

## Role of Marginal Vacuoles in Fnac Thyroid



### Medical Science

KEYWORDS : MVs – Marginal vacuoles

**Dr. Priti Singhal**

Student, Department of Pathology, Rabindra Nath Tagore Medical College, Udaipur, Rajasthan, India

**Dr. Dharmendra Kumar Garg**

Assistant Professor, Department of Pathology, Rabindra Nath Tagore Medical College, Udaipur, Rajasthan, India

**Dr. Sunita Bhargava**

Professor and Head, Department of Pathology, Rabindra Nath Tagore Medical College, Udaipur, Rajasthan, India

### ABSTRACT

*Marginal vacuoles (MVs) are irregular cytoplasmic vacuoles measuring 1-7  $\mu\text{m}$  in diameter, deeply eosinophilic in the periphery with a large unstained central area and tend to gather peripherally in a group of follicular epithelium. We studied the presence of MVs in thyroid enlargements with aims to assess the presence of MVs in diffuse thyroid enlargements, to investigate whether MVs have a diagnostic role in fine needle aspiration cytology of solitary thyroid nodules and to evaluate the degree of correlation between MVs, levels of thyroid hormones and cytological diagnosis. It was concluded that the presence of abundant MVs revealed an association with Primary hyperplasia and hyperthyroid cases; but they can also be seen in patients with Hashimoto's thyroiditis and in euthyroid cases. MVs are infrequent in Colloid goiter and do not correlate well with thyroid function.*

### INTRODUCTION

The critical issue in the management of patients with thyroid disease is to find a way to distinguish pre-operatively, benign nodules from cancers. Radiological imaging, serological and molecular studies have made major advances in the last decade in the diagnosis and management of patients with thyroid disease.

Fine needle aspiration has become the most prominent, and the easiest way, to morphologically evaluate lesions of the thyroid (Schinstine, 2010).

Soderstrom and Nilsson in 1972 were the first to discuss marginal vacuoles (MVs) in the cytoplasm of follicular cells in smears from toxic goiters. They reported that marginal vacuoles along with a nuclear ring pattern in follicular fragments are fairly specific signs of hyperfunction of the thyroid. But subsequently Orelle and Sterrets (2012) observed that although marginal vacuoles were present in Toxic nodular goiter, they may be seen in a smaller percentage of cells in Hashimoto thyroiditis, Diffuse or Nodular goiter and occasionally in a neoplasm including carcinoma. In untreated Graves disease however upto 100% of cells may show fireflares.

Marginal vacuoles (MVs) or fire-flare appearance have been described as irregular cytoplasmic vacuoles measuring 1-7  $\mu\text{m}$  in diameter, deeply eosinophilic in the periphery with a large unstained central area on May-Grünwald-Giemsa (MGG) stained fine needle aspiration (FNA) smears. They tend to gather peripherally in a group of follicular epithelium and hence are called marginal vacuoles. These marginal vacuoles stain poorly or not at all with PAS and are not positive for the acid phosphatases. They are not as distinct in wet fixed, haematoxylin-eosin stained smears as in dry fixed MGG stained smear (Gupta et al, 2013).

The true nature of marginal vacuoles is not known, although ultrastructural studies have indicated that these are dilated cisternae of endoplasmic reticulum generated by hyperactivity and vacuolar content of phagolysosomes (Galera, 1997).

The present study was undertaken to assess the presence

of marginal vacuoles in thyroid enlargements and evaluate the degree of correlation between marginal vacuoles, levels of thyroid hormone and cytological diagnosis.

### AIMS AND OBJECTIVES

To assess the presence of marginal vacuoles in diffuse thyroid enlargements.

To investigate whether marginal vacuoles have a diagnostic role in fine needle aspiration cytology of solitary thyroid nodules.

To evaluate the degree of correlation between marginal vacuoles, levels of thyroid hormones and cytological diagnosis.

