testis, and the like [8].

Infections involving the upper extremities, thoracic wall, and breast silicone breast implants may present as axillary lymphadenopathy in the form of inflammatory and foreign body reactions [9, 10]. The risk of the metastatic deposit is higher in older women [11].

As it is draining from the lower extremities, which are susceptible to different injuries, the frequent causes for inguinal lymphadenopathy are infections and metastasis from the respective sites. Infections and metastatic lesions from the pelvic structures like the cervix, vulva, rectum, and anus can also drain the inguinal lymph nodes [12]. Infections like HIV, infectious mononucleosis, and tuberculosis can present as waning and waxing generalized lymphadenopathy and matted lymph nodes at multiple sites, respectively. Malignant lymphomas can also be shown as indolent waxing and waning or massive generalized lymphadenopathy, depending on the specific types of lymphomas [13, 14].

## 2. Methods

### 2.1. Study Area and Period

The study was conducted from July to September 2020 in

HUCSH, which is found in Hawassa town, Sidama regional state of South Ethiopia. HUCSH is located 270 km southeast of Ethiopia's capital city, Addis Ababa, with an estimated population of around 258,808. HUCSH is the first referral hospital established in the region, serving as a teaching hospital for the College of Medicine and Health Science of Hawassa University, with a catchment population of 10-12 million. It serves about 43,384 patients of all types per year. Cytology and Histopathology services are available in the pathology department.

### 2.2. Study Design, Study Population and Sampling

A facility-based cross-sectional study design was used. All tissue biopsy specimens received, processed, and reported at the HUCSH department from September 2014 to August 2020 were used.

All LN specimens received, processed, and reported at the HUCSH department of pathology are included in the study.

### 2.3. Data Collection and Quality Control

After approval from the Institutional Review Board (IRB) of HUCSH, the principal investigator prepared a checklist after reviewing pertinent literature. The training was given to data collectors on data collection procedures, and the principal investigator, principal investigator, and principal investigator checked the completeness for any inconsistency and ambiguity. Finally, it was fed into the computer and analyzed and interpreted.

### 2.4. Data Analysis

The collected data is cleaned and manually entered into open Epi- version 3 and exported to SPSS version 20 statistical software for analysis. Descriptive analyses like frequency distribution, proportion and dispersion were calculated. The finding is presented using frequency tables, graphs and charts. Both univariate and multivariate analyses were done. A P value of  $\leq 0.05$  was considered statistically significant.

### 2.5. Operational Definition

*Lymphadenopathy:* Lymph node enlargement  $> 1$  cm in extra inguinal regions and  $> 1.5$  cm in inguinal region.

## 3. Result

### 3.1. Socio-demographic Data

In this study, a total number of 188 lymph node biopsies were analyzed with 119 (63.3%) male cases and 69 (36.7%) female cases (M:F = 1.7:1). The age range of the study subjects is 1 to 84 years, with a mean of  $31.28 \pm 18.64$  years.

