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EXPRESSION OF CD56 AND HBME-1 IN SURGICALLY EXCISED THYROID NODULES

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ARTICLE INFO | **ABSTRACT** | **ORIGINAL RESEARCH ARTICLE**

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Introduction: Thyroid nodules represent a wide spectrum of neoplasms with different biological behaviors Majority of thyroid nodules are benign, but malignancy is found in approximately 5–15% of cases. Accurate diagnosis of these thyroid nodules is difficult, because of subtle and subjective histomorphological criteria. Immunohistochemistry method may play a complementary role to clarify diagnostic dilemma. CD56 is a neural cell adhesion molecule expressed on thyroid follicular cells. Down regulation of CD56 can shows correlation with tumour progression. Hector Battifora mesothelial epitope (HBME-1) is a membranous antigen located on follicular thyroid tumour cells and normal thyroid tissue is negative for HBME-1. **Objective:** To observe the expression of CD56 and HBME-1 in the diagnosis of surgically excised thyroid nodules. **Methods:** This cross sectional study was conducted in the Department of Pathology, Chittagong Medical College, Chattogram from March 2019 to February 2021. Immunohistochemistry was done at Armed Forces Institute of Pathology, Dhaka Cantonment. Sixty-three surgically resected thyroid nodules were evaluated to find out their histopathological type. Immunostaining was done by using primary antibody against CD56 (FLEX Monoclonal Mouse Anti-Human CD56 Clone 123C3 Ready to use (LINK). Denmark) and HBME-1 (Anti–Mesothelioma mouse monoclonal antibody HBME-1ab2383. Abcam, UK). Patient's demographic data were collected and recorded in a predesigned data

sheet. Statistical analysis was carried out as required. Ethical practice was ensured in every step of the study. **Results:** Among the 63 cases, mean age (±SD) of the patients was 39.47 ± 13.67 years and male to female ratio of 1:6.9. Thirty-four patients (76.3%) had multiple nodules. Among the 63 patients, 68.3% (43 cases) were histologically diagnosed as benign and 31 .7% (20 cases) as malignant thyroid nodules according 2017 WHO classification of thyroid tumours. Immunohistochemistry was performed using the markers CD56 and HBME-1 for all the 63cases.In present study weak to strong positive expression of CD56 was observed in 33(76.7%) cases out of 43 benign nodules whereas negative CD56 expression was observed in 20(100%) malignant cases. CD56 expression between benign and malignant lesion was statistically significant (p value, 0.002). HBME-1 was showed positive expression for 17(85%) out of 20 cases of malignant nodules and negative expression was observed in benign nodules. No statistically significant (p>0.250) difference was found between HBME-1 expression and histopathological diagnosis. So this study has improved the better understanding of thyroid nodules by expression of these immunomarkers (CD56 and HBME1) and thus may help the patients for selecting appropriate management protocol. **Conclusion:** In this study, Positive HBME-1 staining is a strong indicator of malignancy, although negative staining does not rule it out. IHC with CD56 and HBME-1 is considered to be important ancillary test in the diagnosis of thyroid neoplasms, but it does not replace the conventional histopathological examination.

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INTRODUCTION

Thyroid diseases are the most common endocrine disorders worldwide. In the United States about 40% of populations between 30 and 60 yrs have thyroid nodules [1]. The prevalence of thyroid nodules based on palpation in the generalpopulation is 2–6% [2]. But non palpable thyroid nodules found incidentally on highpopulation Ultra-Sonography suggest a rate of 19-67% [3]. Thyroid cancer accounts for 1-2% of all malignancies and 90% of all neuroendocrine tumours [4]. According to World Health Organization (WHO) GLOBOCAN Statistics, thyroidcancer was responsible for 567,000 new cases and 41,071 deaths in the year 2018 worldwide, ranking in ninth place for incidence. The global incidence rate in women of 10.2 per 100,000 is 3 times higher than in men [5, 6]. Majority of thyroid nodules are benign, but malignancy is found in approximately 5–15% of cases, the 'gold standard' in diagnosis of thyroid nodules is histopathologic evaluation using routine haematoxylin and eosin staining. Diagnostic dilemma may arise when an encapsulated nodule with a follicular pattern of growth exhibits clear nuclei with grooves and distinguishing follicular adenoma from encapsulated follicular variant papillary thyroid carcinoma becomes difficult. [7]. Liu et al [8] proposed well-differentiated tumor with uncertain behavior (WDT-UB) which covered WDT of UMP (WDT-UMP) and non-invasive encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC). These borderline/precursor thyroid tumors were incorporated in the 4th edition WHO

