Journal of Carcinogenesis
Covering Genesis to Therapeutics
Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 23: Issue 1, https://carcinogenesis.com/

Histopathological and Immunohistochemical Spectrum with Evaluation of Ki-67 Labelling Index on various Thyroid neoplasms.

Smriti bhaskar[1*], Hena A. Ansari[2], Anurag Kapoor[3], Sayeedul Hasan Arif[4]

[1*]Assistant Professor, Department of Pathology, Autonomous State Medical College, Sonebhadra, U.P.
[2] Associate Professor, Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh,U.P.
[3]Junior Resident, Department of Biochemistry, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, U.P.
[4]Professor, Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, U.P
***Corresponding Author:**

Email ID: drsmritibhaskar@gmail.com

ABSTRACT

Background: Thyroid lesions encompass a wide spectrum ranging from non-neoplastic conditions to benign and malignant neoplasms. Differentiating these entities, especially follicular patterned lesions, remains a diagnostic challenge. Ki-67, a cellular proliferation marker, has emerged as a useful adjunct in evaluating tumor behavior.
Aim: To analyze the histopathological spectrum of thyroid lesions and to evaluate the role of Ki-67 labelling index in their differentiation.
Materials and Methods: This cross-sectional study included 157 surgically resected thyroid specimens over a period of 5 years (2015–2020). Histopathological examination was performed using hematoxylin and eosin staining. Immunohistochemical analysis of Ki-67 was carried out in 40 selected cases. The Ki-67 labelling index was calculated and statistically analyzed using Chi-square test.
Results: Out of 157 cases, 95 (60.5%) were non-neoplastic and 62 (39.5%) were neoplastic.
Among neoplastic lesions, 18 (11.5%) were benign, 5 (3.2%) were borderline follicular patterned tumors, and 39 (24.8%) were malignant. Papillary thyroid carcinoma was the most common malignancy (80%). Ki-67 expression was absent in non-neoplastic lesions, low in benign tumors (≤3%), and significantly higher in malignant tumors (>3–5%). A statistically significant difference ($p<0.05$) was observed between benign and malignant lesions.
Conclusion: Ki-67 labelling index is a useful adjunct marker in distinguishing benign from malignant thyroid lesions and plays a significant role in evaluating follicular patterned tumors.

Key Words: Thyroid lesions, Ki-67, Histopathology, Thyroid neoplasms, Immunohistochemistry

How to Cite: Smriti Bhaskar, Hena Ansari, Anurag Kapoor, Sayadul Hasan Arif (2024) Histopathological and Immunohistochemical Spectrum with Evaluation of Ki-67Labelling Index on various Thyroid neoplasms. *Journal of Carcinogenesis, Vol.23, No.1*, 916-921

1. INTRODUCTION

Cancer thyroid lesions are among the most common endocrine disorders encountered in clinical practice. They range from non-neoplastic conditions such as colloid goiter and thyroiditis to neoplastic lesions including benign adenomas and malignant carcinomas. The incidence of thyroid cancer has shown a rising trend worldwide, with a higher prevalence in females. Histopathology remains the gold standard for diagnosis; however, certain lesions, particularly follicular patterned tumors, pose diagnostic challenges due to overlapping features. Immunohistochemistry has emerged as an important adjunct in improving diagnostic accuracy.

Ki-67 is a nuclear proliferation marker expressed during active phases of the cell cycle. The Ki-67 labelling index (LI) reflects the proliferative activity of tumor cells and has been studied in various malignancies as a prognostic and diagnostic marker. This study aims to evaluate the histopathological spectrum of thyroid lesions and assess the role of Ki-67 in their differentiation.

2. MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Pathology, Jawaharlal Nehru Medical College, AMU, Aligarh.

Study Design-Retrospective (3 years) and prospective (2 years), Study period: 2015–2020

Sample Size

Total cases: 157 thyroid specimens

Inclusion Criteria

Surgically resected thyroid specimens

Exclusion Criteria

Inadequate or poorly preserved samples

Histopathological Examination

Specimens were fixed in 10% buffered formalin, processed, and stained with hematoxylin and eosin. Detailed microscopic examination was carried out.

