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Study to know the utility of HBME 1 and CK 19 in thyroid neoplasm: A tertiary care hospital and study

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Abstract
Introduction: Thyroid tumors are the most common endocrine tumors. Thyroid cancer is four times more common in women when compare to men. In the differentiation of thyroid lesions, cytokeratin 19 (CK19) and Hector Battifora mesothelial–1 (HBME -1) expressions were examined in many studies and significant results were obtained. In normal thyroid, follicular epithelium shows absence Cytokeratin 19 expression. Many studies reported a strong and diffuse staining pattern of CK19 in PTC. Expression of Hector Battifora mesothelial–1 was demonstrated in malignant thyroid neoplasms, especially PTCs.
Aims: To study the cytological and histomorphological features of thyroid neoplasm; and to analysis the utility of thyroid neoplasm; and to analysis the utility of immunohistochemical staining – HBME1 and CK-19 in thyroid neoplasm.
Results: A total of 29 patients with thyroid neoplasm were surgically operated and specimen were reviewed. Out of which 23 (79.4%) were females and 6 (20.6%) were males. Age of the patients ranged from 16 to 66 years. Expression of CK-19 in PTC seen in 15 (93.75%) cases in that 14 cases showed strong and diffuse positivity and 1 cases showed weak and focal positivity. Expression of CK-19 in FC is absent.
Conclusion: Thyroid neoplasm, cytological, histomorphological features immunohistochemical staining, HBME -1, CK- 19.

Keywords: TPO expression, CK-19 expression

Introduction

Thyroid tumors are the most common endocrine tumors and about 30% of the population of 30 years has thyroid nodules [1]. The overall incidence of thyroid carcinoma has increased more rapidly than that of any other malignancy [2]. Thyroid cancer is four times more common in women when compare to men [3]. Similar increases in frequency rates had been reported by various countries in the world [4]. At present, histopathologic evaluation using Hematoxylin and Eosin staining is the "gold standard" for the diagnosis of thyroid nodules and tumors [5]. Inmost cases the diagnosis of thyroid neoplasms is straight forward. However, pathologists have difficulty with lesions exhibiting equivocal features of benign and malignancy especially when there is a morphological overlap between follicular lesions and follicular variant papillary thyroid carcinoma. Even though the diagnostic criteria for Papillary thyroid carcinoma (PTC) and Follicular thyroid carcinoma (FTC) are clearlyoutlined inmany articles and textbooks. The application of these criteria is subjective and circumstantial. Diagnosis of follicular thyroid lesions lack consistency between interobserver or intraobservereven among expert pathologists, these are also well documented in many studies [6, 9].

In recent years, immunohistochemistry (IHC) markers and molecular markers, using somaticmutation, gene expression, and microRNA analyses are been useful in search of objective measures that differentiate benign from malignant lesions. In the differentiation of thyroid lesions, cytokeratin 19 (CK19) and Hector Battifora mesothelial–1(HBME -1) expressions were examined in many studies and significant results were obtained [10]. In normal thyroid, follicular epithelium shows absence Cytokeratin 19 expression [11, 12]. Many studies reported a strong and diffuse staining pattern of CK19 in PTC. Overexpression of CK19 is a good indicator for PTC; but the sensitivity for follicular carcinoma is low [13].

Overexpression of Hector Battifora mesothelial–1 was demonstrated in malignant thyroid neoplasms, especially PTCs, with the exception of Hurthle cell carcinomas [14, 15]. The objective of this article is to study the cytological and histomorphological features of thyroid neoplasm; and to analysis the utility of immunohistochemical staining – HBME1 and CK-19 in thyroid neoplasm.

Material and methods

Total of 29 cases of surgically resected thyroid neoplasm are taken during the period of June 2018 – May 2019 which was collected from the archive Department of Pathology at SMVMCH, Pondicherry, India. Parameters were obtained from the pathology reports such as age, gender, tumor size, multicentric disease, subtypes.All specimens were fixed in 10% formalin, routine processing and stained with hematoxylin and eosin. Cytological reports of histopathological proven thyroid neoplasm were taken and the diagnosis is compared. Then immunohistochemical staining was performed using two selected markers (CK 19 and HBME-1). Positive controls for HBME-1 (mesothelioma) and CK-19 (skin) were done. A case was considered positive for a particular marker when cytoplasmic 10% or more of the lesional cells was found reactive with the antibody.

