MEDICINE UPDATES JOURNAL

Faculty of Medicine Port Said University

Volum: 28 No: 5 PP: 70 - 87

" *TROP2 Immunohistochemical expression in Classic and Infiltrative Follicular Variants of Papillary Thyroid Carcinoma and its Association with Histopathological Parameters*"

Authors

Ahmed Ali Elmetwally [1], Marwa Hosny Khashaba [2], Mayada Saad Farrag [2], Heba Mohamed Wagih [3], Azza Hassan Zidan [4]

[1] Pathology Laboratory, Ismailia Teaching Oncology Hospital, Ismailia, Egypt.

[2] Department of Pathology, Faculty of Medicine, Port Said University, Port Said, Egypt.

[3] Department of Pathology, Faculty of Medicine, Suez-Canal University, Ismailia, Egypt.

[4] Galala University, Suez, Egypt. - Department of Pathology, Faculty of Medicine, Port Said University, Port Said, Egypt.

Submitted: 2025-08-24

Accepted: 2025-09-13

DOI: 10.21608/muj.2025.417015.1256

ISSN : 2682-2741

ABSTRACT:

Background: Thyroid tumors are very common in Egyptian population, having 2% incidence and 7.73% prevalence. The most common type of malignant thyroid tumors is papillary thyroid carcinoma (PTC). Trophoblast Cell Surface Antigen 2 (TROP-2) antibody is expressed in various types of thyroid lesions.

Aim: To assess immunohistochemical expression of TROP-2 in classic and follicular variants of papillary thyroid carcinoma. Also, to evaluate association of its expression with variable demographic and histopathological parameters.

.

Subjects and Methods: The current study is a cross-sectional analytical study. Thirty-six cases were collected during the period of January 2017 to January 2018. The paraffin blocks are retrieved from archives of pathology laboratory at Suez Canal University Hospital; 18 blocks of classic PTC cases and 18 blocks of follicular variant of PTC (FVPTC).

Results: TROP-2 is positively expressed in 94.4% of classic variants of PTC and in 77.78% of infiltrative FVPTC. There is no statistically significant association between classic and FVPTC and the results of expression of TROP-2 ($p = 0.337$). TROP2 positive expression showed a statistically significant association with higher tumor stage in FVPTC group. The rest of demographic and histopathological parameters have shown no statistically significant association with TROP2 expression in either classic PTC or FVPTC groups.

Conclusions: TROP2 shows frequent membranous positivity in both classic and infiltrative follicular variant of PTC with higher levels of positivity in classic variant, within FVPTC group, TROP2 is positively correlated with higher T stage.

Keywords: TROP-2, classic variant of PTC, infiltrative FVPTC.

INTRODUCTION

Papillary thyroid carcinoma has been subclassified in the latest WHO classifications into 14 different subtypes, based of structural and cytological features, they are Classic/ conventional type, papillary microcarcinoma, encapsulated PTC, infiltrative follicular variant of PTC, diffuse sclerosing variant, tall cell variant, columnar cell variant, cribriform morular variant, hobnail variant, PTC with fibromatosis/ fasciitis like stroma, solid/ trabecular variant, oncocytic variant, spindle cell variant,

clear cell variant and Warthin-like variant (Jung., 2023; Bychkov & Jung., 2024; Lebrun & Salmon., 2024).

There are cellular/nuclear characteristics of papillary thyroid carcinoma such as nuclear enlargement, nuclear elongation, nuclear overlap, irregular nuclear membrane, nuclear pseudoinclusions, longitudinal nuclear grooving and nuclear chromatin clearing (Bychkov & Jung., 2024; Lebrun & Salmon., 2024).

Classic/ conventional variant is characterized by infiltrative complex papillary structures with fibrovascular cores, lined by above mentioned tumor cells. Papillary microcarcinoma is not a morphological subtype, but it is a PTC that is ≤ 1 cm in maximum diameter.

The infiltrative follicular variant is characterized by arranged in follicles lined by similar malignant tumor cells, this variant must be infiltrative, could show vascular emboli and not entirely capsulated, as one of the differential diagnosis is non-invasive follicular neoplasm with papillary like nuclear features which is a low-risk follicular cell derived thyroid neoplasm has similar cytological features but must be capsulated/well defined with no infiltrative foci, presence of papillary structures or vascular capsular invasion (Jung., 2023).

