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## Original Research Article

## Role of hematological and inflammatory marker in granulomatous compared to non-granulomatous lymphadenitis

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## ABSTRACT

Lymphadenopathy can result due to an increase in lymphocytes in the lymph node due to various infections like tuberculosis and lymphoproliferative conditions. Granulomatous lymphadenitis causes an increase in inflammatory biomarkers which can be assessed by simple hemogram using TLC and DLC and ratios derived from it like NLR (Neutrophil Lymphocyte Ratio) and PLR (Platelet Lymphocyte Ratio).

**Aim:** To establish the role of hematological and inflammatory biomarkers in granulomatous and non-granulomatous lymphadenitis.

**Materials and Methods:** The study was performed in a tertiary care center from august 2020 to September 2022. The study included 150 patients with neck mass taking inclusion and exclusion criteria into account. Cytologically proven cases were categorised into granulomatous and non-granulomatous cases depending on cytological evaluation. Different laboratory parameters like TLC, DLC, ESR, CRP, NLR, and PLR were used to compare granulomatous lymphadenitis to non-granulomatous.

**Result:** In the studied population there were 92(61.3%) females and 58(38.7%) males but when compared to the non-granulomatous lymphadenitis group, females predominated by 70.7% hematological markers like NLR, PLR, and CRP in the granulomatous lymphadenitis group was significantly higher. The mean Neutrophil was considerably higher among granulomatous lymphadenitis but in non-granulomatous lymphadenitis, the group showed considerably greater mean lymphocytes.

**Conclusion:** Tuberculosis is the most frequent clinical condition connected to cervical lymphadenopathy in our area. More often than not, women are involved. Hematological and biochemical parameters like NLR, PLR, and CRP can give us some indication before FNAC for the presence of granulomatous and non-granulomatous lymphadenitis. It will help the treating doctor think methodically about early case identification and avoid diagnostic delays in situations like tuberculosis, especially at the primary care level.

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## 1. Introduction

Lymph node enlargement in local and systemic infectious cases is seen as lymphadenopathy. Lymphadenopathy describes the expansion of lymph gland, which brings about non-malignant, malignant & metastatic disease. Non-neoplastic lymphadenopathies mostly include granulomatous lymphadenitis, follicular hyperplasia,

and other causes of reactive lymph node enlargement. An enlarged cervical lymph node is a typical finding in clinical examinations performed in medical practices. Lymphoproliferative disorder or an infection may cause lymphocytes that are intrinsic to the lymph node to proliferate, causing the lymph node to swell. Lymph node harbors various kinds of lymphoid cells which are physiologically in direct connection with bone marrow and peripheral blood. In pathological terms, such diseases are

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mentioned as hematology pathologies. Granulomatous lymphadenitis can be due to various etiologies for example tuberculosis, leprosy, sarcoidosis, autoimmune inflammation, fungal infection, protozoal infection, some neoplasm and even due to reaction against any foreign bodies. Epithelioid cell granulomas are a collection of modified macrophages under the influence of interleukin 2 and interferon-gamma secreted by TH-1 cells along with some intermingled lymphocytes and fibroblasts at the periphery.<sup>1</sup> Granulomatous lymphadenitis is most frequently brought on by tuberculosis in underdeveloped nations like India.<sup>2</sup> Epithelioid cell granulomas can be caseating or non-caseating depending upon etiology. Tubercular granulomas are mostly caseating type.<sup>3</sup> TBL is difficult to identify and frequently occurs in conjunction with other chronic diseases that provide erratic physical and laboratory results. Diagnostic imaging and cytological/histological examination of cervical lymph nodes need to be excised on the path of conclusion. TBL has been connected to altered levels of many cytokines, interleukin 1 and 17 mediators in serum or plasma.<sup>4,5</sup> Neopterin, C reactive protein (CRP), and beta 2 macroglobulin are just a few of the biochemical parameters that have been employed to evaluate therapeutic monitoring, find persistent culture positivity, diagnose radiological problems, find disseminated mycobacterial disease, and more definitely, to distinguish tuberculosis from cancer.<sup>6</sup> Necrotizing non-granulomatous lymphadenitis is a symptom of several illnesses. Inappropriate therapy that might have negative consequences on the patient could result from incorrect understanding of this pathological phrase. Systemic lupus erythematosus (SLE/lupus lymphadenitis) and other infections are prominent prevalent infectious and inflammatory disorders that produce necrotizing lymphadenitis, which excludes mycobacterial infections like tuberculosis (TB). Numerous studies on chronic inflammatory diseases, including tuberculosis (TB), have concentrated on white blood cell (WBC) count, platelets, and various relative ratios of different blood's white cells can be identified by their monocyte/lymphocyte ratio (MLR), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR). Elevated MLR in peripheral blood was described as indicator of TB progression in newborns and adults who are HIV-positive. The NLR ratio was antiquated and shown to predict possibility of TB in persons with HIV as well as aid to distinguish between pulmonary TB and bacterial community-acquired pneumonia.<sup>7</sup> Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) rates calculated according to hemogram data in patients with a white blood cell count within the normal range can be used to evaluate systemic inflammation. Patients with autoimmune diseases, rheumatic disorders, malignancies, and diabetes have a higher PLR. Neutrophil to