Results

A total of 29 patients with thyroid neoplasm were surgically operated and specimen were reviewed. Out of which 23 (79.4%) were females and 6 (20.6%) were males. Age of the patients ranged from 16 to 66 years**.** 11 cases were under 40 – 50 years, 8 cases were under 30 – 40 years, 4 cases were under 20 – 30 years, 3 cases wereunder 50 – 60 years, 2 cases were under 60 – 70 years and 1 case were under 10 – 20 years.

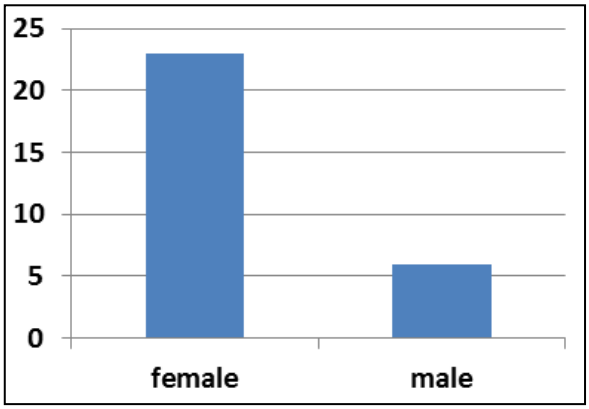

Fig 1: Gender wise distribution of cases

Table 1: Age distribution

Age range	Number of cases	Percent
10-20	1	3.44%
20-30	4	13.79%
30-40	8	27.58%
40-50	11	37.93%
50-60	3	10.34%
60-70	2	6.89%

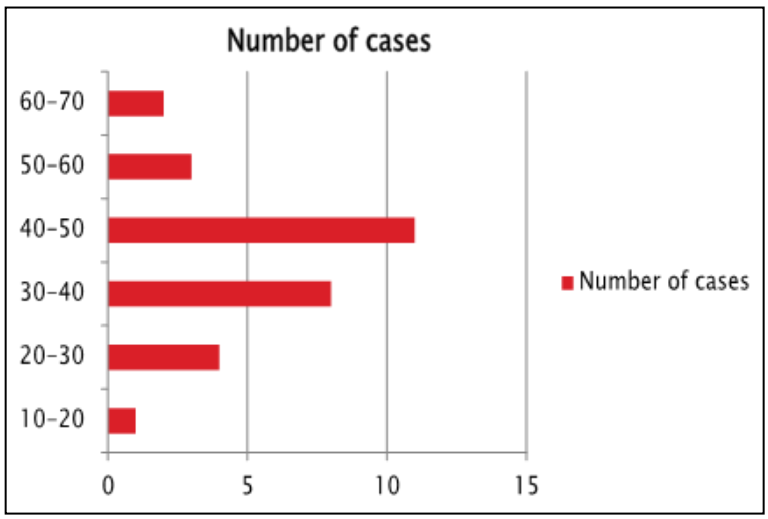

Fig 2: Distribution of cases according to age

Comparison of Histopathology and FNAC

Histopathology of these thyroidectomy specimen showed 16 (58.62%) with PTC. In fine needle aspiration cytology (FNAC) under Bethesda category these 16 cases of PTC was reported as 11 cases under category IV, 3 cases under category V and1 case in each category VI and category IV. Then 5 (17.24%) cases of NIFTP was reported in histopathology in which 3 cases was report under category III and 2 cases reported under category II. 4 cases of follicular adenoma was reported in histopathology in that 3 cases were reported as category II and one case under category III. 3 cases of FVPTC was reported in histopathology in that 2 cases was reported under category III and one case under category II. Then one case follicular carcinoma was reported in histopathology which was reported as category IV in FNAC.