The currently used immunohistochemical cocktail markers that aid in diagnosis of difficult cases are HBME1, CK19 and Galactin 3, but till now no single marker is diagnostic and their accuracy is still controversial. HBME1 has a high specificity in conventional PTC cases, but with lower specificity in follicular variant of PTC (Vella et al., 2022; Abouelfadl et al., 2024).

TROP2 protein is a trans-membrane glycoprotein, it is encoded by tumor associated calcium signal transducer 2 (TACSTD2) gene (Turan & Erkılıç, 2023). It shows higher expression in multiple carcinomas as pancreatic, cervical, breast, lung and ovarian cancers than normal tissues (Abdou et al., 2019; Abdulwahhab et al., 2020).

TROP2 protein has a role in cell cycle progression and cellular proliferation, this is through activation of TROP2 domains, leading to more influx of cytoplasmic calcium, this activates cell cycle (Mcdougall et al., 2015). Also, phosphorylation of its cytoplasmic tail by protein kinases enhances activating mitogen-activated protein kinases (MAPKs), driving tumor growth and inducing cell proliferation (Cubas et al., 2010).

Some studies have shown overexpression of TROP2 protein in PTC (Sun et al., 2021; Abdou et al., 2019). However, TROP2 levels of expression in various variants of PTC should be studied to evaluate their diagnostic accuracy in various subtypes and to assess association with other demographic and histopathological parameters.

MATERIAL AND METHODS

Study setting and Study population:

The current study was a cross-sectional analytical study, executed in the histopathology laboratory Port Said University. Convenience sampling of available thirty-six cases were collected during the period of January 2017 to January 2018. The paraffin blocks were retrieved from archives of pathology laboratory at Suez Canal University Hospital; 18 blocks of classic PTC cases and 18 blocks of infiltrative follicular variant of PTC (FVPTC). Demographic and histopathological parameters were age at time of operation, gender, T stage, lymphovascular invasion, capsular invasion, extrathyroidal extension, lymph node metastasis state and tumor stage.

Inclusion Criteria:

1- Adequate samples diagnosed as classic or infiltrative follicular variant of PTC.

2- Samples with available histopathological and demographic data.

Exclusion Criteria:

1- Samples with scanty material which is not sufficient for proper immunohistochemical staining.
2- Cell blocks of FNAC specimens.

Histopathology and immunohistochemistry procedure:

Sections were cut at 4 µm thickness, stained by hematoxylin and eosin and reviewed by researchers to classify the tumor type based on the latest WHO classifications of endocrine neoplasms (Baloch et al., 2022). Staging of the tumor was based on TNM system according to AJCC, eighth edition (Amin et al., 2017), then assessment of lymphovascular invasion, tumor capsular invasion, extrathyroidal extension and lymph nodal metastasis was performed.

Sections were cut at 3 µm thickness from each block and mounted on positively charged slides, followed by automated TROP2 staining. Mouse purified monoclonal IgG TROP2 antibody (catalogue number sc-376181), at a dilution of 1/100 for 30 minutes, based on the protocol of company data sheet (Santa Cruz biotechnology, Inc), using Venata GX device, by Ventana CC2 retrieval buffer (low ph.) and Ventana detection kit. Positive control of prostate and negative control by omission of antibody have been used.

Evaluation of TROP2 IHC staining:

IHC stained slides were examined by microscope (Olympus BX43) and independent double blinded evaluation by at least two researchers was done for evaluation of IHC expression of TROP2. Expression of TROP-2

was evaluated for intensity as negative/faint staining, moderate and strong staining. Also, evaluated for proportion of staining. Slides were considered as positive for TROP-2 antibody expression if showing moderate or strong positive membranous staining of more than 10 % of stained cells (Yang et al., 2018).

Statistical analysis:

Descriptive analysis and calculation of percentage of different studied groups were done. Association between TROP2 expression and different histopathological and demographic parameters were assessed using appropriate statistical tests according to types of variables. Also, data illustration using tables, figures and charts were done. P- value was considered as significant when ≤0.05. Statistical analysis was done using the statistics software SPSS (Version 23) for windows 10.

Ethical considerations:

The study protocol was reviewed and accepted by the (IRB/IEC) institutional review board and institutional research ethics committee of PSU prior to initiation (ERN: MED (1/6/2023) s.no (95) PTH 904_001).

Funding source: Covered by the researchers.

Conflict of interest: Authors declared absence of conflict of interest related to the research.

Data Availability: All raw data supporting findings are available upon request from the corresponding author (Ahmed A. Elmetwally).