lymphocyte ratio (NLR) is a straightforward marker of the systemic inflammatory response in intensive care patients. It has also been identified as an unrelated prognostic factor for non-infectious disorders, such as acute myocardial infarction, stroke, and a variety of malignancies.<sup>8–10</sup> Additionally, NLR has been demonstrated to be self-sufficient predictor of both short as well as long term death in critically sick patients.<sup>11</sup>

Consequently, we wanted to find out and interpret quantitative levels of these parameters in granulomatous lymphadenitis and reactive lymphadenopathy and will try to find out any association with the disease.

## 2. Materials and Methods

### 2.1. Study design

It was a clinical prospective study that was done in the Department of Pathology, Teerthanker Mahaveer Medical College and Research Centre.

### 2.2. Study setting

The data utilized in this study has been anonymized to protect the identities of the individuals involved. The study was conducted from August 2020 to September 2022. Research was approved by Institutional Ethical Committee

### 2.3. Sample size

The study comprised a total of 150 neck mass cases. Research participants were categorized as granulomatous and reactive lymphadenitis according to their cytological report.

## 3. Method of data collection

A comparison of different laboratory parameters was performed among these 2 categories. A CBC was conducted on Sysmex XN-10, CRP was measured on a semi-automated analyzer 300, and ESR by the Westergren method. We studied parameters such as TLC (Total leucocyte count), DLC (Differential Leucocyte Count), NLR (Neutrophil Lymphocyte Ratio), PLR (Platelet Lymphocyte Ratio), ESR (Erythrocyte Sedimentation Rate), and CRP (C-Reactive Protein).

## 4. Result

In our study, out of a total of 150 cases, 75 were classified as granulomatous and 75 cases as reactive lymphadenitis. In the studied population, there were 70.7% females and 44% males. As indicated in Table 1, our study found a female preponderance in both study groups as indicated in Table 1. The average age of the study group was  $27.55 \pm 0.91$  in granulomatous lymphadenitis and  $26.32 \pm 16.60$  in non-granulomatous. All laboratory parameters in the two groups

of lymphadenitis are shown in Table 1 indicating differences in their mean values. Hematological parameters such as NLR, PLR and CRP were significantly increased in patients of granulomatous disease and showed statistical significance with disease severity ( $P < 0.001$ ) whereas other parameters such as TLC, ESR was not significant.

**Table 1:**

	Granulomatous lymphadenitis	Non-granulomatous lymphadenitis	P-value
<b>Age</b>	27.55±0.91	26.32±16.60	0.614
<b>Sex</b>			
Male	29.3%	48%	0.019
Female	70.7%	52%	
<b>TLC</b>	13158.01±603.1	11667.73±1248.1	0.353
<b>ESR</b>	22.48±5.63	22.72±7.22	0.821
<b>NLR</b>	6.15±3.17	3.76±2.64	0.001
<b>PLR</b>	(1.74±0.63) x104	(1.30±0.73) x104	0.001
<b>CRP</b>	11.71±19.69	2.97±4.07	0.001

## 5. Discussion

Nothing stood out different in mean age between the groups with granulomatous lymphadenitis (27.55years ±12.91SD) and non-granulomatous lymphadenitis (26.32years ±16.60SD). With an overall mean age of 29.04 ± 19.14 years, the findings revealed that 23.4%, 65.2%, and 11.3% of the study participants were in the age groups of fewer than 14 years, 15-59 years, and 60 years, respectively.

