



SIGNIFICANCE OF NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO AS A DIAGNOSTIC AID IN DIFFERENTIATING BETHESDA CATEGORY II THYROID LESIONS : A PROSPECTIVE HOSPITAL BASED STUDY.

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ABSTRACT

Introduction: Thyroid lesions often present as thyroid nodule. Bethesda Category II thyroid lesions comprise of benign thyroid lesions. On FNA sometimes cytologically overlapping features makes it difficult to distinguish between these lesions. NLR has been known to be raised in a number of infectious conditions, stroke, myocardial infarction and malignancies. Studies have shown NLR to be raised in lymphocytic thyroiditis. PLR is also a marker of systemic inflammation and is raised in a number of conditions including cardiovascular diseases, Hashimoto thyroiditis and certain malignancies. The present study aims to study if NLR and PLR can be of diagnostic help in differentiating benign thyroid lesions, besides FNAC and serology to avoid unnecessary surgery and their role as diagnostic aid in cytologically overlapping benign lesions. **Material And Methods:** Study was conducted in the cytology and haematology sections of department of pathology in SMMH medical College, Saharanpur. In the study period June, 2024 to December, 2024, 52 cases were separated which were reported as Bethesda category II lesions on FNAC. Their complete blood counts were taken and peripheral blood smears were prepared. Two groups were created based on cytology findings, Group A included Colloid goitre and Group B lymphocytic thyroiditis. NLR and PLR was calculated and data compiled using SPSS 25 software. **Results:** Out of the 52 cases included in the study 47 patients were female and 5 male. The most common age group in the study was 31-40 years. The mean NLR for colloid goitre group was 2.4369, the mean NLR for lymphocytic thyroiditis was 2.7223, two tailed p value being 0.5544, which was not statistically significant. PLR value for colloid goitre group was 98.700, while PLR value for lymphocytic thyroiditis was 100.37, two tailed p value being 0.8862, which was not statistically significant. **Conclusion:** NLR and PLR although cheap and readily available tests were not found to have significant association with either Colloid goitre or lymphocytic thyroiditis. Therefore they were not found to have a significant role in differentiating between thyroid lesions. FNAC in combination with anti TPO are more reliable for diagnosing Bethesda category II thyroid lesions. Histopathology being the gold standard for confirmatory diagnosis.

KEYWORDS : FNAC , NLR : Neutrophil to lymphocyte ratio, PLR : Platelet to lymphocyte ratio, SD : Standard deviation , SEM : Standard error of mean

INTRODUCTION

Thyroid lesions are common disorders of the endocrine system. They often present as thyroid nodules clinically. Fine needle aspiration and ultrasound are important diagnostic aids for preoperative evaluation of nodules of thyroid.

Palpable nodules are present in about 4 to 7 % of adult patients of thyroid disorders. When radiologically screened and autopsy findings are included, 20-70 % population may have non palpable nodules. Out of these about 5% are malignant¹

Bethesda category II lesions are the benign lesions of thyroid. These include Colloid goitre, Grave's disease, Hashimoto thyroiditis and subacute thyroiditis². Typically these lesions can be identified on the basis of their cytological features and with the help of radiology. Some overlap of cytological features may pose difficulty in diagnosing category II lesions. Colloid may be scant in the smears of goitre and hurthle cell change may be present in these patients whereas lymphocytic thyroiditis may show scant colloid, and granulomas (causing diagnostic difficulty with subacute thyroiditis).³

It is impractical and unnecessary to excise all thyroid nodules, therefore FNAC plays an important role in screening these nodules. Given the dilemma of cytological overlap between category II lesions warrants the need for an affordable and easily available diagnostic test for diagnostic aid, where serology is not available. The fact that large colloid goitres are surgically excised and lymphocytic thyroiditis is treated hormonally and is self limiting adds to the need of an adjuvant test.

Neutrophil to lymphocyte ratio (NLR) is used as one of the important parameters for systemic inflammation and stress. It is easily available and economical parameter and indicates the immune response of various infections and non-infectious stimuli⁴, acute stroke, myocardial infarction, diabetes mellitus, irritable bowel disease⁵, atherosclerosis, post-surgery, COVID 19⁶, and also raised in some malignancies. NLR has been found to be raised in Hashimoto thyroiditis⁷ in some studies, making it a potential marker for monitoring disease activity.