Immunohistochemistry

Ki-67 immunostaining was performed on 40 selected cases. The Ki-67 labelling index was calculated as the percentage of positively stained nuclei among at least 200 tumor cells.

Statistical Analysis

Data were analyzed using Chi-square test. A p-value <0.05 was considered statistically significant.

3.RESULTS

Distribution of Thyroid Lesions
Non-neoplastic: 95 (60.5%)
Neoplastic: 62 (39.5%) Neoplastic Lesions Benign: 18 (11.5%) Borderline (encapsulated follicular tumors): 5 (3.2%) Malignant: 39 (24.8%) Gender Distribution Females: 154 (98%)
Males: 3 (2%)

Histopathological Findings

Control: Cervical carcinoma

Most common non-neoplastic lesion: Colloid goiter (46.3%)

Most common benign tumor: Follicular adenoma (89%)

Most common malignant tumor: Papillary thyroid carcinoma (80%)

Ki-67 Expression, Non-neoplastic: 0% expression, Benign tumors: 1–3% expression, Malignant tumors: >3–5% expression.

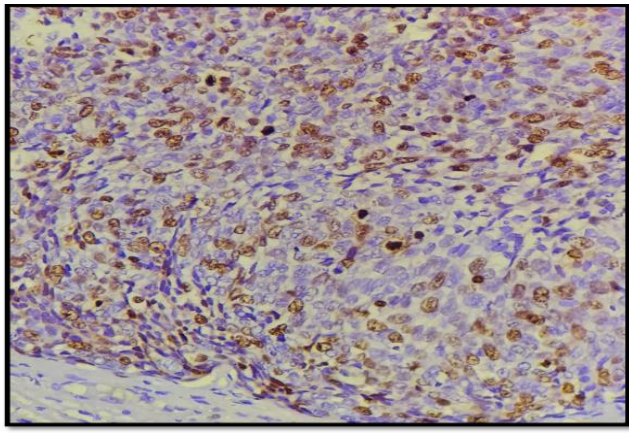


Fig-1.Positive control – cervical carcinoma showing High nuclear positivity in Ki-67 (4-5%)

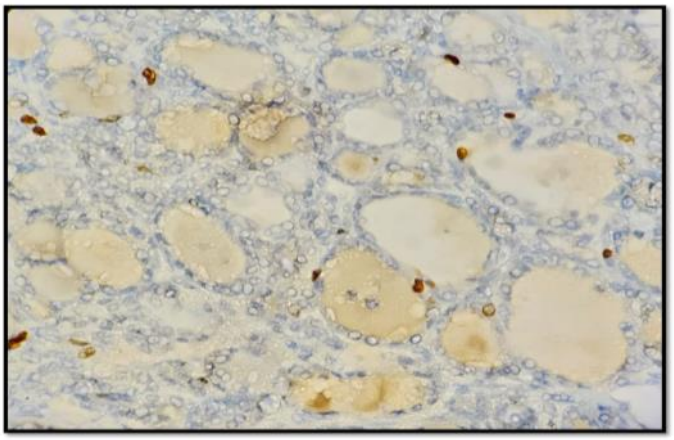


Fig-2: Follicular Adenoma showing Ki-67 nuclear positivity that is 1%

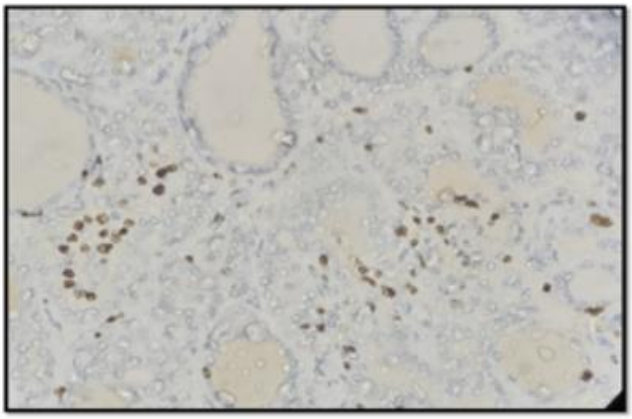


Fig-3: Follicular variant of Papillary Carcinoma Thyroid showing Ki-67 nuclear positivity that is 3%