classification of thyroid tumors as a new tumor entity. Their behavior codes were decided to be 1 (borderline or uncertain behavior), and 0 (benign), 2 (in situ carcinoma) or 3 (malignant) [9,10]. Such morphological features put a burden on pathologist while trying to make diagnosis on H & E slides. Immunohistochemistry method plays a complementary role to clarify these dilemmas. CD56 is a neural cell adhesion molecule from the immunoglobin superfamily that mediates cell to cell adhesion. CD56is expressed in almost all benign thyroid tumor cells. Decreased expression of CD56 has frequently found in malignant thyroid tumour especially papillary thyroid carcinoma. Down regulation of CD56 can stimulate lymphangiogenesis and metastasis and shows correlation with tumour progression [11]. Diagnostic validity of CD56 was of highest sensitivity in differentiating follicular variant papillary thyroid carcinoma from follicular adenoma and follicular carcinoma from follicular adenoma 86% in both. Hector Battifora mesothelial epitope (HBME-1) is a membranous antigen located on microvilli of mesothelial cells and also in follicular thyroid tumour cells [1]. Normal thyroid tissue is negative for HBME-1. In previous study, diagnostic sensitivity was observed highest in differentiating follicular variant papillary thyroid carcinoma from follicular adenoma (100%), follicular variant papillary thyroid carcinoma from follicular carcinoma (100%), Papillary carcinoma from thyroid tumors of uncertain malignant potential (100%) and Papillary carcinoma from other benign non neoplastic lesions (100%) [10]. Patients with differentiated thyroid carcinoma have an excellent prognosis. After all, accurate histopathological examination of the specimen after (hemi) thyroidectomy with lymphadenectomy (if done) is regarded as the gold standard for the management and further therapeutic approach [12]. Borderline/precursor thyroid tumors are indolent tumors biologically and should be treated more conservatively [13]. If diagnosis can be made correctly, these individuals will be spared of unnecessary, aggressive surgical and radioactive iodine therapy and morbidity and financial costs related to these procedures.

OBJECTIVES

General objectives

- To evaluate the contribution of CD56 and HBME-1 immuno-expression in the diagnosis of surgically excised thyroid nodules.

Specific Objectives:

- To study the different histological subtypes of thyroid nodules.
- To assess the association of CD56 expression with histological type.
- To assess the association of HBME-1 expression with histological type.

MATERIALS AND METHODS

Type of the study: Cross sectional observational study.

Place of the study: Department of Pathology, Chittagong Medical College, Chattogram, Bangladesh. Immunohistochemistry was done at Armed Forces Institute of Pathology, Dhaka Cantonment, Dhaka, Bangladesh.

Study period: March 2019 to February 2021.

Study population: Total 63 Patients with clinically palpable thyroid nodules excised in the Department of E.N.T, Chittagong Medical College & Hospital, Chattogram, and other private hospitals in Chattogram were the target population during specified time duration.

Sample collection: The material for the present study was obtained from thyroidectomy specimens (lobectomies, hemithyroidectomies, and subtotal/total thyroidectomies) received at Department of Pathology Chittagong Medical College & Hospital, Chattogram. In all cases, the tissue was fixed in 10% buffered formalin, routinely processed, embedded in paraffin and microtomed sections stained with hematoxylineosin (H&E). Representative blocks were taken for immunohistochemistry.

Sampling technique: Consecutive sampling.

SAMPLE SELECTION CRITERIA

Inclusion criteria:

1. Patients with surgically excised palpable thyroid nodules.
2. Those patients who had given written informed consent for the study.

Exclusion criteria:

1. Patients with any form of malignancy metastasis to thyroid from other sites.
2. Patients previously treated with chemotherapy or radiotherapy for thyroid tumor.
3. Patients unwilling to give written consent.

Data collection procedure: Data was recorded considering the variables of interest by structured interview and then documented in a pre-designed case record form after taking informed written consent from the patients. Socio-economic profile of the patients was classified according to *modified Kuppus-wamy Socioeconomic status* scale. Patients were eligible for inclusion if they were undergone surgical resection of thyroid nodular leisons and all the specimens of each case were submitted for histological examination; and finally diagnosed according to the WHO classification.

Histopathologic Examination: All specimens of each case were processed by conventional histopathology method. Hematoxylin and eosin-stained slides of each case was prepared for proper microscopic evaluation. Sections were studied under light microscope to classify benign and malignant lesions and to select one representative paraffin block for immunohistochemical analysis.

Immunohistochemical Examination: From paraffin-embedded blocks, 4-micrometer thick sections were cut, deparaffinized with xylene and rehydrated through a graded series of alcohol. For antigen retrieval, the samples were carried out with 1 mmol/L of EDTA (pH 6 for HBME-1) with 10 minutes on the hotplate. This was followed by a 10-minute incubation in avidin biotin with tris(hydroxymethyl) aminomethane (Tris) buffer in between. Then the sections were successively stained separately with FLEX Monoclonal Mouse Anti-Human CD56 Clone 123C3 ready to use (LINK). Denmark and Anti –Mesothelioma mouse monoclonal antibody (HBME-1) ab2383. (Abcam UK). DAKO REALTM EnVision TM (HRP RABBIT/MOUSE) (ENV) was used as secondary antibody for both markers. Positive control was taken from sections of tonsils forCD56 immunostain and sections of papillary carcinoma of thyroid for HBME-1 immunostain.