### MATERIAL AND METHODS

The present study was conducted on patients with thyroid lesions who attended the Cytology section of Pathology Department, RNT Medical College, Udaipur. Study approval was obtained from the Ethics Committee of our institute

After taking detailed history and performing clinical examination, the patients were subjected to fine needle aspiration sampling. Smears were air dried and then stained with May-Grunwald-Giemsa stain.

Adequacy of the samples was assessed by using the Hamburger criteria (Hamburger et al, 1998), that is, six clusters of epithelial cells in at least two slides prepared from separate aspirates. A good criterion of adequacy, when appropriately applied, ensures a low false-negative rate.

Grading of marginal vacuoles was done as per the following criteria (Nilsson, 1972).

Grade I (No/scanty MVs): Distinct MVs exceeding 2 $\mu\text{m}$  in diameter demonstrated in <10% of cells.

Grade II (Moderate MVs): MVs seen in 10-50% of the cells examined.

Grade III (Abundant MVs): Presence of MVs in >50% of the cells examined.

The hormonal status of all the patients having thyroid enlargement was taken into account and depending on the values of the thyroid function test, the patients were categorized as euthyroid, hyperthyroid and hypothyroid

The presence and degree of grading of marginal vacuoles was then correlated with the cytological diagnosis of the patient and thyroid hormone status of the patient.

## RESULTS

Statistical analysis was done to evaluate the amount of marginal vacuoles with the hormonal status. It was found that euthyroid and hyperthyroid had high significant correlation with the presence of significant (abundant + moderate) marginal vacuoles (p value of 0.004 and 0.001 respectively). Hypothyroidism had insignificant statistical correlation with the presence of marginal vacuoles (p value 0.62) but had significant correlation with the absence of abundant marginal vacuoles (p value = 0.04).

**Table 1**  
Statistical correlation of marginal vacuoles with the hormonal status

Hormonal status	Abundant marginal vacuoles(a)	Moderate marginal vacuoles (b)	Significant marginal vacuoles (a+b)	P value
Euthyroid n=75	6	16	22	0.004
Hyperthyroid n=26	13	8	21	0.001
Hypothyroid n=29	0	7	7	0.62
Total	19	31	50	

Statistical correlation was done between the presence of marginal vacuoles and various cytological categories. It was observed that primary hyperplasia had significant statistical correlation with the presence of significant (abundant+moderate) marginal vacuoles (p value of 0.04) and insignificant correlation in all other categories. Colloid goiter showed a significant statistical correlation with the absence of marginal vacuoles (p value of 0.05).

**Table 2**  
Statistical correlation of cytological diagnosis with the presence of marginal vacuoles

Cytological diagnosis	Abundant marginal vacuoles (a)	Moderate marginal vacuoles (b)	Significant marginal vacuoles (a+b)	P value
Primary hyperplasia n=16	4	1	5	0.04
Colloid goiter n=62	5	16	21	0.50
Hashimoto's thyroiditis n=25	5	6	11	0.30
Follicular neoplasm n=24	5	8	13	0.29
Total	19	31	50	

Statistical evaluation was done using SPSS version 18.0 (LEAD Technologies, Inc., Charlotte, North Carolina, USA). A  $p \leq 0.05$  was considered as significant and a  $P \leq 0.01$  as highly significant.

## DISCUSSION

In our study, it was observed that Primary hyperplasia had a significant correlation with the presence of significant marginal vacuoles (abundant + moderate) with a p value of 0.04 and insignificant correlation in colloid goiter

(p value=0.50), Hashimoto's thyroiditis (p value=0.30) and Follicular neoplasm (p value= 0.29). Colloid goiter showed a significant statistical correlation with the absence of marginal vacuoles ( $P=0.05$ )

Das 1998 revealed marginal vacuoles in 42.6% of Hyperplastic nodules; that was highly significantly ( $P < .001$ ). Marginal vacuoles were limited to neoplasms with a follicular component and Follicular variant of Papillary carcinoma (FVPC) that was also statistically significant ( $p=0.002$ ).