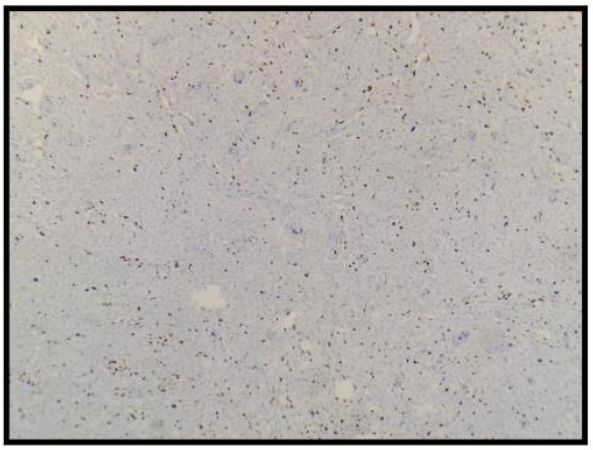


Fig-4: Medullary Carcinoma Thyroid showing Ki-67 nuclear positivity that is 4%

Significant differences were observed:

Non-neoplastic vs neoplastic ($p<0.05$), Benign vs malignant ($p<0.05$),v Malignant vs borderline tumors ($p<0.001$).

Tables and figure

Table 1: Distribution of Thyroid Lesions

Category	Number of Cases	Percentage
Non-neoplastic	95	60.5%
Neoplastic	62	39.5%