Immunohistochemically Evaluation: The membranous expression of CD56 and HBME-1 was scored by the intensity of staining and percentage of positive cells. The scoring was done by using the 5HPF objective lens and counting at least 100 cells for immunoreactivity in 4 corners and central. The staining intensity was estimated as 0-no stain/ colorless, 1-slight staining/ yellowish, 2-moderate staining/ brown-yellow, 3-maximal staining/dark brown. Percentage of positive cells for CD56 (0- <10% positive cells, 1-<25% positive cells, 2- 26-50% positive cells, 3->50%) and for HMBE-1 (0- <5% positive cells, 1+- <30% positive cells, 2+-<50% positive cells, 3->50. The expression intensity was computed as the multiplication of the percentage of positive cells by staining intensity. The lesion was considered positive for a marker when the expression intensity was at least 2.

Statistical analysis of data: software Statistical Package for the Social Sciences, version 27 (SPSS Inc., Chicago, IL) was used for data analysis. Results were shown as table and expressed as frequency & percentage for qualitative data and mean ± SD for quantitative data and McNemartest was applied for compared of the two markers (CD56 expression & HBME-1 immunostaining) with histopathological examination. A 'p' value <0.05 was

considered as statistically significant because of all analysis were consider as 95% confidence level.

RESULTS AND OBSERVATIONS

The present study was carried to evaluate the diagnostic role of CD56 & HBME-1 immunoexpression in thyroid nodules. For these purposes total of 63 cases of surgically resected thyroid nodules sample were enrolled in this study. After details gross examinations of the specimens, hematoxylin and eosin stained sections were examined under the microscope for histological examination andCD56 & HBME-1 immunostaining were done.

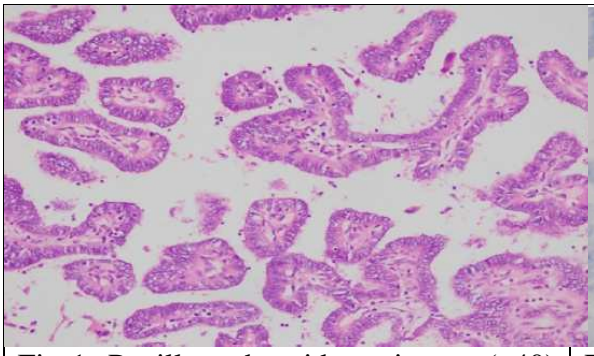

Fig-1: Papillary thyroid carcinoma (x40) H & E.

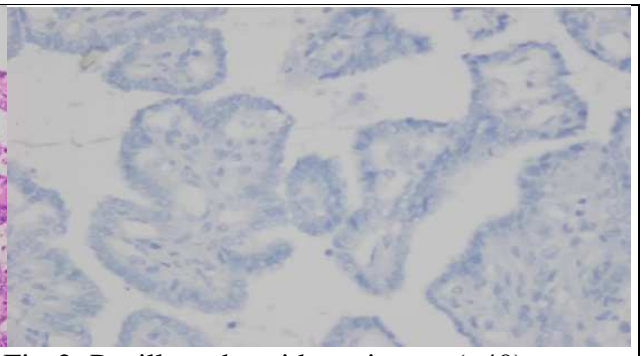

Fig-2: Papillary thyroid carcinoma (x40). CD56 expression: Negative

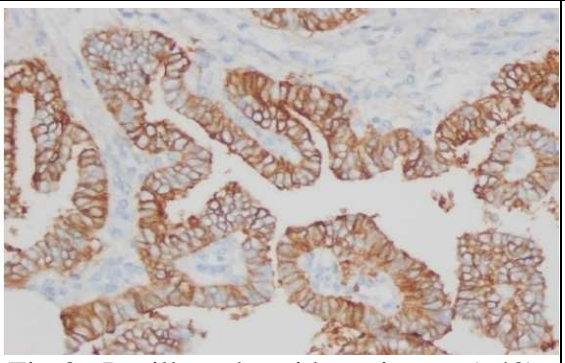

Fig-3: Papillary thyroid carcinoma (x40). HBME-1 expression: Strong positive (+++).

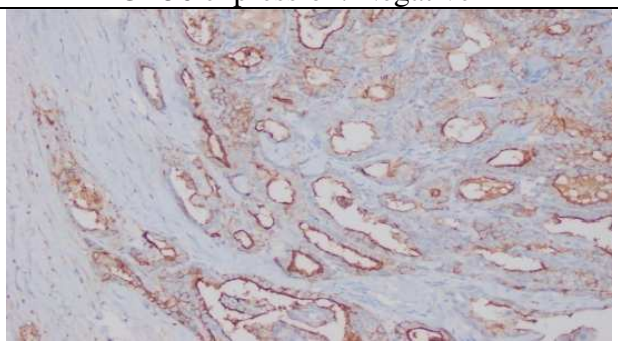

Fig-4: Papillary thyroid carcinoma (x40). HBME-1 expression: Capsular invasion. Strong positive (+++).