RESULTS

Histopathological and demographic characteristics:

This study was done on 36 cases of PTC cases; 18 cases were of classic variant of PTC and 18 cases were of infiltrative FVPTC. The demographic and histopathological data of these cases are listed in **(Table 1 and Table 2)**.

There was a statistically significant association between the female gender of cases and infiltrative FVPTC, compared to the classic variant of PTC **(P= 0.0029) (Table 2)**.

The rest of demographic and histopathological parameters as age of cases at time of excision, lymphovascular invasion, capsular invasion, extra thyroid extension, T stage, lymph nodal invasion status and stage showed no statistically significant differences between classic and follicular variants of PTC **(Table 1 and 2)**.

TROP2 IHC expression:

Cases of PTC were immunohistochemically stained for TROP2, 31 cases were positive for TROP-2, representing 86.11% of all cases. Twenty cases showed strong TROP2 expression, 11 cases showed moderate TROP-2 staining.

Seventeen cases of classic variant of PTC group out of 18 were positive for TROP2, representing 94.44% of group cases while 14 out of 18 cases of infiltrative FVPTC group were positive for TROP2, representing 77.78% **(Figure 1)**. So, there was no statistically significant association between the expression results of TROP2 and both classic and infiltrative follicular variant of PTC (p=0.3377) **(Table 3 and figure 2)**. Also, there was no statistically significant association between the intensity

or proportion of TROP2 expression in both groups (p= 0.427 and 0.659 respectively) **(Table 3)**.

Association between TROP2 expression and different demographic and histopathological characteristics

There was no statistically significant association between results of TROP2 expression and variable demographic and histopathological parameters in all cases of PTC (p >0.05), classic variant of PTC and infiltrative FVPTC **(Table 4, 5 and 6).** However, there was a statistically significant association between TROP2 expression and higher T stage (T3) in cases of infiltrative FVPTC compared to lower stages stage (T1 and T2) **(p= 0.0261) (Table 6)**.

DISCUSSION

Papillary thyroid carcinoma is a common tumor affecting Egyptian people and all over the world. Our study has been conducted to assess TROP2 expression in cases of papillary thyroid carcinoma. Addressing its most common variants; classic variant and infiltrative FVPTC. Also, assessment of association between the expression of TROP2 and variable demographic and histopathological parameters have been performed.

TROP2 is known to be a transmembrane glycoprotein. It is highly expressed in multiple carcinomas compared to normal tissues (Abdou et al., 2019; Abdulwahhab et al., 2020; Turan & Erkılıç, 2023). TROP-2 enhances tumoral cellular migration and metastasis (Guerra et al., 2023). It also shows membranous staining in thyroid lesions (Yang et al., 2018).

This study has been conducted on 36 cases of PTC, 18 cases of classic PTC and 18 cases of infiltrative FVPTC. In our study TROP-2 antibody showed exclusive membranous staining in 31 out of 36 cases of PTC. This pattern of expression of TROP-2 is like other studies as stated by Addati at al., and Attia et al. (Addati et al., 2015; Attia et al., 2024). Other studies have shown both membranous and cytoplasmic staining, this is likely due to different manufacturers of antibodies and different antigen retrieval methods (Yang et al., 2018; Abdou et al., 2019).

Cases of PTC were IHC stained for TROP2, 31 cases were positive for TROP-2, representing 86.11% of all cases. There are many studies that showed a similar level of expression (80-90%) in cases of PTC (Nesreen et al., 2018; Raouf et al., 2020), mostly due to adopting a similar method of interpretation of positivity.

Other studies have shown much lower levels of expression up to 50% due to less time of incubation of primary antibody and different producers of primary antibody (Murtezaoglu & Gucer., 2017). Also, other studies have shown a higher level of expression (more than 95%) in cases of PTC, likely due to adoption of different methods of interpretation of positivity (Yang et al., 2018; Saffar et al., 2021; Attia et al., 2024).

In our study TROP2 showed a positive expression in 94.44% (17/18) of classic PTC cases and in 77.78% (14/18) of infiltrative FVPTC cases, with no statistically significant association of TROP2 expression between them.

These results were similar to Nesreen et al. (2018) and Raouf et al. (2020) studies, due to similar manufacturer of the primary antibody. In the same time; our results were contradictory to those of Murtezaoglu & Gucer (2017) and Abdou et al. (2019) studies, due to different manufacturer, being a

polyclonal antibody and shorter incubation period in Murtezaoglu & Gucer study and adopting a different method of evaluation of TROP-2 positivity by only considering strong TROP-2 staining as positive.