Table 2: Distribution of Neoplastic Lesions

Type	Cases	Percentage
Benign	18	11.5%
Borderline	5	3.2%
Malignant	39	24.8%

Table 3: Ki-67 Expression

Category	Ki- 67 Expression
Non- neoplastic	0%
Benign	≤3%
Malignant	>3–5%

Figure 1

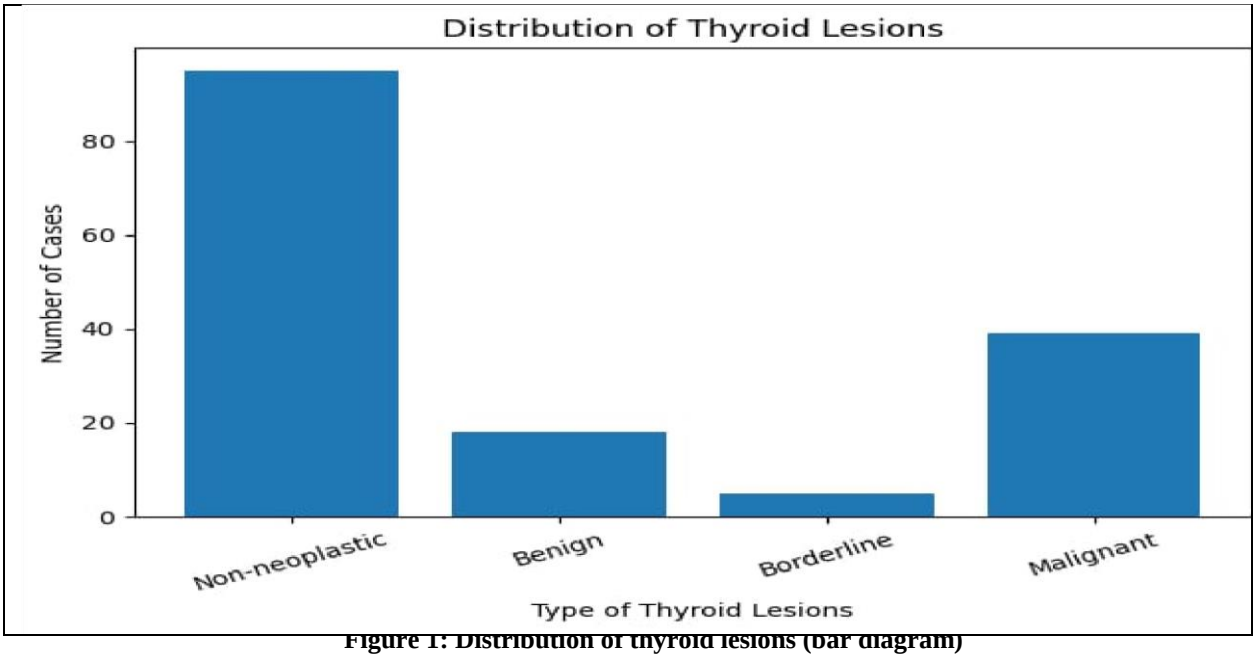


Figure 1: Distribution of thyroid lesions (bar diagram)

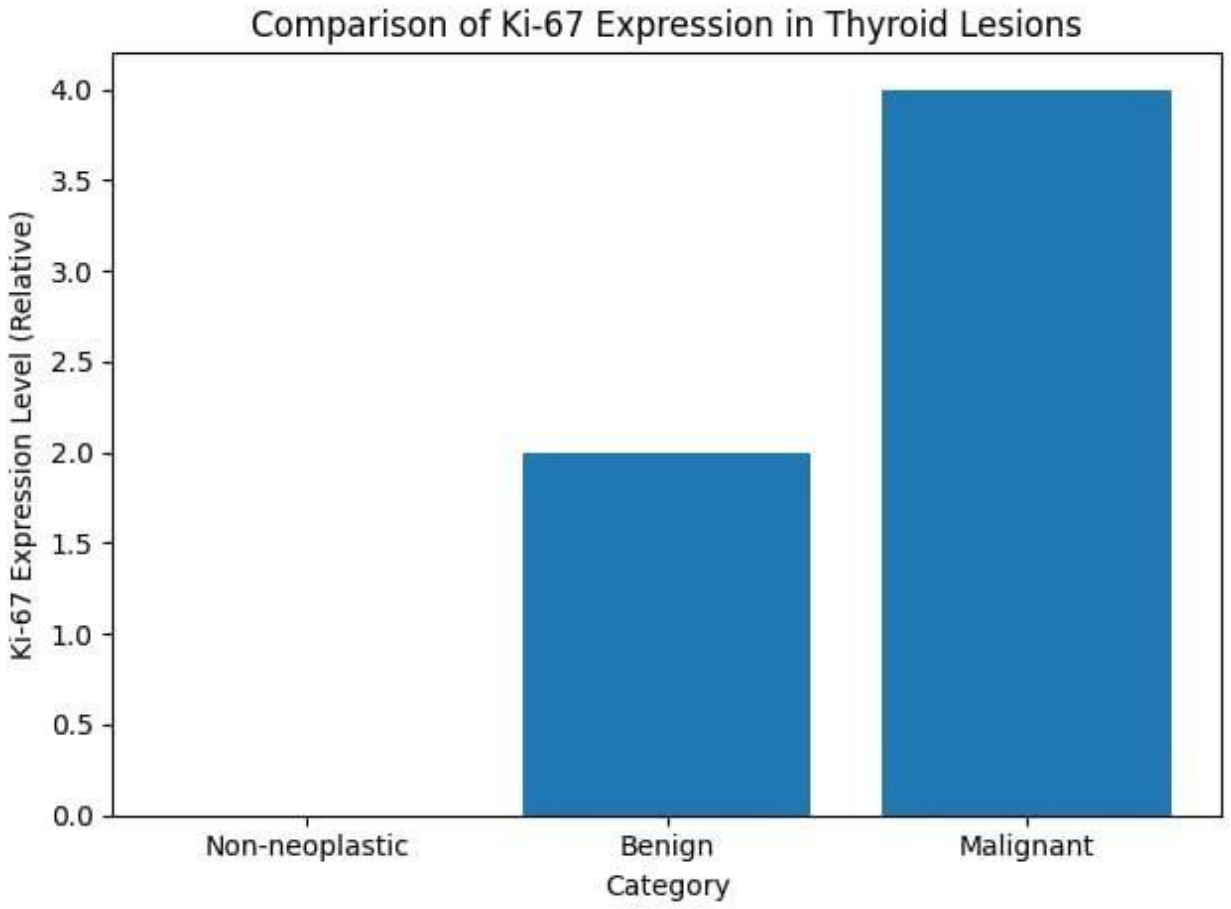
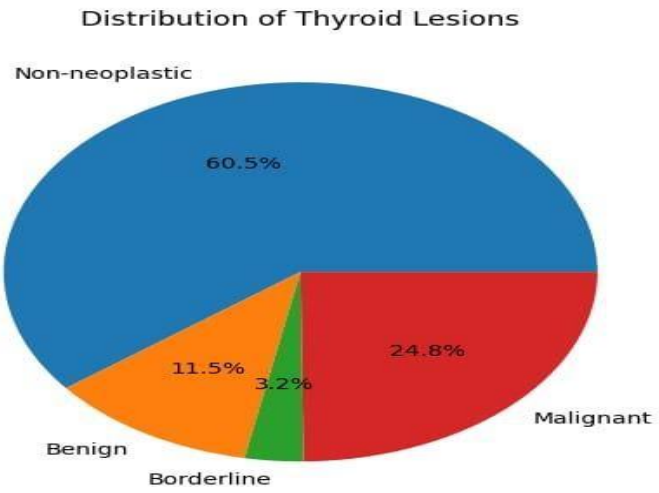