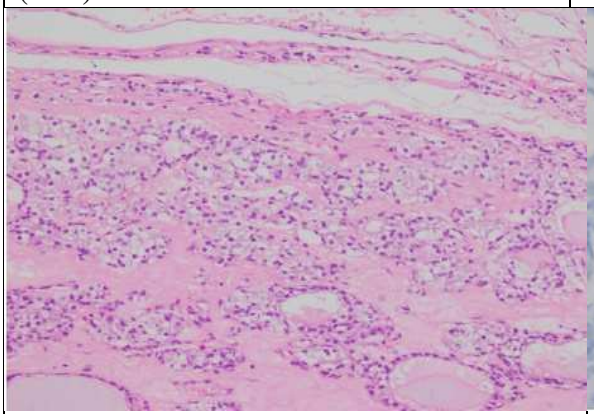

Fig-5: Follicular carcinoma (x20) H&E.

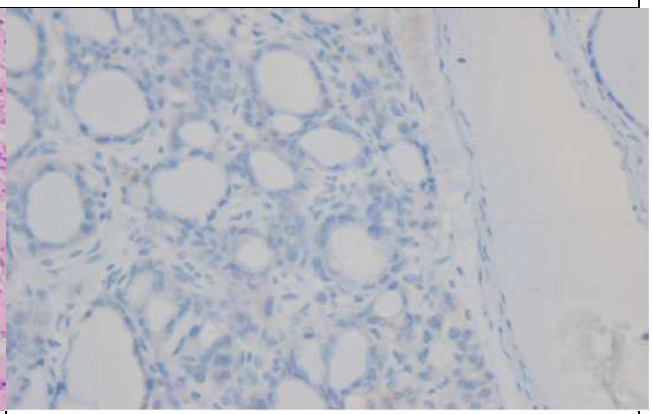

Fig-6: Follicular carcinoma (x40). CD56 expression: Negative.

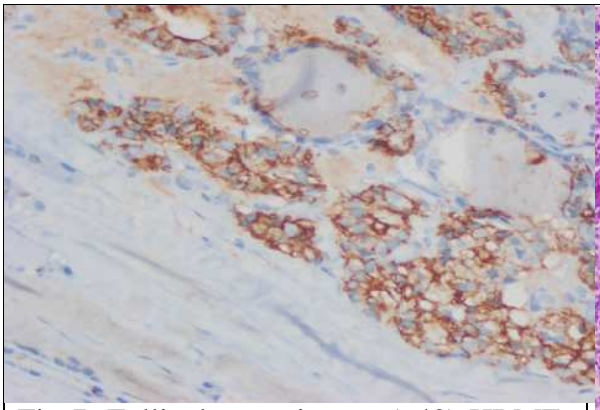

Fig-7: Follicular carcinoma (x40) HBME-1 expression: Capsular invasion, Strong positive (+++).

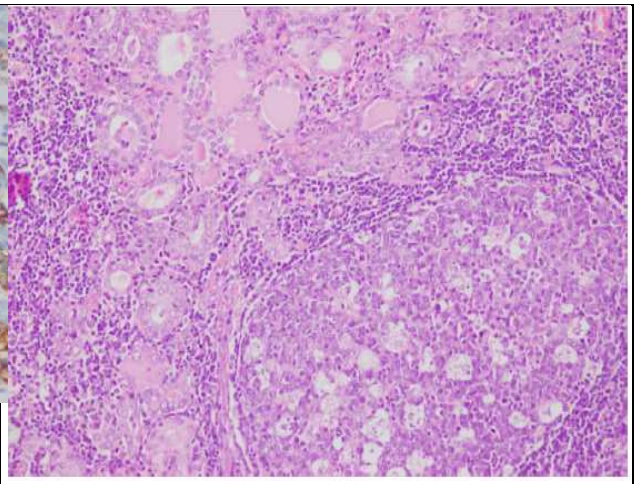

Fig-8: Hasimoto thyroiditis (x20) H&E.

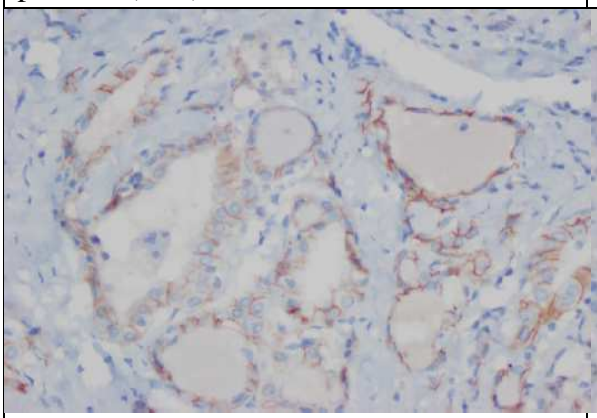

Fig-9: Hasimoto thyroiditis (x40) CD56 expression: Moderate positive (++).