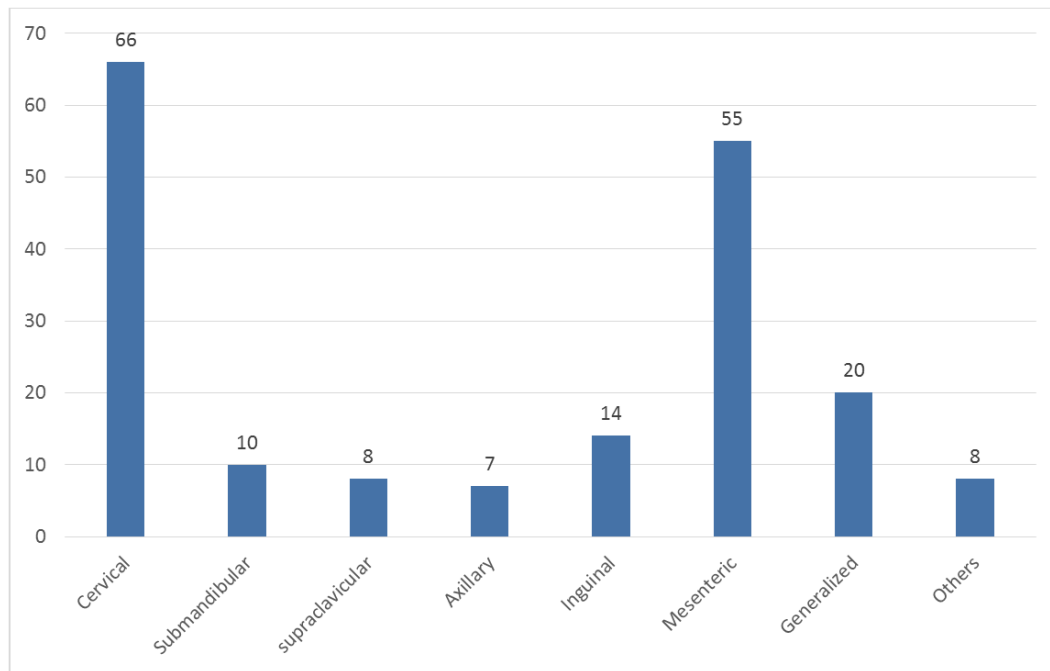
#### *Clinical Data*

#### *Distribution of LAP with Regard to LN Groups*

Localized LAP is found in 168 (89.4%) of the study subjects and the remaining 20 (10.6%) are generalized. Among localized LN groups, cervical, mesenteric, and inguinal LN groups are the most commonly biopsied groups

accounting for 66 (35.1%) 55 (29.3%) and 14 (7.4%) respectively (Figure 1). Regarding the size, 72.2% of benign

reactive conditions are with a size of less than 2cm, whereas 74.5% of lymphomas have a size of at least 2cm.

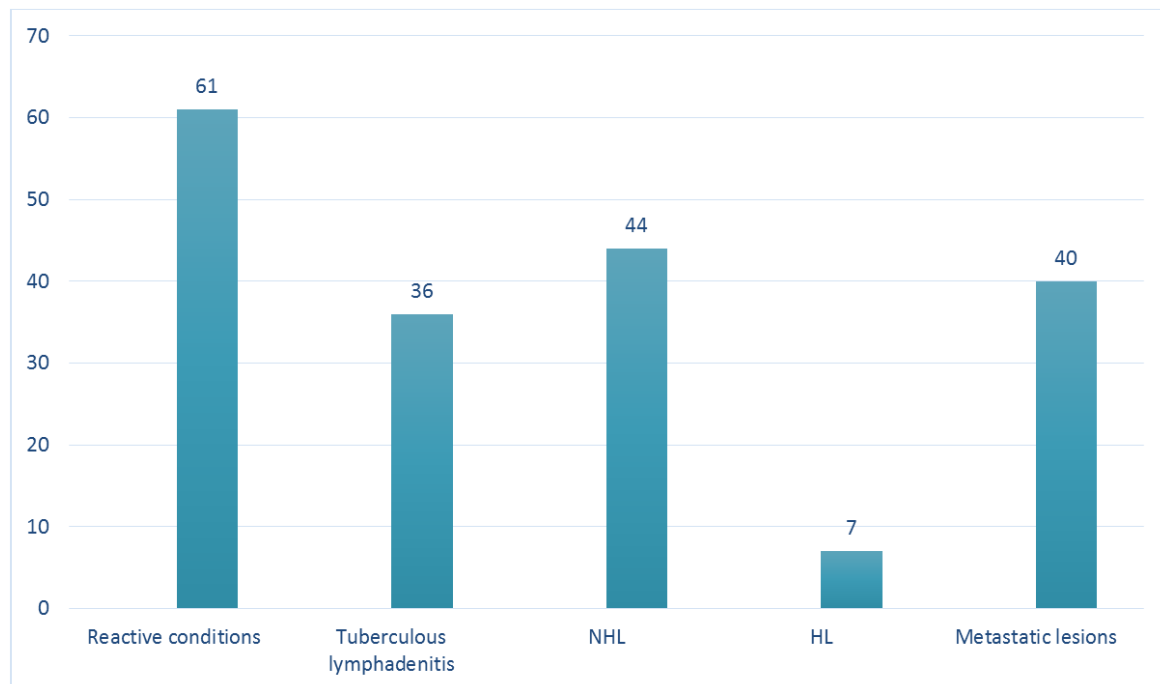


**Figure 1.** Distribution of LAP in patients with LN biopsy at HUCSH 2014-2020.

### 3.2. Patterns of Histopathologic Diagnosis

Histopathologically reactive nonspecific conditions (including cortical, paracortical hyperplasia and sinus histiocytosis) and lymphomas (both Hodgkin's and non

Hodgkin's) are the most common histopathologic findings consisting of 61 (32.4%) and 44 (23.4%) respectively followed by metastatic lesions (n=40, 21.3%) and tuberculosis lymphadenitis (n=36, 19.1%) (Figure 2).