Platelet to lymphocyte ratio is also an important marker to assess systemic inflammation, studies have shown that it is raised in certain malignancies⁸ and in patients with cardiovascular risk⁹. Development of systemic inflammation is seen Hashimoto thyroiditis patients and studies have shown PLR to be raised in patients of Hashimoto thyroiditis.

The present study aims to evaluate the significance of NLR and PLR in diagnosing Bethesda category II thyroid lesions, as an adjunct to cytological findings and serology, as NLR and PLR are easily available and affordable and as the treatment modality in these lesions is different from each other.

MATERIAL AND METHODS

This prospective cross sectional study was done in the department of Pathology, SMMH Government Medical College, Saharanpur on a study group of 52 patients from June '24 to December '24. The study group comprised of two groups: Group A and Group B. Group A included 26 patients diagnosed as colloid goitre on cytology and 26 patients diagnosed as lymphocytic thyroiditis were taken in the study group B.

FNAC of patients with palpable thyroid swelling was done using a 24 gauge needle and 20 ml syringe. Ultrasound guided FNAC was done for deep seated lesions. Smears were stained using May-Grunwald Giemsa stain and Pap stain and evaluated. Bethesda Category II lesions were included in the study.

Thyroid profile of these patients was done using Abbot architect plus hormone analyser and CBC was done using a Cell dyn Ruby five part cell counter and peripheral blood smears were prepared and stained using Leishman stain.

Neutrophil to lymphocyte ratio was calculated using the formula :
NLR : Absolute Neutrophil Count/Absolute lymphocyte count

Platelet to lymphocyte count was calculated using the formula :
PLR : Platelet Count/Absolute Lymphocyte Count

Inclusion Criteria: 1. All patients with palpable thyroid lesions
2. Patients willing to give consent for the study
3. Patients with

Bethesda Category II on cytology

Exclusion Criteria : 1. Patients unwilling to give consent to the study
2. Patients with Bethesda Category I, III, IV, V, VI thyroid lesions
3. Patients with chronic diseases like coronary artery disease, haematological disease, malignancy, liver and kidney diseases

In patients showing cytological overlap between colloid goitre and lymphocytic thyroiditis, serology and histopathology was done wherever it was necessary to categorise the lesions.

RESULTS:

Out of 52 patients, 47 were female and 5 male :

Table 1. Percentage Of Males And Females In The Study

GENDER	No. of Patients	Percentage
Female	47	90.3%
Male	05	9.7%

Age Distribution:

Out of 52 patients, maximum patients were found to be of the age group 31-40 years followed by 41-50 years age group

Table 2. Age Distribution

Age group (in years)	No. of Patients	% of patients
1-10	0	0
11-20	05	9.6
21-30	09	17.4
31-40	18	34.7
41-50	12	23.0
51-60	04	7.7
61-70	02	3.8
71-80	02	3.8

On evaluating the thyroid profile of the study sample the following results were found :In the 26 patients diagnosed as colloid goitre majority were hypothyroid.

Table 3. Thyroid Hormone Profile In Patients With Colloid Goitre

	No. of patients	% of patients
Euthyroid	9	34.6
Hyperthyroid	3	11.5
Hypothyroid	14	53.9

In the 26 patients diagnosed as lymphocytic thyroiditis majority were hypothyroid.

Table 4. Thyroid Hormone Profile With Patients With Lymphocytic Thyroiditis

	No. of patients	% of patients
Euthyroid	10	38.5
Hyperthyroid	05	19.2
Hypothyroid	11	42.3

Neutrophil To Lymphocyte Ratio:

The mean value of neutrophil to lymphocyte ratio was calculated for Group A and Group B and compared using unpaired t test.

Table 5. Neutrophil To Lymphocyte Ratio Group A And Group B

GROUP	GROUP A	GROUP B
Mean	2.4369	2.7223
SD	1.5453	1.8946
SEM	0.3031	0.3716
N	26	26

Confidence Interval:

The mean of group A minus group B = 0.2854

95% confidence interval of this difference - 1.2485 to 0.6777

Intermediate Values Used In Calculation :

t = 0.5952

df = 50

standard error of difference : 0.479

P Value And Statistical Significance :

The two tailed P value = 0.5544, By conventional criteria this difference is considered to be not statistically significant.