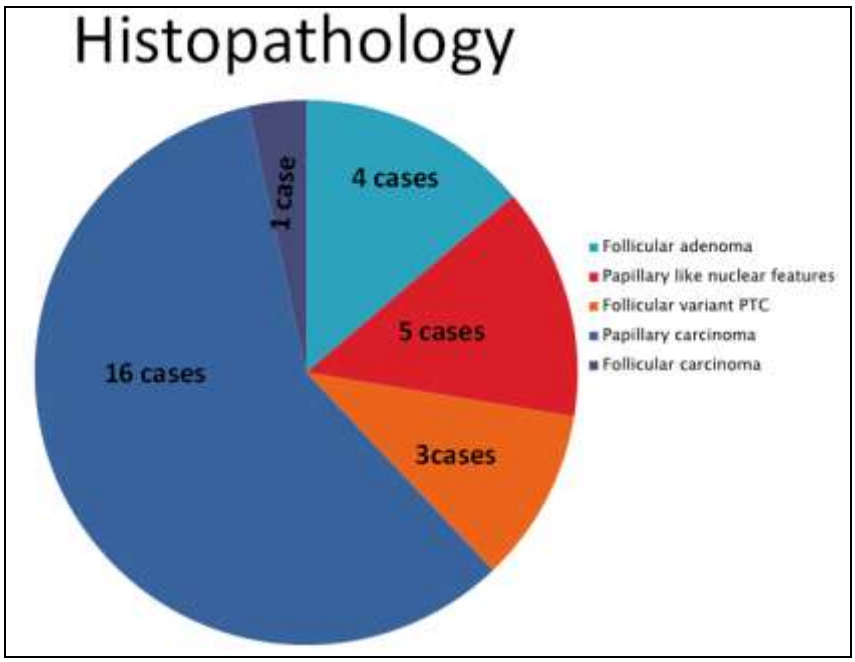

Fig 3: Histopathological distribution of thyroid neoplasms

Cytology of thyroid – Bethesda category

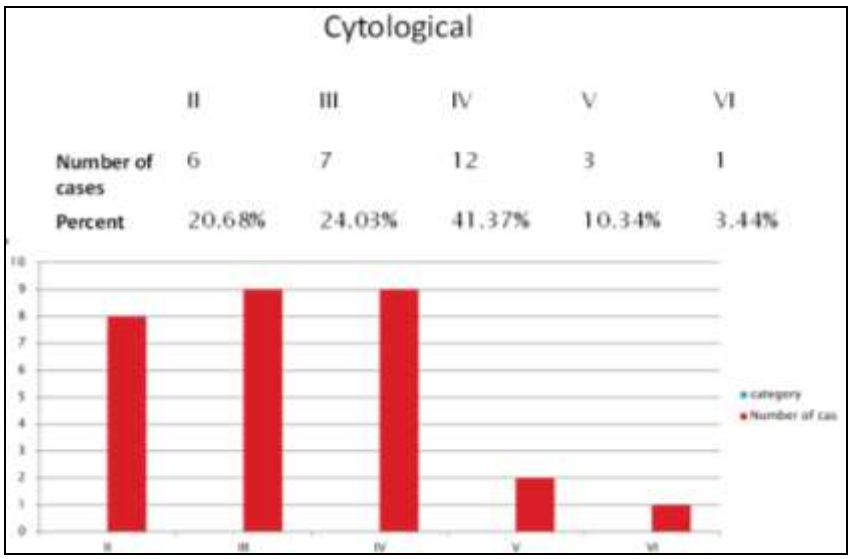

Fig 4: Cytological distribution of thyroid neoplasms

Comparison of Histopathological diagnosis with FNAC of thyroid neoplastic lesions.

Histopath Diagnosis	Number of cases	Percent	BC-I	BC-II	BC-III	BC-IV	BC-V	BC-VI
Follicular adenoma	4	13.79%		3	1			
NIFTP	5	17.24%		2	3			
Follicular variant PTC	3	10.34%		1	2			
Papillary carcinoma	16	58.62%			1	11	3	1
Follicular carcinoma	1	3.44%				1		