In our study there was no statistically significant association between all demographic parameters and cases of PTC. Many studies have shown similar results (Yang et al., 2018; Abdou et al., 2019; Attia et al., 2024).

Also, our study has shown no statistically significant association between all histopathological parameters and cases of PTC. This is in line with many studies (Yang et al., 2018; Attia et al., 2024) as they used a similar method for interpretation of positivity of TROP2. This is contrary to Abdou et al. study, that has shown a significant association of lymph nodal metastasis and TROP2 positivity, with no other significant associations with other histopathological parameters (Abdou et al., 2019).

Concerning association with demographic and histopathological parameters with TROP2 in classic or infiltrative FVPTC, these relations have not been addressed by other researchers.

There is no statistically significant association between all demographic and histopathological parameters in cases of classic PTC and TROP2 expression. However, regarding infiltrative FVPTC there is a statistically significant association between higher T stage and positivity of TROP2. The rest of all demographic and histopathological parameters in cases of infiltrative FVPTC have shown no statistically significant association with TROP2 expression.

Table (1): Comparison between classic PTC and infiltrative FVPTC according to demographic data

		Classic PTC (n = 18)		FVPTC (n = 18)		P
		No.	%	No.	%	
Age	**Less than 55**	13	72.2	11	61.11	0.4795
	55 or more	5	27.8	7	38.89	
Gender	**Male**	9	50	1	5.56	**0.0029** FET *
	Female	9	50	17	94.44	

χ^2: Chi square test FET: Fisher Exact test
p: p value for comparing between the two studied groups
*: Statistically significant at $p \leq 0.05$

Table (2): Comparison between classic PTC and infiltrative FVPTC according to histopathological parameters

		Classic PTC (n = 18)		FVPTC (n = 18)		P
		No.	%	No.	%	
Lymphovascular invasion state	**No**	16	88.89	18	100	0.4857
	Yes	2	11.11	0	0	
Capsular Invasion	**No**	1	5.56	4	22.22	0.3377
	Yes	17	94.44	14	77.78	
Extra-thyroid extension	**No**	17	94.44	16	88.89	1
	Yes	1	5.56	2	11.11	
T stage	**T1**	5	0.0	5	17.7	0.313
	T2	7	4.0	3	19.0	
	T3	6	44.0	10	22.8	
LN stage	**NX/0**	15	83.33	15	83.33	1
	N1	3	16.67	3	16.67	
Stage	**I**	16	88.89	14	77.78	0.6581
	II	2	11.11	4	22.22	

FET: Fisher Exact test
p: p value for comparing between the two studied groups

Table (3): Comparison between classic PTC and infiltrative FVPTC according to TROP2 staining

TROP2		Classic PTC (n = 18)		FVPTC (n = 18)		P
		No.	%	No.	%	
Intensity	Negative/faint Moderate Strong	1 6 11	5.56 33.33 61.11	4 5 9	22.22 27.78 50	0.427
Result	Negative Positive	1 17	5.56 94.44	4 14	22.22 77.78	0.3377
Proportion	Min. – Max. Mean ± SD.	0.0 – 100.0 53 ± 43.428		0.0 – 100.0 61 ± 37.096		0.659

SD: Standard deviation p: p value for comparing between the two studied groups.

Table (4): Relation between TROP2 Result with demographic and histopathological data and in all PTC cases (n = 36)

		N	TROP2 Result				p
			Negative (n = 5)		Positive (n = 31)		
			No.	%	No.	%	
Gender	Male Female	10 26	1 4	10 15.39	9 22	90 84.61	^{FE}p= 1.000
Age	Less than 55 55 or more	24 12	5 0	20.83 0	19 12	79.17 100	^{FE}p= 0.1464
Lymphovascular invasion state	No Yes	34 2	5 0	14.7 0	29 2	85.3 100	^{FE}p= 1.000
Capsular Invasion	No Yes	31 5	5 0	16.13 0	26 5	83.87 100	^{FE}p= 1.000
Extra-thyroid extension	No Yes	33 3	5 0	15.15 0	28 3	84.85 100	^{FE}p= 1.000
T stage	T1 T2 T3	10 10 16	2 3 0	20 30 0	8 7 16	80 70 100	^{FE}p= 0.0705
LN stage	NX/0 N1	30 6	5 0	16.67 0	25 6	83.33 100	^{FE}p= 0.5638
Stage	I II	30 6	5 0	16.67 0	25 6	83.33 100	^{FE}p= 0.5638