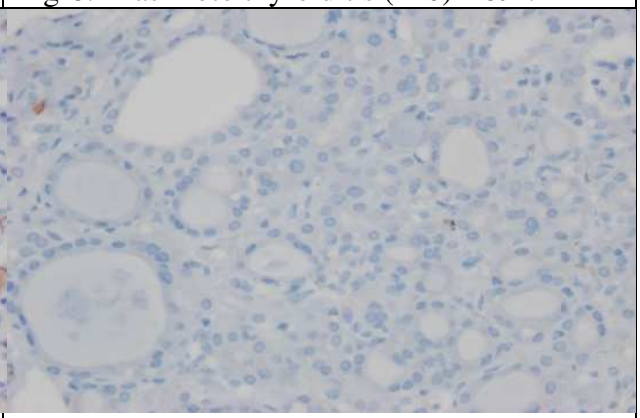

Fig-10: Hasimoto thyroiditis (x40) HBME-1 expression: Negative.

Distribution of the patients according to age (n=63):

Among the 63 cases of present study, 20 patients (31.7%) were in between 26-35 years of age, followed by 17 patients (27%) in between 36-45 years of age. The mean age (±SD) of the patients was 39.47 ± 13.67 years with the youngest and eldest patient in this study were 16 years and 74 years of old respectively (Table 1).

Table-1: Distribution of the patients according to age (n=63)

Age (Years)	**Frequency**	**Percent**
16-25	7	11.1
26-35	20	31.7
36-45	17	27.0
46-55	11	17.5
56-65	6	9.5
66-74	2	3.2
Mean ± SD (Min-Max)	39.47 ± 13.67 (16-74)	
Median	38	
Mode	40	

Gender:

Female was predominant (55 cases; 87.3 %) and male to female ratio was 1: 6.9 (Table 2). This study showed frank predominance of thyroid nodule in female patients.

Table-2: Distribution of the patients according to gender (n=63)

Gender	**Frequency**	**Percent**
Male	8	12.7
Female	55	87.3

Dietary iodine intake:

Out of 63 cases, 29 patients (46%) consume iodized salt and 34 patients (54%) consumed non-iodized salt (Table 3).

Table-3: Distribution of the patients according to dietary iodine intake (n=63)

Dietary iodine intake	Frequency	Percent
Yes	29	46.0
No	34	54.0
Total	**63**	**100.0**

Family history:

Maximum patients (59cases; 93.7%) had no significant family history. Four patients (6.3%) had a family history of the thyroid nodule (Table 4).

Table-4: Distribution of the patients according to family history (n=63)

Family history	**Frequency**	**Percent**
Yes	4	**6.3**
No	59	**93.7**
Total	**63**	**100.0**

Histopathological types:

In present study, among 63 cases of nodules, 37 cases (58.7%) were histopathologically diagnosed as multinodulargoitre (MNG). Hasimoto thyroiditis and follicular adenoma both were 3 cases (4.8%) respectively. Histopathologically diagnosed malignant nodules include – 10 cases of papillary thyroid carcinoma (15.9%), 5 cases (7.9%) of follicular variant PTC and 5 cases (7.9%) of follicular carcinoma. Histological typing was done according to 2017 WHO classification of thyroid tumors.

Table-5: Distribution of the patients according to histological types (n=63)

Histological Diagnosis	**Frequency**	**Percent**
Benign		
Multinodular Goitre (MNG)	37	58.7
Hasimoto Thyroiditis	3	4.8
Follicular Adenoma (FA)	3	4.8
Malignant		
Classic Papillary Thyroid	10	15.9

Carcinoma(PTC)		
Follicular variant PTC	5	7.9
Follicular Carcinoma (FC)	5	7.9
Total	63	100

Histopathological diagnosis (n=63)

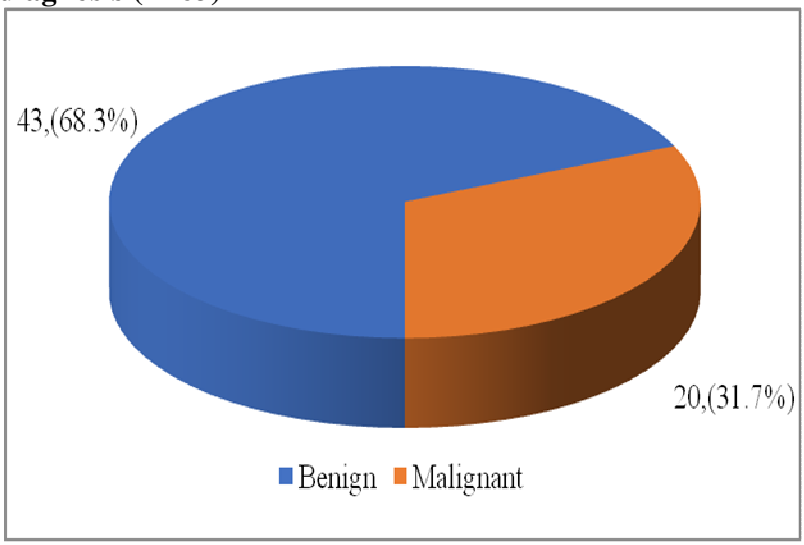

Fig-11: Pie chart of the patients according to histopathological diagnosis (n=63).