Platelet To Lymphocyte Ratio :

The mean value of platelet to lymphocyte ratio was calculated for

Group A and Group B and compared using unpaired t test

Table 6. Platelet To Lymphocyte Ratio Group A And Group B

Group	Group A	Group B
Mean	98.700	100.37
SD	45.455	38.274
SEM	8.915	7.506
N	26	26

Confidence Interval :

The mean of group A minus group B = 1.677

95% confidence interval of this difference - 25.084 to 21.730

Intermediate Values Used In Calculation :

t = 0.1439

df = 50

standard error of difference : 11.654

P Value And Statistical Significance :

The two tailed P value = 0.8862, By conventional criteria this difference is considered to be not statistically significant.

It was observed that Neutrophil to lymphocyte ratio and Platelet to lymphocyte ratio did not have statistically significant difference in values between the two study groups, Colloid goitre and lymphocytic thyroiditis. According to the present study it is not a reliable diagnostic aid in differentiating between these two Bethesda Category II lesions

DISCUSSION

Fine needle aspiration (FNA) is known to be the safest, minimally invasive and highly accurate diagnostic modality in thyroid lesions. It has a sensitivity of about 93.4% and a positive predictive value of about 98.6%.³

The use of FNA has decreased the number of surgeries being done for benign lesions. Its indications include evaluating thyroid swellings, whether diffuse or nodular and to establish whether the thyroid lesion is inflammatory, autoimmune or nodular goitre to avoid unnecessary surgery.

Colloid goitre is identified by presence of cytological features like macrofollicles, cohesive cells, uniform evenly spaced cells, presence of colloid and macrophages. Hurthle cell change, multinucleated giant cells may also be present. These features along with scant colloid and degenerating bare nuclei can pose cytological overlap with lymphocytic thyroiditis.¹

Autoimmune thyroiditis eg. lymphocytic thyroiditis presents as a diffuse goitre that is painless with or without nodularity. Most patients are hypothyroid. Characteristic mixed lymphoid population and hurthle cell change is generally present, but scant colloid and presence of tingible body macrophages can cause diagnostic difficulties with colloid goitre. Presence of nodularity in the lesion as well as hypothyroid profile may further add to the overlap.¹

This warrants the need of additional tests that are easily available and cheap apart from serology and histopathology. The present study aims at evaluating whether Neutrophil to lymphocyte ratio (NLR) and Platelet to lymphocyte ratio (PLR) offer any diagnostic clue in differentiating between these two major Bethesda Category II lesions.

Neutrophil and lymphocyte count undergo certain temporary changes under inflammatory conditions¹⁰. NLR is calculated by dividing absolute neutrophil count by absolute lymphocyte count. An elevated NLR can be seen in several bacterial and fungal infections, acute stroke, myocardial infarction, atherosclerosis, post-surgery and cancer¹¹. It reflects relationship between innate immunity (neutrophils) and adaptive immunity (lymphocytes). Recent studies show abnormal NLR levels in relation to autoimmune diseases.

Platelet to lymphocyte ratio (PLR) is calculated by dividing absolute platelet count by the absolute lymphocyte count. It is also recommended as a potential marker of inflammation¹². It can be used as index for differential diagnosis of certain diseases like cancer, inflammatory diseases and patients with cardiovascular risk.

Bilge M et al studied 145 Hashimoto thyroiditis patients with 60 healthy age matched patients. NLR and PLR were higher as compared to the control groups. NLR (2.29 ± 0.65 vs 1.68 ± 0.40) and PLR

(164.95±55.14 vs 106.88±32.19), $p < 0.001$ for all comparisons.¹³

Arpaci D et al found that NLR and PLR are significantly different in the group of Hashimoto thyroiditis patients as compared to the control group, $p < 0.05$.¹⁴

In the study conducted by Onalan E et al Group of 121 patients of Hashimoto thyroiditis and 100 patients control group, NLR was significantly higher in the HT group as compared to the control group and PLR was significantly lower in the HT group as compared to the control group.¹⁰

Studies evaluating the association of NLR and PLR to colloid goitre are scarce.