FET: Fisher Exact test p: p value for Relation TROP2 Result and different parameters

Table (5): Relation between TROP2 results with demographic and histopathological data and in classic PTC group (n = 18)

		N	TROP2 Result				p
			Negative (n = 1)		Positive (n = 17)		
			No.	%	No.	%	
Gender	**Male**	9	0	0	9	100	^{FE}p= 1.000
	Female	9	1	11.11	8	88.89	
Age	**Less than 55**	13	1	7.69	12	92.31	^{FE}p= 1.000
	55 or more	5	0	0	5	100	
Lymphovacular invasion state	**No**	16	1	6.67	15	93.33	^{FE}p= 1.000
	Yes	2	0	0	2	100	
Capsular Invasion	**No**	17	1	5.88	16	94.12	^{FE}p= 1.000
	Yes	1	0	0	1	100	
Extra-thyroid extension	**No**	17	1	5.88	16	94.12	^{FE}p= 1.000
	Yes	1	0	0	1	100	
T stage	**T1**	5	0	100	5	100	^{FE}p= 1.000
	T2	7	1	14.29	6	85.71	
	T3	6	0	100	6	100	
LN stage	**NX/0**	15	1	6.67	14	93.33	^{FE}p= 1.000
	N1	3	0	0.0	3	100.0	
Stage	**I**	16	1	6.67	15	93.33	^{FE}p= 1.000
	II	2	0	0	2	100	

FET: Fisher Exact test

p: p value for Relation TROP2 Result and different parameters

Table (6): Relation between TROP2 Result with demographic and histopathological data and in infiltrative FVPTC group (n = 18)

		N	TROP2 Result				p
			Negative (n = 4)		Positive (n = 14)		
			No.	%	No.	%	
Gender	**Male**	1	1	100	0	0	^{FE}p=
	Female	17	3	17.65	14	82.35	0.222
Age	**Less than 55**	11	4	36.36	7	63.64	^{FE}p=
	55 or more	7	0	0	7	100	0.1193
Lymphovascular invasion state	**No**	18	4	22.22	14	77.78	^{FE}p=
	Yes	0	0	0	0	0	1.000
Capsular Invasion	**No**	14	4	28.57	10	71.43	^{FE}p=
	Yes	4	0	0	4	100	0.5242
Extra-thyroid extension	**No**	16	4	25	12	75	^{FE}p=
	Yes	2	0	0	2	100	1.000
T stage	**T1**	5	2	40	3	60	
	T2	3	2	66.67	1	33.33	
	T3	10	0	0	10	100	**^{FE}p= 0.0261***
LN stage	**NX/0**	15	4	26.67	11	73.33	^{FE}p=
	N1	3	0	0	3	100	0.5539
Stage	**I**	14	4	28.57	10	71.43	^{FE}p=
	II	4	0	0.0	4	100.0	0.5242