Das 2006 observed the frequency of marginal vacuoles in Hyperplastic nodules (90.9%,  $P = 0.0196$ ) and in a significantly higher number of Follicular neoplasm (FN; 85.7%,  $P = 0.0069$ ).

A highly significant ( $p<0.001$ ) statistical correlation was observed in Primary hyperplasia by Bamanikar et al (2015).

On studying the association of hormonal status with the presence of marginal vacuoles, it was found that there was an overall significant correlation in all three hormonal groups with marginal vacuoles. On intragroup comparison, it was found that euthyroid and hyperthyroid patients had a significant correlation with a  $P$  value of 0.004 and 0.001, respectively. The statistical correlation of hypothyroid group with the presence of marginal vacuoles was insignificant with a  $P$  value of 0.62 but had a significant correlation with the absence of abundant marginal vacuoles with a  $p$  value of 0.04.

Volavsek 1996 observed, marginal vacuoles or/and marginal vacuole like structures more frequently (69%) in hyperthyroid patients with a  $p$  value  $< 0.05$ .

These findings in the present study were in consonance with the study conducted by Gupta et al,2013 where he observed a significant correlation in all three hormonal groups with marginal vacuoles ( $P = 0.001$ ).

Another study carried out by Bamanikar et al, 2015 also revealed abundant marginal vacuoles in hyperthyroid 11 of 15 (73.3%) followed by euthyroid 4 of 15 (26.7%). There were no abundant marginal vacuoles observed in hypothyroid cases. Thus, there was an overall significant association in all three hormonal groups with presence of marginal vacuoles ( $P = 0.03$ ).

## CONCLUSION

After analyzing the results of the present study, it was concluded that the presence of abundant "fire-flares" revealed an association with Primary hyperplasia and hyperthyroid cases; but they can also be seen in patients with Hashimoto's thyroiditis and in euthyroid cases. Marginal vacuoles are infrequent in Colloid goiter and do not correlate well with thyroid function. Further studies are needed on a larger sample size to corroborate the above conclusions because of the limited sampling size in the present study.

## REFERENCES

- Schinstine M: A brief description of the Bethesda System for reporting thyroid fine needle aspirates. *Hawaii Med J* 69(7); 176-8, 2010.
- Soderstrom N and Nilsson G. Cytologic diagnosis of thyrotoxicosis. *Acta Med Scand* 205:263-5, 1972
- Orell SR, Sterrett GF. 5th ed. New York: Elsevier Churchill Livingstone; Fine needle aspiration cytology;124,2012
- Gupta A, Manish S, Shivani K, Atul G, Onis S, Viplesh K: Cytomorphologic significance of marginal vacuoles in diffuse thyroid enlargement. *Journal of Cytology* 30(2):125-139, 2013
- Galera-Davidson H. Diagnostic problem in thyroid FNA. *Diagn Cytopathol* 17:422-8, 1997.

6. Nilsson G: Marginal vacuoles in fine needle aspiration biopsy smears of toxic goiters; *Acta Pathologica Microbiologica Scandinavica Section A Pathology*; 80A(3), 289-293, 1972
7. Das DK, Jain S, Tripathi RP, Parkash S, Khan IU, Rajwanshi A, et al. Marginal vacuole in thyroid aspirate. *Acta Cytologica* 42:1121-8, 1998.
8. Das DK. Marginal vacuoles (fire-flare appearance) in fine needle aspiration smears of thyroid lesions: Does it represent diffusing out of thyroid hormones at the base of follicular cells? *Diagn Cytopathol* 34:277-83, 2006.
9. Bamanikar S, Bamanikar A, Nair R, Chandanwale S, Kumar H, Buch A. Significance of Marginal Vacuoles in Fine Needle Aspiration Cytology of Diffuse Thyroid Swelling. *J Cytol Histol* ;2015
10. Volavsek M, Us Krasovek M, Auerspera M, Hocevar M, Golouh R. *Diagnostic Cytopathology* 15(2):93-97, 1996.