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Correlation Between Nutritional Deficiencies (E.G., Iron, Zinc) And Lymph Node Cytology Patterns: Study In Hilly Area Of Uttarakhand

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ABSTRACT

Background: Micronutrient deficiencies, particularly of iron and zinc, are prevalent in resource-limited regions and have known effects on immune function. This study aimed to evaluate the correlation between nutritional deficiencies and cytological patterns observed in lymph node aspirates from patients in the hilly region of Uttarakhand.

Materials and Methods: This cross-sectional study included 234 patients with peripheral lymphadenopathy who underwent fine-needle aspiration cytology (FNAC) and serum nutritional assessment. Cytological patterns were classified as reactive hyperplasia, granulomatous lymphadenitis, suppurative inflammation, or neoplastic. Serum iron and zinc levels were measured, and associations between deficiencies and cytological patterns were analyzed statistically.

Results: Iron deficiency was present in 53.8% of patients, zinc deficiency in 44.4%, and both deficiencies in 30.8%. Reactive lymphoid hyperplasia (41.9%) and granulomatous lymphadenitis (33.8%) were the most common cytological findings. A statistically significant correlation was found between iron deficiency and reactive lymphoid hyperplasia ($p < 0.01$), while no significant correlation was observed for zinc deficiency with specific patterns, though a higher frequency of granulomatous changes was noted in zinc-deficient individuals.

Conclusion: Iron and zinc deficiencies are common among patients with lymphadenopathy in hilly regions. Iron deficiency is significantly associated with reactive lymphoid hyperplasia, suggesting an immune-modulatory influence on cytological response. Nutritional profiling may enhance diagnostic interpretation and guide holistic patient management in endemic and underserved populations

Keywords: *Iron deficiency, zinc deficiency, lymphadenopathy, FNAC, reactive hyperplasia, granulomatous lymphadenitis, Uttarakhand, nutritional status*

1. INTRODUCTION

Lymphadenopathy is a common clinical finding that often prompts cytological evaluation to identify underlying infectious, inflammatory, or neoplastic etiologies. Fine-needle aspiration cytology (FNAC) remains a rapid, minimally invasive, and cost-effective diagnostic modality in evaluating lymph node enlargements, particularly in resource-constrained settings [1]. The cytomorphological spectrum of lymph node lesions includes reactive hyperplasia, granulomatous inflammation, suppurative changes, and malignancy, among others [2].

Nutritional deficiencies, especially of micronutrients such as iron and zinc, have a profound impact on immune competence and inflammatory response. Iron plays a central role in immune cell proliferation and cytokine activity, while zinc is essential for the function of T-lymphocytes, natural killer cells, and maintenance of epithelial barriers [3,4]. Deficiencies in these nutrients can alter lymphoid architecture and modulate the host response to infectious agents, potentially influencing the cytological patterns observed in lymph node aspirates.

The hilly regions of Uttarakhand present unique public health challenges due to geographical isolation, dietary insufficiencies, and limited access to healthcare services. Nutritional anemia and trace element deficiencies remain prevalent, particularly among lower socio-economic groups and rural populations [5]. At the same time, infectious causes such as tuberculosis, which often present with granulomatous lymphadenitis, remain endemic in these regions [6].

While several studies have evaluated the cytomorphological spectrum of lymphadenopathy, limited data exist correlating nutritional deficiencies with specific cytological patterns. Understanding this relationship may provide insight into the interplay between host nutritional status and lymph node pathology and assist clinicians in formulating more targeted diagnostic and therapeutic strategies

The present study was conducted to evaluate the prevalence of iron and zinc deficiencies among patients presenting with lymphadenopathy and to correlate these deficiencies with specific cytological patterns observed on FNAC in the hilly region of Uttarakhand.

2. MATERIAL AND METHODS

Study Design and Setting: This was a hospital-based, cross-sectional observational study conducted at an Indian medical college located in the hilly region of Uttarakhand.