**Figure 2.** Patterns of histopathologic diagnosis of LN biopsy in HUCSH 2014-2020.

The majority, 86.9% of nonspecific reactive conditions have less than one month, whereas 89% of malignant

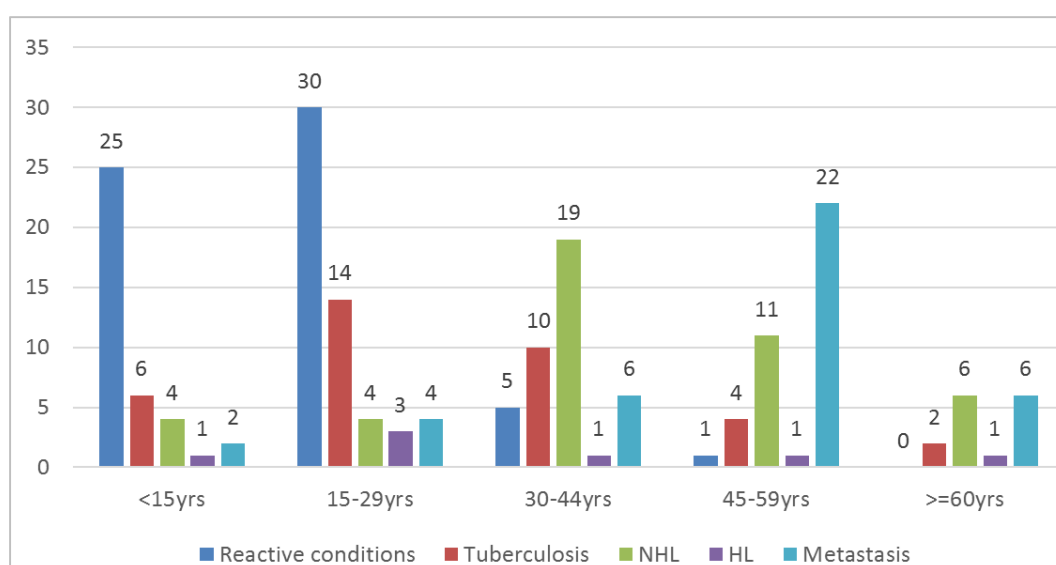
conditions collectively presented with LAP of more than 1-month duration.

Histopathologically reactive nonspecific conditions (including cortical, paracortical hyperplasia and sinus histiocytosis) and lymphomas (both Hodgkin's and non-Hodgkin's) are the most common histopathologic findings consisting of 61 (32.4%) and 44 (23.4%) respectively followed by metastatic lesions (n=40, 21.3%) and tuberculosis lymphadenitis (n=36, 19.1%).

Cervical LNs are commonest groups to be involved by tuberculous lymphadenitis (n=17, 47.2%) and to harbor metastatic deposits (n=23, 57.5%). Generalized LAP is the most typical presentation for NHL (n=16, 36.4%) whereas

mesenteric groups are the primary sites to be affected by nonspecific reactive conditions (n=45, 73.8%).

Non-neoplastic conditions like reactive lymphoid hyperplasia and tuberculous lymphadenitis are more common in patients under 45 years of age. (Figure 3)., The majority of metastatic lesions (70%), are seen in patients with the age of older than 45 years with the age range of 12 – 75 years, and mean age of  $46 \pm 14.942$  years, which shows a strong association between the patient's age and the risk of harbouring metastatic lesions ( $X^2 = 41.639$ ,  $df = 3$ ,  $p < 0.001$ ). As compared to patients with the age of <15 yrs, those with the age of above 45 years have high probability of harboring metastatic deposits with high statistical significance.