Figure 2: Ki-67 expression across lesions



4. DISCUSSION

Principal Findings-This study demonstrates that the majority of thyroid lesions are nonneoplastic (60.5%) with a marked female predominance (98%). Among neoplastic lesions, papillary thyroid carcinoma (PTC) constituted the most common malignancy (80%). Ki-67 labelling index (LI) showed a stepwise increase from non-neoplastic (0%) to benign (≤3%) and malignant lesions (>3–5%), with statistically significant differences between benign and malignant groups ($p<0.05$).

Comparison with Existing Literature

The predominance of non-neoplastic thyroid lesions and female preponderance observed in this study is consistent with earlier reports by Pellegriti et al. and Unnikrishnan et al., who noted higher incidence rates in females and increasing global trends in thyroid disorders (1,2). Similar distributions have been reported in Indian cohorts by Veedu et al. (3).

Papillary thyroid carcinoma being the most frequent malignancy aligns with global cancer registry data and studies by Nikiforov et al., where PTC accounts for the majority of thyroid cancers (4). The high proportion of follicular variant PTC (FVPTC) in our study further supports observations by Lloyd et al. regarding evolving histopathological classifications (5).

Role of Ki-67 in Thyroid Lesions

Ki-67 is a well-established proliferation marker expressed during active phases of the cell cycle. In the present study, all non-neoplastic lesions were negative for Ki-67 expression, whereas benign lesions showed low proliferative activity and malignant tumors exhibited significantly higher Ki-67 LI. These findings are in agreement with studies by Pujani et al. and Choudhury et al., which demonstrated statistically significant differences in Ki-67 expression between benign and malignant thyroid lesions (6,7).

Kakudo et al. proposed risk stratification of thyroid tumors based on Ki-67 LI, categorizing them into low, intermediate, and high-risk groups (8). Our findings corroborate this classification, as malignant tumors consistently showed higher Ki-67 expression**.**

Follicular Patterned Lesions

Differentiating follicular adenoma, follicular carcinoma, and borderline tumors such as NIFTP and FTUMP remains a diagnostic challenge. In our study, Ki-67 expression did not show significant differences between benign and borderline lesions ($p>0.05$), indicating overlapping proliferative activity. However, a significant difference was observed when compared with malignant lesions ($p<0.001$).These observations are consistent with Mu et al., who reported that Ki67 LI is higher in malignant follicular tumors compared to adenomas and borderline lesions

(9). Similarly, Wang et al. demonstrated that Ki-67 can aid in distinguishing aggressive variants of thyroid carcinoma (10).