Study Population: Patients of all age groups presenting with peripheral lymphadenopathy and referred for fine-needle aspiration cytology (FNAC) were included. The study aimed to explore the correlation between nutritional deficiencies—primarily iron and zinc—and the cytological patterns observed in lymph node aspirates.

Inclusion and Exclusion Criteria: The study included patients presenting with clinically palpable peripheral lymph nodes who were scheduled for fine-needle aspiration cytology (FNAC). Only those who provided informed consent for nutritional assessment and blood sampling were considered eligible. Additionally, participants were required to be permanent residents of the hilly regions of Uttarakhand, having lived there continuously for a minimum of five years.

Exclusion criteria encompassed individuals with known malignancies, immunosuppressive disorders such as HIV, or those currently receiving immunosuppressive therapy. Patients whose aspirates were deemed inadequate or hemorrhagic were also excluded from the analysis. Furthermore, pregnant and lactating women were not enrolled in the study, as their nutritional indices could be physiologically altered and potentially confound the results.

Sample Size: A total of 234 patients meeting the eligibility criteria were enrolled consecutively.

Data Collection and Procedure: All participants underwent a thorough clinical assessment, including a detailed history, physical examination, and systemic evaluation. FNAC was carried out using standard protocols with 22–23 gauge needles under strict aseptic precautions. The aspirated material was smeared on glass slides and stained using May-GrünwaldGiemsa (MGG) and Ziehl-Neelsen (ZN) stains. Based on cytomorphological features, the lymph node aspirates were categorized into distinct diagnostic groups, including reactive lymphoid hyperplasia, granulomatous lymphadenitis, suppurative lymphadenitis, and neoplastic lesions.

Concurrently, venous blood samples were collected from each participant to evaluate nutritional status. Serum iron and ferritin concentrations were measured using chemiluminescent immunoassay techniques, while serum zinc levels were assessed via atomic absorption spectrophotometry. Hemoglobin levels were determined using an automated hematology analyzer. Nutritional deficiencies were defined based on standard reference cut-offs: iron deficiency was diagnosed when serum ferritin was less than 15 ng/mL in males and less than 12 ng/mL in females, whereas zinc deficiency was defined as serum zinc levels below 70 µg/dL.

Statistical Analysis: Data were compiled using Microsoft Excel and analyzed using SPSS. Descriptive statistics were used to summarize demographic and laboratory findings. Association between nutritional deficiencies and cytological patterns was assessed using Chi-square test or Fisher's exact test, and p-values <0.05 were considered statistically significant.

3. RESULTS

Table 1: Demographic Profile of the Study Population (N = 234)

Variable	Category	Frequency (n)	Percentage (%)
Age Group (years)	<18	36	15.4
	18–40	124	53.0
	>40	74	31.6
Gender	Male	127	54.3
	Female	107	45.7
Residence	Rural (Hilly)	234	100.0

The majority of patients were in the 18–40 year age group. Slight male predominance was observed. All patients were residents of the hilly regions of Uttarakhand (Table 1).

Table 2: Cytological Diagnosis of Lymph Node Aspirates

Cytology Pattern	Frequency (n)	Percentage (%)
Reactive lymphoid hyperplasia	98	41.9
Granulomatous lymphadenitis	79	33.8
Suppurative lymphadenitis	26	11.1
Tubercular lymphadenitis (AFB+)	18	7.7
Metastatic malignancy	8	3.4
Lymphoma (suspicious)	5	2.1

Reactive and granulomatous lymphadenitis were the most common cytological patterns, together comprising over 75% of cases. A smaller subset showed tubercular and neoplastic patterns(Table 2).

Table 3: Prevalence of Nutritional Deficiencies (N = 234)

Deficiency	Number of Cases (n)	Percentage (%)
Iron deficiency	126	53.8
Zinc deficiency	104	44.4
Both iron & zinc	72	30.8
No deficiency	58	24.8

Over half of the patients had iron deficiency, and nearly one-third had both iron and zinc deficiencies. Only one-fourth of patients had normal nutritional indices (Table 3).