Figure 11 shows among the 63 patients, 43cases (68.3%) were histologically reported as benign and 20 cases (31.7%) as malignant according 2017 WHO classification of thyroid

Histopathological diagnosis and number of the nodule (n=63):

Among 29 cases of single nodule, 17 cases (58.6%) were malignant nodules, and the rest 12 cases (41.4%) were benign. On the other hand, among 34 cases of multiple nodules, mostly represented nodular goiter and other benign lesions -31 (91.2%) and only 3cases (8.8%) were malignant nodules. So, single nodules have a high possibility of being malignant. This association reached statistical significance ($p<0.05$) and was calculated by chi-square test (Table-6).

Table-6: Histopathological diagnosis and number of the nodule (n=63)

No. of nodule	Histopathological Diagnosis		p-value*
	Malignant	Benign	
Single (29)	17 (58.6)	12 (41.4)	<0.001
Multiple(34)	3 (8.8)	31 (91.2)	
Total	20 (31.7)	43 (68.3)	

CD56and HBME-1 expression with different histological types (n=63):

The positive CD56 expression was observed in 33/63 (52.4%) cases, which included 28/37 (76.7%) cases of MNG, 3/3 (100%) cases of Hashimoto's thyroiditis and 2 / 3(66.7%) cases of FA. Positive expression of HBME-1 in 17 out of 63 cases (27%) of thyroid nodule. It was negative in histomorphological diagnosed benign cases whereas 17 out of 20 (85%) malignant cases showed positive expression.

Table-7: CD56and HBME-1 expression with different histological types (n=63)

Histopathological Diagnosis	CD56 expression		HBME-1 expression	
	Positive	Negative	Positive	Negative
Multinodular Goitre (MNG)	28 (75.7)	9 (24.3)	0 (0.0)	37 (100.0)
Hasimoto Thyroiditis	3 (100.0)	0 (0.0)	0 (0.0)	3 (100.0)
Follicular Adenoma (FA)	2 (66.7)	1 (33.3)	0 (0.0)	3 (100.0)
Classic PTC	0 (0.0)	10 (100.0)	8 (80.0)	2 (20.0)
Follicular variant PTC	0 (0.0)	5 (100.0)	4 (80.0)	1 (20.0)
Follicular Carcinoma (FC)	0 (0.0)	5 (100.0)	5 (100.0)	0 (0.0)

CD56 expression:

In present study, CD56 was positive in 33 cases out of 43 benign cases. CD56 was negative in malignant cases. The expression of CD56 was statistically significant means there was a difference in diagnosis of benign nodule by CD56 expression and histopathological examination. It was calculated by Mc Nemar test (Table-8).

Table 8: CD56 expression with histopathological diagnosis (n=63)

CD56 expression	Histopathological Diagnosis		p-value*
	Benign	Malignant	
Positive	33(76.7)	0 (0)	0.002
Negative	10 (23.3)	20 (100.0)	
Total	43 (100.0)	20 (100.0)	

HBME-1 expression:

HBME-1 was expressed positive in 17 out of 20 malignant cases. Benign cases were negative for HBME-1. The expression of HBME-1 was not statistically significant ($p>0.05$) means no difference was observed between histopathological examination and HBME-1 expression for diagnosis of benign and malignant nodules. It was calculated by McNemar test.

Table-9: HBME-1 expression with Histopathological Diagnosis (n=63)

HBME-1 expression	Histopathological Diagnosis		p-value*
	Malignant	Benign	
Positive	17 (85.0)	0 (0.0)	0.250
Negative	3 (15.0)	43 (100.0)	
Total	20 (100.0)	43 (100.0)	

DISCUSSION

In the diagnosis of thyroid nodules, gold standard is histopathological evaluation. In the cases of morphological overlap, immunohistochemistry is needed for differential diagnosis [14]. The purpose of this study is to observe the expressions of CD56 and HBME-1 antibodies in surgically excised thyroid nodular lesions for diagnosis of benign and malignant nodules. A total 63 histopathologically diagnosed cases of surgically excised thyroid nodules were enrolled in this study. In present study, the mean age (±SD) of the patients was 39.47 ± 13.67 years with female predominance (55 cases; 87.3%). Male to female ratio was found 1: 6.9. These findings are nearly similar to the study of Durmus *et al* [14], who found a mean age of 48.2 for malignant and 50.8 for benign lesions (range: 21-77 years) with 83.6%