Fig 5: Comparison of histopathological diagnosis with FNAC

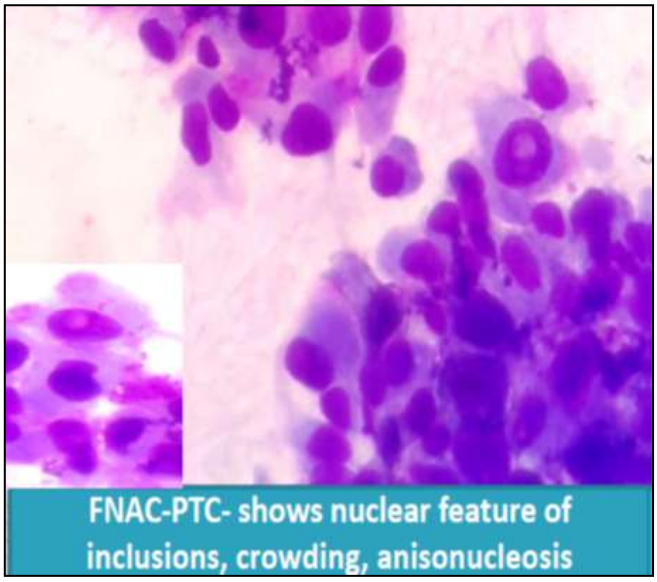

Fig 6: FNAC – Papillary carcinoma with nuclear inclusion, crowding and anisonucleosis

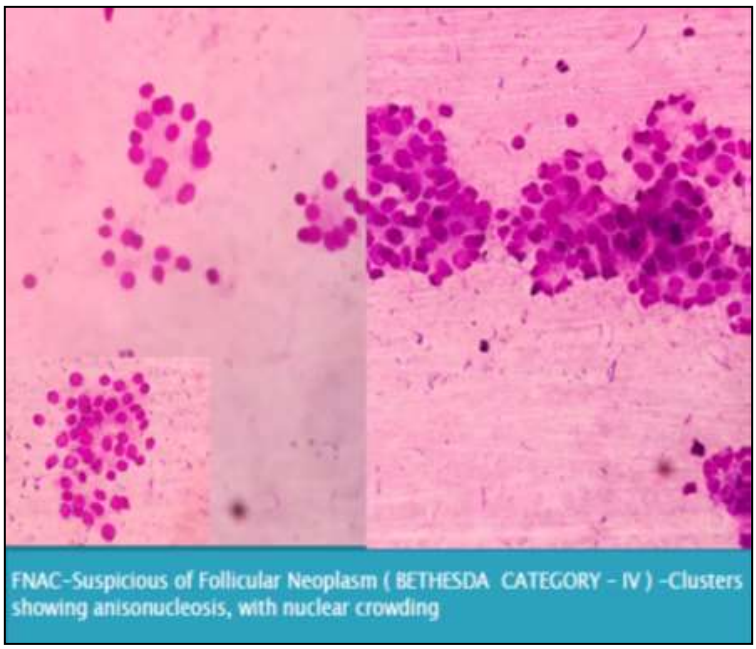

Fig 7: FNAC – Suspicious of Follicular Neoplasm (Bethesdacategory- IV) with nuclear crowding and anisonucleosis

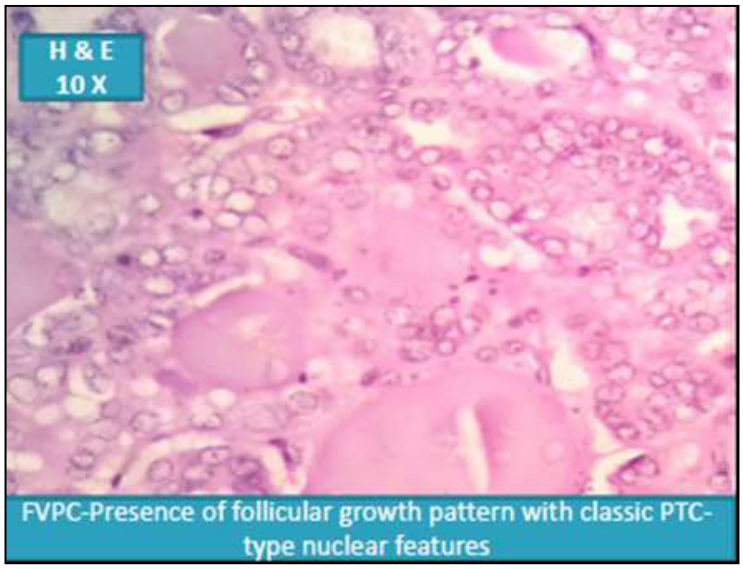

Fig 8: H&E 10X Follicular growth pattern with classic papillary carcinoma nuclear features