Table 4: Correlation between Iron Deficiency and Cytological Patterns

Cytology Pattern	Iron Deficient (n=126)	Iron Normal (n=108)	p-value
Reactive lymphoid hyperplasia	65	33	<0.01
Granulomatous lymphadenitis	40	39	0.230
Suppurative lymphadenitis	11	15	0.147
Tubercular lymphadenitis	6	12	0.079
Metastatic/Neoplastic	4	9	0.218

Iron deficiency was significantly associated with reactive lymphoid hyperplasia ($p < 0.01$), suggesting a potential link with non-specific immune activation. Other patterns showed no statistically significant correlation (Table 4).

Table 5: Correlation between Zinc Deficiency and Cytological Patterns

Cytology Pattern	Zinc Deficient (n=104)	Zinc Normal (n=130)	p-value
Reactive lymphoid hyperplasia	47	51	0.671
Granulomatous lymphadenitis	32	47	0.098
Suppurative/TB lymphadenitis	18	26	0.881
Neoplastic (incl. metastasis)	7	6	0.213

No significant association was observed between zinc deficiency and specific cytological patterns, although a trend was noted toward higher frequency of granulomatous pathology in the zinc-deficient group (Table 5).

4. DISCUSSION

In this study, we explored the relationship between iron and zinc deficiencies and the cytological patterns observed in lymph node FNAC specimens from a population residing in the hilly terrain of Uttarakhand. The most frequently encountered patterns were reactive lymphoid hyperplasia and granulomatous lymphadenitis, which is consistent with findings from similar rural and semi-urban settings in India [7,8].

A significant association was noted between iron deficiency and reactive lymphoid hyperplasia, suggesting a link between nutritional anemia and non-specific immune activation. Iron deficiency has been shown to impair cell-mediated immunity and alter cytokine responses, potentially leading to chronic antigenic stimulation and reactive lymphoid proliferation [9]. This aligns with previous immunological research where iron-deficient individuals demonstrated impaired lymphocyte function and thymic atrophy [10].

Zinc deficiency, although common in our cohort, did not show a statistically significant correlation with specific cytological patterns. However, a trend toward increased granulomatous pathology was observed. This may be explained by zinc's role in macrophage activation and phagocytosis, which are central to granuloma formation in diseases such as tuberculosis and sarcoidosis [11,12]. Studies have demonstrated impaired granuloma maturation and delayed resolution of inflammation in zinc-deficient individuals [13].

The relatively high prevalence of both iron and zinc deficiencies in this population can be attributed to geographical and socioeconomic factors. Mountainous regions often suffer from limited dietary diversity, micronutrient-poor soil, and lower healthcare access, compounding the risk of nutritional deficiencies [14]. These deficiencies not only predispose individuals to infections but may also modify their pathological responses, thereby influencing cytological features observed on FNAC.

Interestingly, patients with dual deficiencies (iron and zinc) presented with both reactive and granulomatous patterns, though the numbers were insufficient to establish statistical significance. This indicates a potential cumulative immunological effect of combined deficiencies, warranting further research with larger sample sizes.

This study underscores the importance of assessing nutritional status in patients presenting with lymphadenopathy, especially in endemic and resource-limited settings. FNAC findings, when interpreted alongside micronutrient profiles, may offer deeper insights into underlying immune and infectious dynamics.

Limitations of the study include its cross-sectional nature and lack of confirmatory histopathological or microbiological correlation in all cases. Additionally, serum zinc levels can be influenced by acute-phase reactions, which were not controlled for in this study.

5. CONCLUSION

This study highlights a significant burden of iron and zinc deficiencies among individuals presenting with peripheral lymphadenopathy in the hilly region of Uttarakhand. A statistically significant correlation was observed between iron deficiency and reactive lymphoid hyperplasia, suggesting an immunomodulatory role of micronutrients in shaping cytological patterns. Although zinc deficiency did not show a strong individual association with any specific pattern, a trend toward increased granulomatous changes was noted. The findings emphasize the need for integrated nutritional screening in patients undergoing lymph node evaluation, particularly in resource-limited or endemic settings. Addressing nutritional deficiencies may not only improve immune response but also refine diagnostic interpretations in cytopathology

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