Females were significantly more among granulomatous lymphadenitis group (70%) compared to non-granulomatous lymphadenitis group(52%). T Sagirgolu et al. (2017)<sup>12</sup> and Rohini et al (2016),<sup>13</sup> confirmed through a study that mean TLC in cases of lymphadenopathy is higher than in control groups (0.008) but in the present study, there was no significant difference in mean TLC between non-granulomatous lymphadenitis (11667.73±1248.12) and granulomatous lymphadenitis groups(13158.01±603.56). The mean Lymphocyte was significantly more among non-granulomatous lymphadenitis (24.37±11.07 vs 16.01±6.83). The mean Neutrophil was significantly more among the granulomatous lymphadenitis group (79.53±8.09vs 69.03±13.14). This may be due to an equal rise of TLC in cases of granulomatous and reactive lymphadenitis due to superadded infection and it is balanced in both cases or this difference has occurred due to geographical variation in the pattern of disease. It was found in the current research that there was no significant difference in mean ESR between non-granulomatous lymphadenitis (22.72±7.22) and granulomatous lymphadenitis (22.48±5.63) groups and this output does not match with Rohini et al. (2016),<sup>13</sup> who

assessed hematological parameters in tuberculosis groups versus control. The result of which stated that there was raised ESR in tubercular groups than in control. This may be due to the small sample size in recent study.

Dirican et al (2014),<sup>14</sup> found that NLR is considerably greater in sarcoidosis patients compared to healthy control and also stated that patients with extrapulmonary involvement had higher NLR levels. This study is in accordance with the present study where NLR is remarkably more among granulomatous (6.15±3.17) compared to non-granulomatous lymphadenitis(3.76±2.64) category. Additionally, recognized as a diagnostic indicator of bacterial infection is lymphocytopenia.<sup>15</sup> This study does not match the output of a recent study where the granulomatous lymphadenitis group had increased NLR. Therefore, it is proposed that NLR could be predictive of bacterial infections and stressful situations. The lack of differences in NLR levels between TB lymphadenitis and controls in our investigation may indicate that parenchymal infiltration is a possible cause of NLR increase. Singh et al.<sup>16</sup> (2017) investigated found that hematological changes associated with tuberculosis and found thrombocytosis in cases of pulmonary tuberculosis groups. This means PLR will be more in cases with pulmonary tuberculosis and this research matches result of recent study where PLR was significantly more in cases of granulomatous (1.74±0.63) compared with non-granulomatous (1.30±0.73) lymphadenitis. This probably explains the pulmonary manifestation in our study group of granulomatous lymphadenopathies. In line with the research of Rohini et al. (2016) there was a significant difference in mean CRP between the groups with granulomatous lymphadenitis (11.71±19.09) and non-granulomatous lymphadenitis (2.97±4.07),<sup>13</sup> and Ştefanescu et al,<sup>17</sup> (2021) where there was continuous elevation of CRP in tuberculosis patients as stated that continuous elevation CRP, is linked with a chronic inflammatory condition.

## 6. Conclusion

Haematological markers have been examined in a number of trials to determine their value in predicting the likelihood that TB illness would develop, detecting active tuberculosis infections, and tracking treatment response. For the proper identification of active TB, there has to be a significant adjustment made to the way conventional blood tests are used. Measures and ratios for complete blood counts have been proposed as hallmark indicators in inflammatory or infectious diseases, such as pulmonary tuberculosis.

The most frequent clinical issue associated with cervical lymphadenopathy is tuberculosis in our geographical region. Females are more commonly involved. Important warning signs and symptoms include organomegaly, consistency, fixed lymph nodes, and B symptoms

which should be taken into account while evaluating lymphadenopathy but hematological parameters like DLC and biochemical parameters like CRP can give us some clue prior to FNAC for the presence of granulomatous and non-granulomatous lymphadenitis. It will assist the treating physician, particularly at the primary care level, in thinking systematically about early case identification and preventing diagnostic delays in instances like tuberculosis. It may be very beneficial for basic healthcare providers at the urban and rural levels, where advanced diagnostic tools to identify lymph node illnesses are often not yet accessible owing to budget limitations. Inflammatory markers NLR and PLR are new and can be used to differentiate Granulomatous and non-granulomatous infections. Further, trials should be made with increased sample size. Many lymphadenopathy patients had vague symptoms and required further testing to get a definitive diagnosis. Additional research may be done by including a large number of patients.

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None.

## 8. Conflict of Interest

None.

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