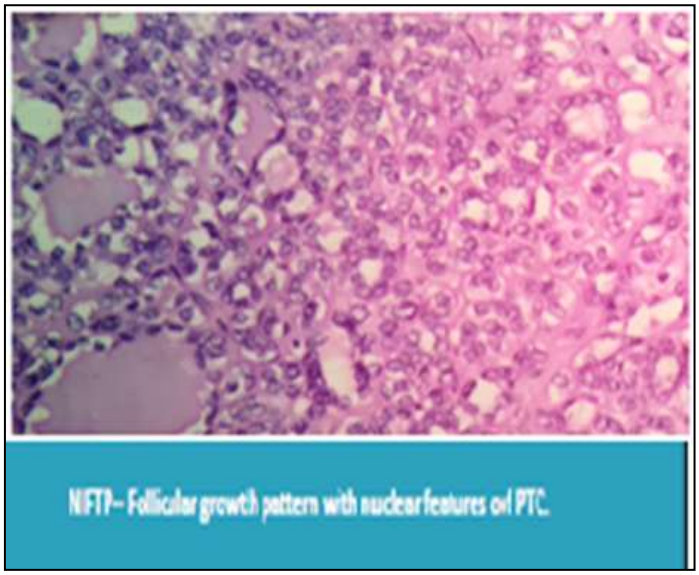

Fig 9: H&E 40X: Follicular growth pattern with nuclear features of papillary carcinoma

Expression of HBME 1 in thyroid Neoplam

16 cases of papillary carcinoma were identified and all were positive for HBME 1. 15 cases expressed strong and diffuse positivity. One case showed weak and focal positivity. 3 cases of FVPC were identified; 2 cases were positivity for HBME 1. One case expressed strong and weak positivity and another one case expressed weak and focal positivity. Then 5 cases in NIFTP were identidied; one cases expressed weak and focal positivity for HBME 1. HBME1 expression is absent in Follicular adenoma and Follicular carcinoma.

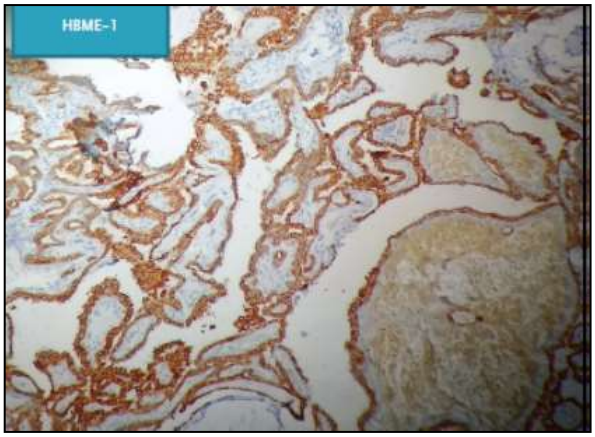

Fig 10: HBME 1 diffuse and strong positivity in papillary thyroid carcinoma (PTC) 100X

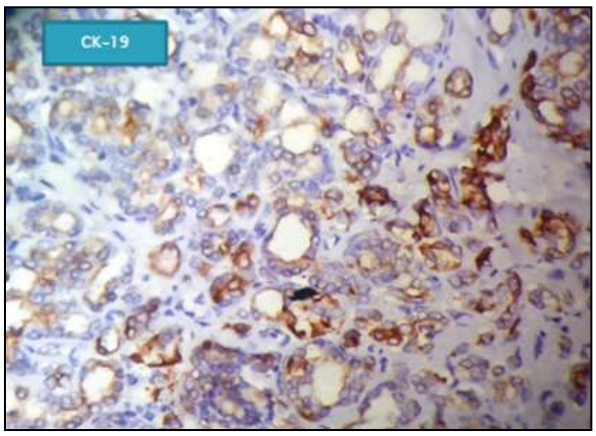

Fig 11: CK 19 diffuse and strong positivity in PTC 100X

Correlation of immunohistochemical staining results with histological diagnosis of thyroid lesions

Markers	FA (4)	NIFTP (5)	FVPC (3)	PTC (16)	FC (1)
HBME 1	0 0%	1 20%	2 66.6%	15 93.75%	0 0%
Strong and diffuse	–		1	15	0
Weak and focal		1	1	1	0
CK-19	1 20%	2 40%	3 100%	15 93.75%	0 0%
Strong and diffuse		0	1	14	0
Weak and focal	1	2	2	1	0

