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Tuberculosis in Superficial Lymphadenopathy Based on Fine Needle Aspiration Cytology: A Cross Sectional Study

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Author`s Contribution

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ABSTRACT

Objective: To investigate the prevalence of tuberculosis among individuals presenting with superficial lymphadenopathy using Fine Needle Aspiration Cytology (FNAC) as a diagnostic method.

Methodology: This cross-sectional research spanned three years, conducted at HBS General Hospital in Islamabad from July 2016 to June 2019. The study enrolled individuals meeting specified inclusion and exclusion criteria, presenting with superficial lymph node enlargement. All participants provided written consent before undergoing fine needle aspiration cytology (FNAC), and the diagnosis of tuberculosis relied on histopathological findings.

Results: Among 632 patients aged 15 to 60 years who underwent FNAC following clinical examination and relevant lab investigations, 85.4% (n=540) exhibited cervical lymphadenopathy. Among these, 57.7% (n=312) were diagnosed with tuberculous lymphadenitis, comprising 58.3% females (n=182) and 41.6% males (n=130). Axillary lymphadenopathy was observed in 5.53% (n=35) of patients, among whom 3.64% females (n=23) and 2.1% males (n=13) were diagnosed with tuberculous lymphadenopathy. Generalized lymphadenopathy was seen in 5.1% (n=32) of cases, with 0.94% males (n=6) and 0.79% (n=5) demonstrating histological evidence of TB on FNAC. Inguinal lymphadenopathy was observed in 3.95% (n=25) of patients, including 0.94% males (n=5) and 0.47% females (n=3).

Conclusion: Lymphadenopathy, a prevalent clinical condition, encompasses various underlying causes, ranging from manageable tuberculosis to malignant conditions. FNAC serves as a safe and rapid diagnostic technique, reducing the need for excisional biopsies. In this study, cervical lymph nodes were most frequently affected by tuberculous lymphadenopathy, particularly among females.

Key Words: Lymph Node Disease, Lymphadenopathy, Lymph Node Biopsy, Enlarged Lymph Nodes, Neoplasm

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Introduction

Lymphadenopathy, defined as an anomaly in the size or composition of lymph nodes, can occur due to the infiltration or dispersion of inflammatory or neoplastic cells into these nodes. It is a manifestation of a wide range of medical conditions.[1] Lymphadenopathy presents as enlarged lymph nodes and is a common observation in clinical practice, whether in acute or chronic cases. Lymph nodes that are palpable and exceed 5 mm in size are considered abnormal. The annual occurrence of unexplained lymphadenopathy stands at 0.6%, with only 1.1% of cases being linked to malignancies, a percentage that rises with age. Approximately half of healthy children

may have palpable lymph nodes at any given time.[2] In children, lymphadenopathy is typically benign or related to infections. In both adults and children, lymphadenopathy persisting for less than two weeks or for over 12 months without changes in size is less likely to be of neoplastic origin.[3,4] Exceptions include low-grade Hodgkin lymphoma and non-Hodgkin lymphoma, both of which are associated with systemic symptoms.[5]

An excision biopsy of the lymph node is the preferred method for diagnosis, although it necessitates either local or general anesthesia. An alternative diagnostic approach with minimal trauma and cost is fine needle aspiration cytology (FNAC).[6] FNAC was initially performed in 1904 by Captain E.D.W. Greig and Lieutenant A.C.H. Grey, both marine officers. The first tumor diagnosis using FNAC was accomplished in 1914 by English physician Gordon R. in 1921. De May succinctly summarized the advantages of FNAC using the acronym SAFE, which stands for simple, accurate, fast, and cost-effective. FNAC can readily distinguish between malignant and nonmalignant lesions.[5] When performed with radiological guidance such as ultrasound and computed tomography scans, FNAC can enhance its diagnostic yield.[6]

In reviews of patients with lymphadenopathy, 17.5% were diagnosed with malignancies, including 11.4% with lymphoproliferative disorders and 6.1% with metastasis. Reactive conditions accounted for 31% of cases, while 26% had other non-malignant diseases.[7] A study conducted in Pakistan involving 498 patients with cervical lymphadenopathy revealed that 8% had Hodgkin lymphoma (in stages 2 and 3).[8]

Tuberculous lymphadenitis manifests as painless masses and may potentially lead to the formation of cold abscesses. In KPK, Pakistan, a reported 39% of cases involving cervical lymphadenopathy were attributed to Tuberculous causes.[7] Granulomatous lymphadenopathy poses a broad range of potential diagnoses, including sarcoidosis, carcinoma, lymphoma, sarcoma, fungal infections, cat scratch fever, and toxoplasmosis.