female patients. The male to female ratio was 1:5.2, which is much similar to the present result. Female sex was an independent risk factor for the development of Thyroid nodules. It was demonstrated in vitro studies that 17-estradiolmaystimulatethegrowth of normal thyroid cells and that thyroid follicular cells contained functional estrogen receptors [15]. This study showed that 46% (29) patients consume household iodized salt and 54% (34) patients consume non-iodized /inadequate iodized salt (commonly known as open salt). Benign disease mainly multinodulargoitre was seen in 25 (73.5%) patients under low coverage of adequately iodized household salt and 18 (62.1%) patients with consuming adequately iodized salt. Yusuf et al. [16] was conducted a Similar survey in Bangladesh. They observed inverse relationship between the coverage of adequately iodized household salt and the prevalence of iodine deficiency in children and women, which is similar to this study. In this study, 34 (54%) patients had multiple thyroid nodules and 29 (46%) patients had solitary nodules. Most of the multiple thyroid nodules 31 (91.2%) were histologically benign and only 3 (8.8%) were malignant. In the case of a solitary nodule, predominant nodules 17 (58.6%) were malignant followed by 12 (41.4%) were benign. Jena et al. [17] found that Solitary thyroid nodules have a high likelihood of harboring a malignancy. Among 63 cases of thyroid nodules in the current study 59 (93.7%) patients had no family history of thyroid disease. Only 4 (6.3%) patients had a family history of goitre and thyroid carcinoma. Three patients with multinodular goiter had a family history of MNG in their first degree relatives and one patient had a malignant thyroid disease (PTC) who was the son of a father having thyroid carcinoma. Among the patients according to histopathological classification, 43 (68.3%) patients had identified benign disease, 20 (31.7%) patients had identified malignant disease. CD56 is expressed in normal thyroid follicular cells with frequent low expression in malignant thyroid tumours. CD56 is a neural cell adhesion molecule and its expression may affect the migratory capability of tumour cells [11]. Positive CD56 expression was observed in 33/63 cases, which included 33 (76.7%) cases of benign. Negative expression was observed in 10/43 (23.3%) cases of benign cases. Several factors in tissue processing, included specimen fixation time, fixatives, reagent quality or failure to antigen retrival, variation in antibody dilution, incubation period were responsible for differences in CD56 expression among MNG. Different studies showed significant negative CD56 expression (from 92.5% to 100%) incases of malignancy mainly papillary carcinoma, FVPTC and FC. Park et al. [18] have worked CD56, galectin-3, and CK19 immunohistochemically in thyroidcarcinomas and benign thyroid nodules. There was no staining with CD56 in92.5% of PTC cases. In our study, CD56 negative staining100% for PTC was quite similar to the previous study. Park et al. also observed Staining percentages of CD56 for FA and NH cases were 93.3% and 90.5%. In our study Staining percentages of CD56 for benign lesions were 66.7% and 75.7%, which showed less CD56 sensitivity than their studies. In present study CD56 expression was negative in23.3% of benign tumour and 100% in malignant tumors (p=.002). Similarly, Alshenawy using a cut-off of 10% tumor cell staining, found that 7 of 8 cases (87.5%) of FVPTC to be negative for CD56 [11]. El Demellawy et al. [19] showed CD56 as an extremely useful marker in the distinction between PTCs and follicular lesions or neoplasms. According to their results, a diffuse expression of CD56 was present in normal and neoplastic follicular epithelium, but was absent in PTCs. In the present scenario, the HBME-1 marker is most promising antibody for identifying thyroid malignancy. HBME-1 stains mostly follicular

derived malignant tumors, including both well-differentiated and poorly differentiated carcinomas. HBME-1 proved to be the most specific marker in distinguishing benign from malignant thyroid pathology. In study, observed positive expression of HBME-1 in 17 out of 63 cases (27%). It was negative in histomorphological diagnosed benign cases. Histomorphologically diagnosed 17 out of 20 malignant cases (85%) showed positive expression. In a study, PALO *et* al. found positive expression of HBME-1 in 87.5% of malignant cases. Nasr *et al.* have worked a lot of immunohistochemical markers in 51 PTC and 57 benign thyroid lesions [20]. They have found HBME-1 staining in 96% of the malignant group and staining was not observed in 93% of benign lesions. This was quite similar to our study. Cheung et al. reported HBME-1 positivity in 70% classic PTC and 45% FVPC with no expression 7.5% of malignant cases. This study was compatible with present study.

CONCLUSION

In this study, Positive HBME-1 staining is a strong indicator of malignancy, although negative staining does not rule it out. Combination of the two markers HBME-1 and CD56 is found more useful in resolving the various patterned follicular lesions but it does not replace the conventional histopathological examination.

RECOMMENDATIONS

Expression of CD56 and HBME-1 can be used for detecting thyroid nodular character. Larger sample size, longer duration, multicenter studies with reliable, reproducible and equivalent standardized techniques, use of other biomarkers, molecular studies and follow up would bring out more and precise representative data.

LIMITATIONS

Study samples were taken from a single institute which may not reflect the exact scenario of whole country. Relatively small sample size due to financial constraints. Mutation could have been studied by RT-PCR & FISH for further analysis.

Conflict of Interest: None.