Fig 12: Correlation of IHC staining with histological diagnosis of thyroid lesion

Expression of CK – 19 in thyroid Neoplam

16 cases of papillary carcinoma were identified in that 15 cases expressed positive for CK 19 in which 14 cases expressed strong and diffuse positivity and one case expressed weak and focal positivity. 3 cases of FVPC were identified in which all 3 cases expressed postivity for CK 19; one case expressed strong and diffuse positivity and 2 cases expressed weak and focal positivity. Out of 5 cases in NIFTP 2 cases expressed weak and focal positivity for CK 19. Out of 4 cases in follicular adenoma only one case showed weak and focal positivity for CK 19. CK 19 expression was absent in Follicular carcinoma.

Other studies	PTC	FVPTC	FTC
Barroeta *et al.* [14]	91%	100%	43%
Cheung *et al.* [16].	66%	57%	0%
Saleh *et al.* [17].	85%	85%	83%
Present study	93.75%	66.6%	0%

Discussion

The age range and mean incidence is slightly higher as compared with previous studies.We found that majority of patients (37.93%) were in their fourth decade of life. Thyroid neoplasms were 4 times more common in females

as compared to males.In histopathology 16 cases of papillary carcinoma was reported in that 11 cases (41.3%) was reported under Bethesda category IV. Expect the papillary micro carcinoma, Follicular variant papillary carcinoma and NIFTP given in Besthesda category- II and Besthesda category III, this could be because of the focal involvement of the thyroid.

HBME 1 expression

According to this study that HBME1 expression is absent in Follicular adenoma and Follicular carcinoma. It has been found that HBME1 expression is present in NIFTP in 1(20%) cases but it as weak and focal expression. Expression of HBME1 in FVPC seen 2(66.6%)cases in that one case showed strong and diffuse positivity and another one case showed weak and focal expression. Expression of HBME1 in PTC seen in 16(93.75%) cases, in that 15cases showed strong and diffuse expression of HBME1 and 1 cases showed weak and focal expression. Barroeta *et al.* in their study showed 91% positivity for PTC, 100% for FVPTC and 43% for FTC. Cheung *et al.* in their study showed 66% positivity for PTC, 57% for FVPTC and 0% for FTC [14]. Saleh *et al.* in their study showed 85% positivity for PTC, 85% for FVPTC and 83% for FTC [16]. Hence comparing this study with others the result are equivocal.

CK 19 expression

It has been found that in Follicular adenoma, 1 (20%) case showed weak and focal expression for CK-19 but this expression less while comparing to PTC, FVPC. Expression of CK-19 in NIFTP is seen 2 cases (40%) but the expression is weak and focal.It has been found that expression in FVPC seen in all the 3(100%) cases but only 1 cases showed strong and diffuse positivity and other 2 cases showed weak and focal expression. Expression of CK-19 in PTC seen in 15 (93.75%) cases in that 14 cases showed strong and diffuse positivity and 1 cases showed weak and focal positivity. Expression of CK-19 in FC is absent. However, other studies showed variable results and yet others demonstrated that the CK19 expression is mostly focal and weak in FC and FA. Barroeta *et al.* in their study showed 91% positivity for PTC, 75% for FVPTC and 71% for FTC. Cheung *et al.*in their study showed 45% for FVPTC and 50% for FTC. Saleh *et al.* in their study showed 90% positivity for PTC, 92% for FVPTC and 75% for FTC. Torregrossa *et al.* in their study showed 95% positivity for PTC, 60% for FVPTC and 85% for FTC. Hence comparing this study with others the result are equivocal.

Conclusion

A benign FNAC diagnosis should be viewed with caution as false negative results do occur. These patients should be followed up and any clinical suspicion of malignancy even in the presence of benign FNAC requires surgery. Immunoexpression of CK19 and HBME-1 is an important supplementary test in the diagnosis of thyroid neoplasms, albeit it does not replace the conventional histomorphological examination. Therefore, we recommend using these panels as useful to differentiate Non invasive follicular thyroid neoplasm with papillary like nuclear features, Follicular variant of papillary thyroid carcinoma and Follicular adenoma.

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