FET: Fisher Exact test *: Statistically significant at $p \leq 0.05$

p: p value for Relation TROP2 Result and different parameters

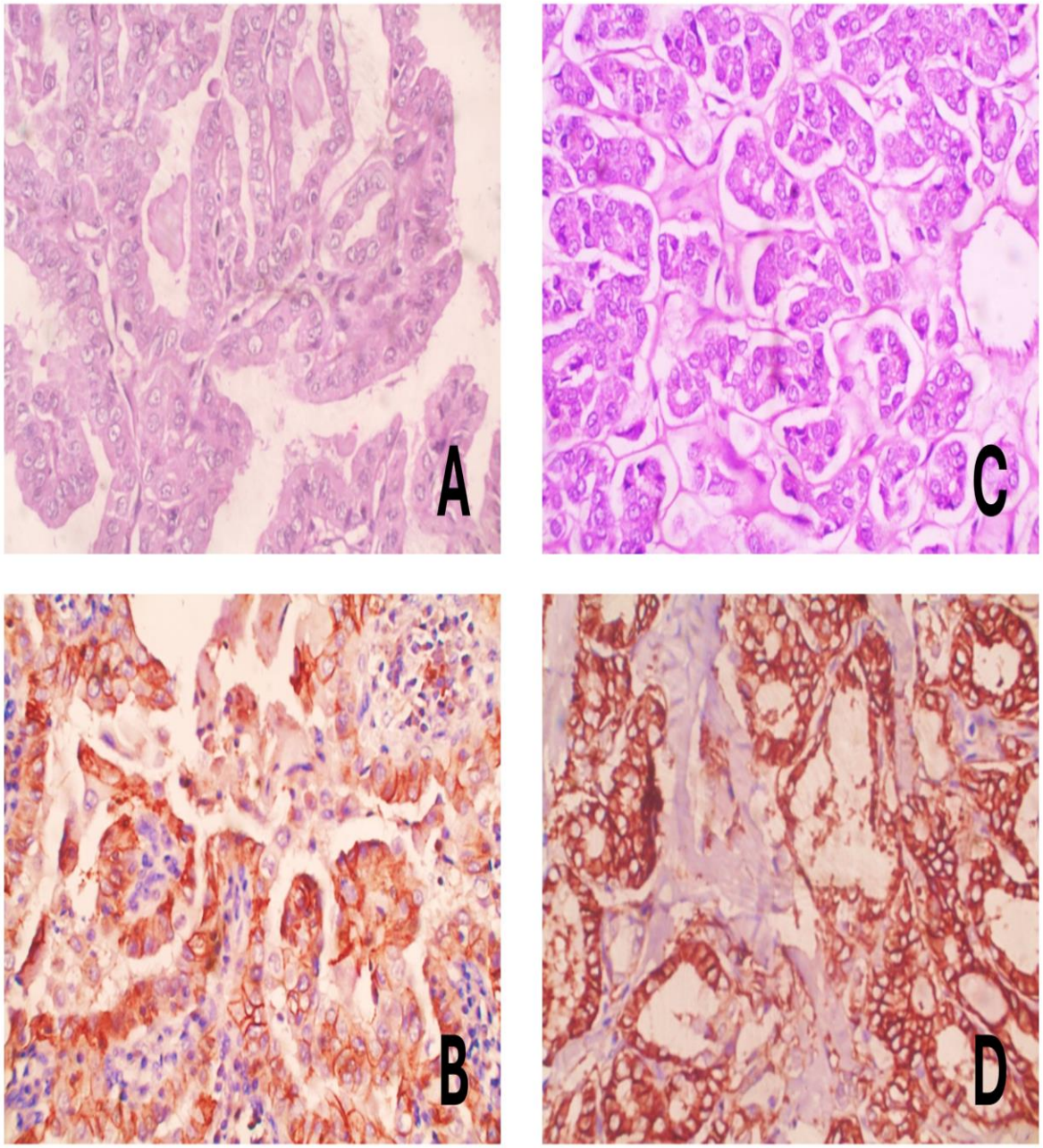

Figure (1); A. Classic papillary thyroid carcinoma. Tumor cells are arranged in complex papillary architecture with fibrovascular cores. Tumor cells are oval, enlarged and overlapping (H&E, 400x). B. Strong positive membranous immunohistochemical expression of TROP-2 in 100% of tumor cells in a case of Classic variant of papillary thyroid carcinoma (TROP-2, DAB, hematoxylin, 400x). C. Infiltrative follicular variant of papillary thyroid carcinoma. Tumor cells are arranged in follicles. Nuclei of tumor cells are enlarged, oval, overlapping, show clearing and focal nuclear grooving (H&E, 400x). D. Strong positive membranous immunohistochemical expression of TROP-2 in 100% of

tumor cells in a case of infiltrative follicular variant of papillary thyroid carcinoma (TROP-2, DAB, hematoxylin, 400x).