In contrast to the above studies in our present study, no statistically significant association was found between NLR and PLR in Group A (Colloid goitre group) and Group B (Lymphocytic thyroiditis group). In terms of NLR the findings of our study are similar to Sharma Et al where no statistical significance was found between HT and NLR. The mean NLR in the thyroiditis group was 2.72 and that in the Colloid goitre group was 2.43 in our study. 2 tailed P value was 0.5544 which is not statistically significant. In the study by Sharma et al mean for HT group was 3.17 and control group was 3.26 with a p value of 0.869 which is not statistically significant.¹⁵

In our study the mean PLR value for thyroiditis patients was 100.37, and that for colloid goitre patients was 98.7 with a two tailed p value of 0.8862 which is not statistically significant.

NLR and PLR though cheap and easily available, are not reliable indicators when it comes to distinguishing between benign lesions of thyroid. FNAC combined with serological studies and radiology are more beneficial in diagnosing such lesions. Histopathology remains the gold standard for diagnosis.

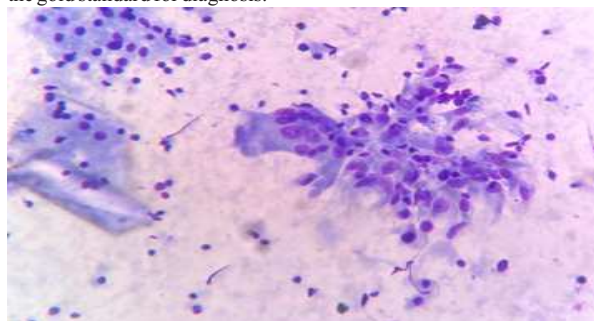


Figure 1: Epithelioid cells in Lymphocytic thyroiditis

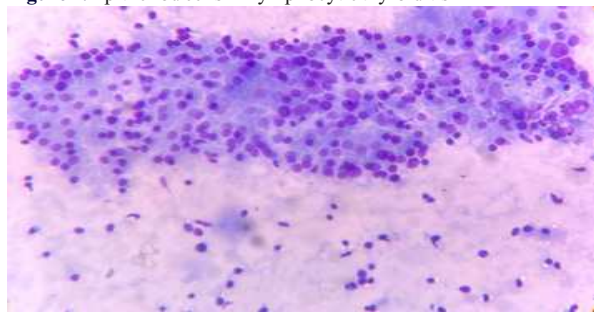


Figure 2: Lymphocytic impingement, oncocytic change in Lymphocytic thyroiditis.

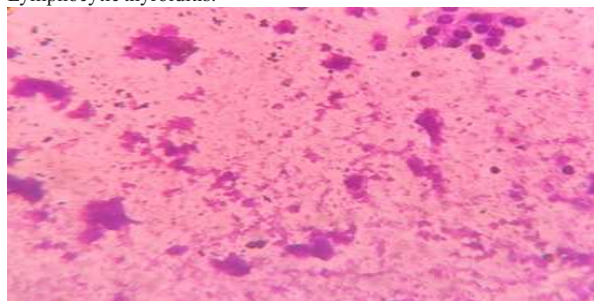


Figure 3: Colloid goitre.

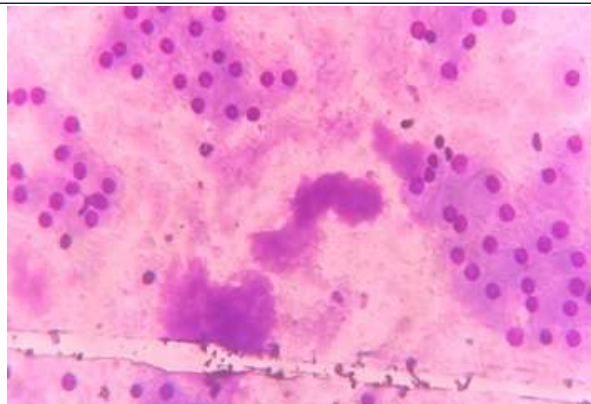


Figure 4: Category II lesion showing oncocytic change with colloid

CONCLUSION

Our study highlights the diagnostic role of NLR and PLR in distinguishing between Bethesda category II thyroid lesions particularly lymphocytic thyroiditis and colloid goitre. NLR and PLR although are indicators of inflammation, raised in a number of infectious, benign and cancerous conditions, when coming to thyroid lesions, particularly benign lesions the data has mixed findings. Some studies show significant statistical relationship between thyroiditis and NLR and PLR, while some with just NLR and some did not find statistical significance with NLR. In our present study we did not find statistically significant relationship between NLR and PLR with either thyroiditis or colloid goitre, irrespective of their thyroid hormone status.