**Figure 3.** Correlation of age and histopathologic diagnosis at HUCSH and YMSC.

## 4. Discussion

Cervical LNs are the most affected groups comprising 35.1% in our study; similar results was also found in Nigerian studies {Kano (46%), Lagos (39.3%), Ilorin (42.6%)}, and Turkey (38.3%) [15-18].

Reactive nonspecific lymphadenitis comprises 32.4% in our study which is comparable with some of Nigerian studies {Lagos (34%) and Ibadan (35%)}, Nepal (36%) while higher than the finding in some others Nigerian studies {Kano (27%), Benin (19%)}, and TASH, Ethiopia (26%), this can be explained by the inclusion of mesenteric LNs majority of which are diagnosed as reactive nonspecific lymphadenitis. [15, 16, 19-22].

19.1% of our study subjects are diagnosed with tuberculous lymphadenitis which is in a proximity with the results of Nigerian studies {Lagos (17.4%) and Benin city (26%)}, and Iraqi (25%). [16, 21, 23]. Whereas this figure is much lower than other studies in TASH, Ethiopia (47.8%), Nepal (47%), and Pakistan (49.3%) [22, 20, 24] this could be due to the growing utilization of HAART, selection or referral bias and the figure is much higher than that of

Chicago (5.8%) [25] This is mainly due to low socioeconomic status and associated unsanitary conditions with subsequent risk of acquiring various infections including tuberculosis.

Cervical groups of LN are the commonest site of involvement for tuberculous lymphadenitis (47.2%) which is also comparable with the result in Nepal (52.2%) [20], and lower than studies in India (56%) and Benin (65%) [26, 21], this can also be explained by the inclusion of mesenteric LN groups in which tuberculous lymphadenitis is the second most common finding as opposed to other studies which are done on peripheral LAP exclusively.

Majorities of tuberculous lymphadenitis were found in patients with age of fewer than 45 years of age (80.3%) which is also comparable with Kano (80%) and Benin city (75.4%) [15, 21].

Metastatic lesions are estimated to be 21.3% in our study; similar results are also found in Nigerian studies {Kano (19%), Ilorin (19.3%), Benin City (22.7%)}, and TASH Ethiopia (19.8%) [15, 17, 21, 22] whereas it is higher than results of Iraqi (11.7%), and Nepal (10.9%) [23, 20] this could also be due to referral and selection bias. Studies in industrialized nations show higher figures of metastatic

lesions like Thailand (53.2%) [27]; this could contribute to environmental and genetic factors. Cervical LNs are the commonest LN groups to be involved by metastatic lesions (57.5%), which is also closely parallel with a study in Turkey (50%) and Benin city (52%) [18, 21].

Lymphomas cumulatively comprises 27.1% (86.3% of the cases are NHL and the remaining 13.7% is Hodgkin's lymphoma) which is in agreement with the figure in Ibadan (24%), Ilorin (28.2%), and Benin city (26.3%) [19, 17, 21] all with NHL predominance whereas the finding in Pakistan (25.4%) [24] even though the cumulative figure is comparable there is a slight HL predominance, this regional discrepancy may be due to genetic and environmental factors.

The majority of lymphoma cases in our study have the size of at least 2cm (74.5%), comparable results are also seen in Pakistan (88%) [24].

## 5. Conclusion

This study's histopathologic pattern of Lymph Node (LN) disease was comparable with other developing countries. Reactive nonspecific conditions and tuberculous lymphadenitis are more common before the age of 45 years. Metastatic lesions are more common after the age of 45 years. non-Hodgkin's lymphoma is more common than Hodgkin's lymphoma. Early detection and investigation of LN enlargement help avoid a delayed diagnosis of a potentially curable disease. We recommend the further studies to determine the predictors.

## Authors' Contribution

*TIK*: Initiated the research, wrote the research proposal, conducted the study, did data entry and analysis, and wrote the manuscript. *AMN*: Involved in the -up of the submission, data analysis and write-up of the manuscript. *BLY*: Involved in the proposal and write-up of the manuscript. *SAA*: Involved in the proposal and write-up of the manuscript. *DDW*: Involved in the proposal and write-up of the manuscript. *YZ*: Involved in the submission and write-up of the manuscript. *ASB*: Involved in the proposal and write-up of the manuscript. All authors read and approve the manuscript.

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## Competing Interests

The authors declare that they have no competing interests.

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