The tuberculin test has demonstrated that more than 80% of the Asian and African population test positive, in contrast to developed nations like the United States, where only 5-10% yield positive results in the tuberculin test.[8] Tuberculosis diagnosis hinges on the presence of epithelioid granulomas, with or without multinucleate giant cells and caseation necrosis. FNAC has emerged as a crucial diagnostic tool for cases of lymphadenopathy, effectively distinguishing between tuberculosis, lymphoma, and metastatic carcinoma.[9]

Our study aimed to assess the prevalence of tuberculosis in cases of superficial lymphadenopathy within a tertiary care hospital in Islamabad.

Methodology

This descriptive cross-sectional research was conducted at HBS General Hospital in Islamabad, spanning a three-year period from July 2015 to June 2018. Approval was granted by the hospital's ethical review board. Sample size was calculated using Open EPI at a 95% confidence interval and with a margin of error at 7%. The study included individuals aged 15 to 70 years who presented with painless superficial lymph node enlargement at various body locations. There were no gender or age restrictions for participation. Patients with either a primary complaint of superficial lymphadenopathy or those who were discovered to have it during physical examinations were eligible for inclusion. Diagnosis was confirmed through FNAC conducted by a pathologist. Additional investigations such as Complete Blood Counts, ESR levels, Hepatitis B surface antigen, HCV, HIV serology, chest and abdominal radiography, and abdominal ultrasound were also performed. Radiography encompassed both posterior, anterior and anteroposterior views for chest X-rays. Prior to participating in the study, participants provided oral and written consent and were informed that they could withdraw from the study at any point before its conclusion. Previously diagnosed patients of tuberculosis on treatment, lymph nodes difficult to aspirate, patients on medication for lymphadenopathy., patients with cancer on chemotherapy and patients on immunosuppressive treatment was defined as an exclusion criteria.

Patients were instructed to undergo FNAC under the guidance of a pathologist, after which they were advised to return to their respective physicians with their histopathology reports. Information was gathered using a predefined form and subsequently analyzed using SPSS version 22. Quantitative data was summarized by reporting the mean and standard deviation. Qualitative data was summarized by reporting the frequencies and percentages. The statistical significance level was set at 0.05.

Results

632 patients with superficial lymphadenopathy were finally enrolled for the study. Of these, 54.11% (n=342) were females and 45.99% (n=290) were males, resulting in a female-to-male ratio of 1.17:1. Among the enrolled patients, 85.44% (n=540) had cervical lymphadenopathy, Out of these, 49.36% (n=312) were diagnosed with tuberculosis through FNAC. In the case of axillary lymphadenopathy, observed in 35 patients, 3.63% (n=23) were found to have tuberculosis. Generalized lymphadenopathy was seen in 32 patients, with a tuberculosis prevalence of 1.74%. The results are outline in table I.

Within the subgroup of 312 patients with Tuberculous cervical lymphadenopathy, 58.3% (n=182) were females, while 41.6% (n=130) were males. The majority of cases within this group were aged between 15 to 30 years, with a female predominance (n=137). The female-to-male ratio in this age group was 1.52:1, with 20.56% of males and 28.79% of females having tuberculous cervical lymphadenitis in our sample (Table II and III).

Axillary lymphadenopathy was observed in 35 patients, with 10 females and 13 males diagnosed with tuberculosis through FNAC. Maximum patients with axillary lymphadenopathy presented between 21 to 30 years of age, with a female-to-male ratio of 1.5:1, indicating female predominance in this category.

Generalized lymphadenopathy was noted in 32 patients, with 11 of them having tuberculosis. Out of these 11 cases, 5 were females and 6 were males. The peak age for presentation in this group was between 21 to 30 years.