Our study has the limitation of small sample size and being conducted at a single hospital.

Based on our present study it can be concluded that NLR and PLR though cost effective and readily available are not reliable indicators when it comes to distinguishing benign thyroid lesions. FNAC combined with serology and radiology is more reliable and histopathology is the gold standard for confirming such lesions.

Ethical Clearance

Ethical clearance was obtained from Institutional ethical committee, SMMH medical college Saharanpur before commencing the study

Conflict Of Interest

The authors declare no conflict of interest

Author Contribution

Concept : Dr Swati Singh and Dr Neetu Goyal

Data collection : Dr Pooja Arora and Dr Bhavna Jain

Manuscript Drafting : Dr Swati Singh, Dr Neetu Goyal and dr Pooja Arora

REFERENCES

1. Cibas ES. Thyroid. In: Cibas ES, Ducatman BS, editors. Diagnostic principles and clinical correlates. 4th ed. Philadelphia: Elsevier, 2014. p747
2. Elsheikh TM, Priollet BC, Hong SW, Sidawy MK. In: Ali SZ, Cibas ES, editors. The Bethesda system for reporting thyroid pathology. 2nd ed. Switzerland: Springer International Publishing. 2018. p1919-25.
3. Jayaram G, Orell SR. Thyroid. In: Houston M, Nash S, editors. Orell and Sterett's Fine needle aspiration cytology. 5th ed. Philadelphia: Elsevier Publishing, 2012. p122-28.
4. Zahorec R, Llisty BL. Neutrophil to lymphocyte ratio, past, present and future perspective. 2021. p1-2
5. Zhang J et al. The value of neutrophil-to-lymphocyte ratio combined with the thyroid imaging and reporting system in the diagnosis of the nature of thyroid nodules. J Clin Lab Anal. 2022. p2.
6. Aktas G. Hematological predictors of novel Coronavirus infection. Rev Assoc Med Bras (1992). 2021;67(suppl 1):1-2.
7. Aktas G, Sit M, Dikbas O, et al. Elevated neutrophil-to lymphocyte ratio in the diagnosis of Hashimoto's thyroiditis. Rev Assoc Med Bras. 1992;2017(63):1065-1068.
8. Feng J, Huang Y, Chen Q. Preoperative platelet lymphocyte lymphocyte (PLR) is a predictive factor for neutrophil to lymphocyte ratio (NLR) in patients with esophageal squamous carcinoma. World J Surg. Oncol. 2014;12:58. doi:10.1186/1477-7819-12-58.
9. Kurtul A, Ornek E. Platelet to Lymphocyte Ratio in Cardiovascular Diseases: A Systematic Review. Angiology. 2019 Oct;70(9):802-818.
10. Onalan E, Dönder E. Neutrophil and platelet to lymphocyte ratio in patients with hypothyroid Hashimoto's thyroiditis. Acta Biomed. 2020 May 11;91(2):310-314
11. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci. 2022 Mar 26;23(7).
12. Erge E, Kiziltunc C, Balci SB, Atak Tel BM, Bilgin S, Duman TT, Aktas G. A Novel

- Inflammatory Marker for the Diagnosis of Hashimoto's Thyroiditis: Platelet-Count-to-Lymphocyte-Count Ratio. *Diseases*. 2023 Jan 22;11(1):15.
13. Bilge M ,Yesilova A ,Adas M ,Helvacı A. Neutrophil and Platelet to lymphocyte ratio in with Euthyroid Hashimoto's Thyroiditis. *Exp Clin Endocrinol Diabetes* 2019;2019127(08):545-549.
 14. Arpacı D, Gurol G, Ergenc H, Yazar H, Tocoglu AG, Ciftci IH, Tamer A. A Controversial New Approach to Address Hematological Parameters in Hashimoto's Thyroiditis. *Clin Lab*. 2016 Jul 1;62(7):1225-1231
 15. Sharma G, Kumar A, Mittal A, Singh R, Chaudhary N. Diagnostic Utility of the Neutrophil-Lymphocyte Ratio and Absolute Lymphocyte Count in Distinguishing Thyroiditis vs Other Benign Causes of Thyroid Enlargement. *Cureus*. 2025 Mar 28;17(3)