Clinical Implications

The findings of this study suggest that Ki-67 LI can serve as a useful adjunct to histopathology, particularly in:

Differentiating benign from malignant thyroid neoplasms Supporting diagnosis in follicular patterned lesions

Assessing tumor proliferative activity and aggressiveness

However, Ki-67 should not be used as a standalone diagnostic marker and must be interpreted in conjunction with

histopathological features.

Strengths and Limitations

Strengths:

•Combined retrospective and prospective design

•Inclusion of a wide spectrum of thyroid lesions

•Application of immunohistochemistry with statistical analysis

Limitations:

Limited number of cases subjected to Ki-67 analysis (n=40)

Lack of longterm follow up for prognostic correlation

Single center study, limiting generalizability

Future Directions

Further multicentric studies with larger sample sizes and incorporation of additional molecular markers are recommended to enhance diagnostic accuracy and prognostic stratification of thyroid lesions.

5.CONCLUSION

The study demonstrates that thyroid lesions are predominantly non-neoplastic with a strong female preponderance. Ki-67 labelling index is a valuable adjunct tool in distinguishing benign from malignant thyroid lesions and provides additional diagnostic support in follicular patterned tumors.

Authors' Contributions

Smriti Bhaskar (Principal Investigator): Conceptualization and study design; supervision of research work; histopathological evaluation; interpretation of data; drafting and final approval of the manuscript.

Hena Ansari: Guidance in study design and methodology; review of histopathological findings; critical revision of manuscript for important intellectual content.

Anurag Kapoor: statistical analysis and interpretation of results; preparation of tables, figures, and graphical representations; literature review; drafting and editing of the manuscript.

REFERNCES

1. Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer. Nat Rev Endocrinol. 2013;9(6):327–36.
2. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15(Suppl 2):S78–81.
3. Veedu PT, et al. Trends in thyroid cancer incidence in India. NCRP Report. 2018.
4. Nikiforov YE, Seethala RR, Tallini G, et al. Nomenclature revision for encapsulated follicular variant of papillary thyroid carcinoma. JAMA Oncol. 2016;2(8):1023–9.
5. Lloyd RV, Osamura RY, Klöppel G, Rosai J. WHO Classification of Tumours of Endocrine Organs. 4th ed. IARC; 2017.
6. Pujani M, et al. Role of Ki-67 in thyroid lesions. J Cytol. 2010;27(3):105–10.
7. Choudhury M, et al. Ki-67 expression in thyroid neoplasms. Indian J Pathol Microbiol. 2011;54(3):456–60.
8. Kakudo K, et al. Ki-67 labeling index in thyroid tumors. Endocr J. 2015;62(1):1–8.
9. Mu N, et al. Diagnostic value of Ki-67 in thyroid tumors. Oncol Lett. 2018;15(2):123–30.
10. Wang W, et al. Ki-67 proliferation index in thyroid carcinoma. Medicine (Baltimore). 2018;97(30):e11589.
11. Gerdes J, et al. Production of a mouse monoclonal antibody reactive with a human nuclear antigen. Int J Cancer. 1984;31:13–20.
12. Alexander EK, et al. Preoperative diagnosis of thyroid nodules with indeterminate cytology. N Engl J Med. 2012;367:705–15.
13. Hsiao SJ, et al. Application of immunohistochemistry in thyroid tumors. Arch Pathol Lab Med. 2014;138:162–9.
14. Bejarano PA, et al. Diagnostic markers in thyroid pathology. Mod Pathol. 2007;20:123–9.
15. Park YJ, et al. Immunohistochemical markers in thyroid lesions. Thyroid. 2007;17:1–8.