BIBLIOGRAPHY:

1. Saleh, H.A., Jin, B., Barnwell, J. and Alzohaili, O.,(2010). Utility of immunohistochemical markers in differentiating benign from malignant follicular- derived thyroid nodules. Diagnostic Pathology, 5(1).
2. Tamhane, S. and Gharib, H. (2016). Thyroid nodule update on diagnosis and management. Clinical Diabetes and Endocrinology, 2(1).
3. Hossain , M,A., Sarkar,M,J. , Dutta ,U,K., Karim,M,A. , Alam,Z,A.,(2014) Frequency of Malignancy in Solitary Thyroid Nodule and Multi-nodular Goitre. Bangladesh J Otorhinolaryngol 2014; 20(2): 55-65
4. Ozolins, A., Narbut, Z., Strumfa, I., Volanska, G., Stepanovs, K,. Gardovskis, J.,(2012) Immunohistochemical Expression of HBME-1, E- cadherinand CD56 in the Differential Diagnosis of Thyroid Nodules. , Medicina (Kaunas) 2012; 48(10):507-14.
5. Dirikoc, A., Faki, S., Baser, H., Özdemir, D., Aydin, C., Ersoy, R., Kilic, M., Kilicarslan, A. and Çakir, B. (2017). Thyroid malignancy risk in different clinical thyroid diseases. Turkish Journal of Medical Sciences, 47, 1509– 1519.
6. Topstad, D., Dickinson, J, A., (2017) Thyroid cancer incidence in Canada: a national cancer registry analysis. 10.9778/cmajo.20160162.
7. Naik, D., Jebasingh, Kf., and Thomas, N., (2018). Management of thyroid nodules in adults. Current Medical Issues, 16(2), 42.
8. Yao, Y., Chen, X., Wu, S., Liang, G., Zhang, H., Zhu, Q., et al., (2018). Thyroid nodules in centenarians: prevalence and relationship to lifestyle

characteristics and dietary habits. Clinical Interventions in Aging, Volume 13, 515–522.

9. Vecchia,V,C,, Malvezzi ,M., Bosetti,C., Garavello,W. , Bertuccio,P., Levi ,F.,et al (2015).Thyroid cancer mortality and incidence: A global overview Int. J. Cancer: 136, 2187–2195.
10. Alshenawy, H., (2014). Utility of immunohistochemical markers in differential diagnosis of follicular cell-derived thyroid lesions. Journal of Microscopy and Ultrastructure, 2(3),127.
11. Muthusamy S. , Shah SH ., Suhaimi SNA ., Kassim N ., Mahasin M ., Saleh MFH., Isa NM (2018) CD56 expression in benign and malignant thyroid lesions Malaysia J Pathol40(2) . 111 – 119.
12. Schmidbauer, B., Menhart, K.,, Hellwig ,D., Grosse,J.,(2017) Differentiated Thyroid Cancer Treatment: State of the Art. Int.J.Mol.Sci.2017,18,1292.
13. Kakudo, K., K, Adel., Naggar, El., P, Steven., Hodak., Khanafshar, E., E, Yuri., Nikiforov., *et* al,.(2018) Noninvasive follicular thyroid neoplasm with papillary- like nuclear features (NIFTP) in thyroid tumor classification, 1–7 Available online at doi:10.1111/pin.12673.
14. Durmus, E.S., Ozcan, D., Yarikkaya, E., Kurt, A. and Arslan, A. (2016). CD56, HBME-1 and cytokeratin 19 expressions in papillary thyroid carcinoma and nodular thyroid lesions. Journal of Research in Medical Sciences, 21(1), 49.
15. Jiang, H., Tian, Y., Yan, W., Kong, Y., Wang, H., Wang, A., et al (2016). The Prevalence of Thyroid Nodules and an Analysis of Related Lifestyle Factors in BeijingCommunities.InternationalJournalofEnvironmentalResearchandPublic Health.
16. Yusuf, H., Rahman, A. K. M, Chowdhury F P., Mohiduzzaman, M., Banu, C.P., Sattar, M.A., et al(2008) Iodine deficiency disorders in Bangladesh, 2004-05: ten years of iodized salt intervention brings remarkable achievement in lowering goitre and iodine deficiency among children and women. Asia Pac J ClinNutr 2008;17 (4):620-628.
17. Jena, A., Patnayak, R., Prakash, J., Sachan, A., Suresh, V., and Lakshmi A., (2015) Malignancy in solitary thyroid nodule: A clinicoradiopathological evaluation. 19(4): 498–503 Available online at doi:10.4103/2230-8210.159056.
18. Park, W.Y., Jeong, S. M., Lee ,JH., Kang ,HJ., Sin, DH., Choi ,KU., et al., (2009). Diagnostic value of decreased expression of CD56 protein in papillary carcinoma of the thyroid gland. Basic and Applied Pathology.2009; 2:63–8.
19. El, Demellawy .D., Nasr AL, Babay S,, Alowami, S,. (2009) Diagnostic utility of CD56 immunohistochemistry in papillary carcinoma of the thyroid. Pathol Res Pract.2009; 205(5):303–9.
20. Nasr, M.R, Mukhopadhyay, S., Zhang, S., Katzenstein, A.L., (2006). Immunohistochemical markers in diagnosis of papillary Thyroid carcinoma: Utility of HBME1 combined with CK19 immunostaining. Mod Pathol. 2006; 19 (12):1631–7.