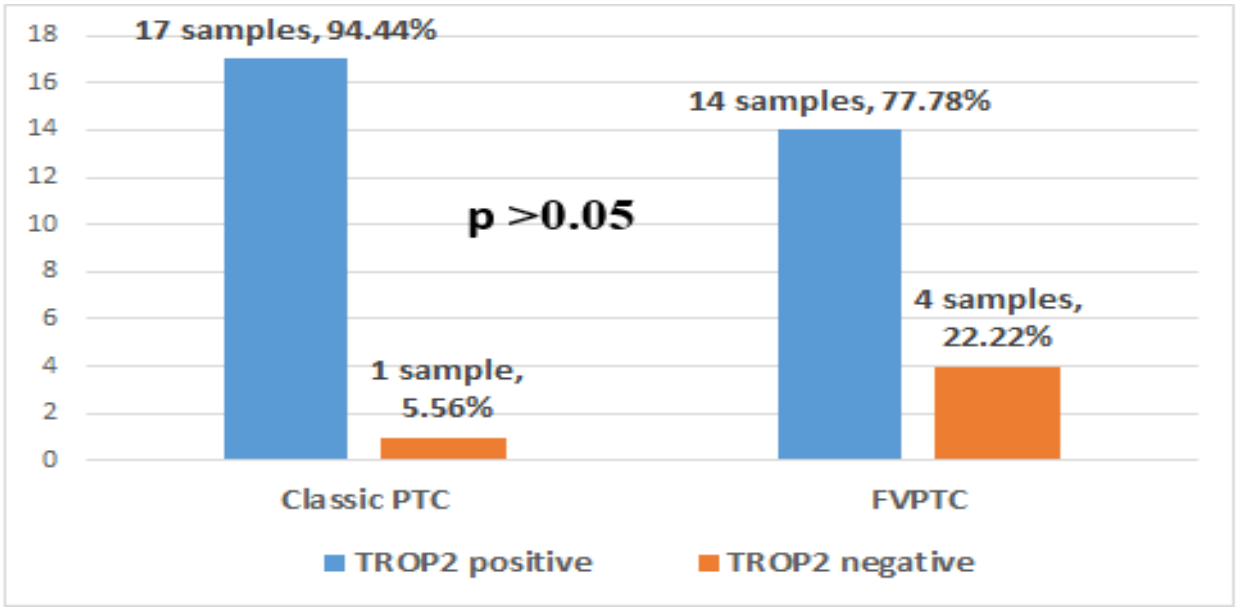

Figure (2): Distribution of classic PTC and infiltrative FVPTC according to TROP2 expression results.

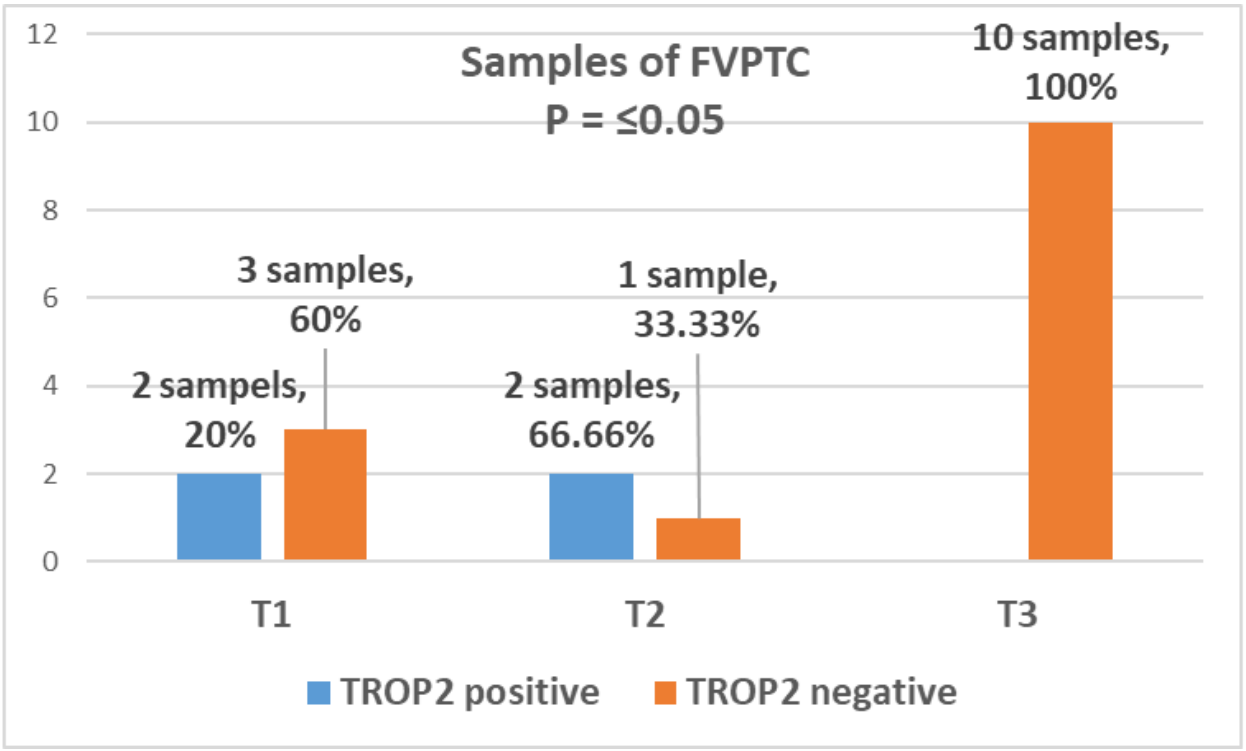

Figure (3): Distribution of T stage in infiltrative FVPTC according to TROP2 expression results.