Inguinal lymphadenopathy was observed in 25 patients (3.95% of enrolled patients), with 8 of them (1.26%) diagnosed with tuberculosis through FNAC. Similar to other categories, the maximum number of patients with inguinal lymphadenopathy also presented between 21 to 30 years of age, with a female predominance (Table I, II, and III).

From the pattern of distribution of lymphadenopathy, it was evident that tuberculosis was more prevalent in cervical lymph nodes.

Discussion

The absence of an evident cause for peripheral lymphadenopathy observed during a physical examination poses a challenging diagnostic scenario. Lymphadenopathy can stem from a wide spectrum of diseases, and when a person has enlarged lymph nodes, particularly in developing countries, tuberculosis emerges

Table I: Gender distribution and lymph node site (based on histopathology, HP)

Gender	**Male**	**Female**
	290	342
Site of lymph node	**No of patients**	**Tuberculosis on HP**
Cervical	540	312 (57.7%)
Axillary	35	23 (3.63%)
Generalized	32	11 (1.74%)
Inguinal	25	8 (1.26%)

Table II: Distribution of TB lymphadenitis (%age) in various age groups with sex and site

Age	**Cervical (n=312)**		**Axillary (n=23)**		**Inguinal (n=25)**		**Generalized (n=32)**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
15- 20	42	59	2	4	7	4	6	4
21- 30	48	78	6	8	2	12	8	10
31 -40	25	24	2	0	0	0	2	1
41 -50	10	17	1	0	0	0	1	0
51- 60	5	4	0	0	0	0	0	0
61 -70	0	0	0	0	0	0	0	0

Table III: Distribution of TB lymphadenitis (%age) overall with sex and site

Tuberculous lymphadenopathy	**Males**		**females**	
	Number	**%age**	**Number**	**%age**
Cervical (n=312)	130	20.56	182	28.79
Axillary (n=23)	13	2.05	10	1.58
Generalized (n=11)	6	0.94	5	0.79
Inguinal (n=8)	5	0.94	3	0.47

as a prominent consideration among potential diagnoses. In developed nations, most instances of tuberculous lymphadenitis have been observed among immigrants originating from regions with a high prevalence of tuberculosis. Despite a decrease in its incidence, tuberculosis continues to be one of the most frequently occurring infectious diseases.[10-13]

The diagnosis of tuberculous lymphadenopathy relies on histological criteria. The presence of granulomas and caseation necrosis, accompanied by Langerhans-type giant cells, serves as conclusive evidence of tuberculosis. A well-organized granuloma featuring a central cluster of epithelioid cells, surrounding histiocytes in a mantle-like arrangement, occasional giant cells, and plasma cells is indicative of tuberculosis. In our current study, the primary histological indicator of tuberculosis was the presence of caseation necrosis, a finding that aligns with previous research.[14,15]

In our research, Tuberculous Cervical lymphadenopathy emerged as the predominant presentation, accounting for 57.7% of cases, a statistic that aligns with findings from other studies.[13,15] For instance, a study reported that 37.2% of lymph nodes examined exhibited Tuberculous characteristics on histological examination. Furthermore, cervical lymphadenopathy stood out as the most common manifestation of lymphadenitis.[16]

Indian investigations also concurred with our findings, indicating that tuberculosis predominantly affected cervical lymph nodes.[17] Similarly, a study conducted in Turkey identified lymph nodes as the most frequent site of extra-pulmonary tuberculosis.[18] Notably, a study in the United States demonstrated that Tuberculous lymphadenitis was more prevalent among females than males in the Asian and North African population.[19]

Our study, in particular, demonstrated a higher prevalence of tuberculous lymphadenitis in cervical lymph nodes among females (58.3%) in contrast to males (41.66%). However, when examining other lymph node sites such as axillary, inguinal, and generalized regions, it became evident that more males exhibited tuberculous lymphadenitis compared to females. Nevertheless, in cases of extra-pulmonary tuberculosis, several studies in the region reported a female predominance.[20] Our study's results were in line with an investigation which, despite its small sample size, yielded nearly identical results.[21]

Conclusion

Lymphadenopathy is a common clinical disorder the underlying pathology may range from treatable tuberculosis to malignant disorders. FNAC is a safe and quick method for diagnosis which reduces the need for excisional biopsy. Most common site of tuberculous lymphadenopathy in present study was cervical lymph nodes with female predominance.

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