REFERENCES

Abdou, A. G., Shabaan, M., Abdallha, R., & Nabil, N. (2019). Diagnostic Value of TROP-2 and CK19 Expression in Papillary Thyroid Carcinoma in Both Surgical and Cytological Specimens. *Clinical Pathology*, *12(2), 1-16*.

Abdulwahhab, O. S., Latif, H., & Kadhim, T. J. (2020). Immunohistochemical Expression of Trop2 and Brav-V600e Proteins in Papillary Thyroid Carcinoma, Hashimoto's Thyroiditis and Grave's Disease in Correlation with Certain Clinico-Pathological Parameters. *Biochem. Cell. Arch*, *20*(2), 4641–4646.

Abouelfadl, D. M., Shabana, M. E., Soliman, A. S. A., & Yassen, N. N. (2024). Evaluation of the immunohistochemical expression of Nrf2, galectin-3, and CK19 in papillary thyroid carcinoma and its mimics. *Egyptian Journal of Pathology*, *44*(2), 150–158.

Addati, T., Achille, G., Centrone, M., Petroni, S., Popescu, O., Russo, S., Grammatica, L., & Simone, G. (2015). TROP-2 expression in papillary thyroid cancer: a preliminary cyto-histological study. *Cytopathology: Official Journal of the British Society for Clinical Cytology*, *26*(5), 303–311.

Amin, M. B., Edge, S., Greene, F., Byrd, D. R., Brookland, R. K., Washington, M.K. Gershenwald, J. E., Compton, C. C., Hess, K. R., Sullivan, D. C., Jessup, J. M., Brierley, J. D., Gaspar, L. E., Schilsky, R. L., & Balch, C. M. (2017). AJCC Cancer Staging Manual (8th edition). *Springer International Publishing: American Joint Commission on Cancer*, 1–997.

Attia, A. S., Hussein, S., Sameh, H., Khalil, A., Waley, A. B., Matar, I., & Sameh, R. (2024). Diagnostic and prognostic utility of TROP-2, SLP-2, and CXCL12 expression in papillary thyroid carcinoma. *Cancer Biomarkers*, *39*(3), 211–221.

Baloch, Z. W., Asa, S. L., Barletta, J. A., Ghossein, R. A., Juhlin, C. C., Jung, C. K., LiVolsi, V. A., Papotti, M. G., Sobrinho-Simões, M., Tallini, G., & Mete, O. (2022). Overview of the 2022 WHO Classification of Thyroid Neoplasms. *Endocrine Pathology 2022 33:1*, *33*(1), 27–63.

Bychkov, A., & Jung, C. K. (2024). What's new in thyroid pathology 2024: updates from the new WHO classification and Bethesda system. *Journal of Pathology and Translational Medicine*, *58*(2), 98.

Cubas, R., Zhang, S., Li, M., Chen, C., & Yao, Q. (2010). Trop2 expression contributes to tumor pathogenesis by activating the ERK MAPK pathway. *Molecular Cancer*, *9*, 253.

Guerra, E., Trerotola, M., & Alberti, S. (2023). Targeting Trop-2 as a Cancer Driver. Mol Cancer Ther (2023) 22 (6): 790–804.

Jung, C. K. (2023). Histological Classification of Thyroid Tumors by the New Fifth Edition of the WHO Classification. *Thyroid FNA Cytology*, 83–89. https://doi.org/10.1007/978-981-99-6782-7_14.

Lebrun, L., & Salmon, I. (2024). Pathology and new insights in thyroid neoplasms in the 2022 WHO classification. *Current Opinion in Oncology*, *36*(1), 13–21.

Mcdougall, A. R. A., Tolcos, M., Hooper, S. B., Cole, T. J., & Wallace, M. J. (2015). Trop2: from development to disease. *Developmental Dynamics: An Official Publication of the American Association of Anatomists*, *244*(2), 99–109.

Murtezaoglu, A. R., & Gucer, H. (2017). Diagnostic value of TROP-2 expression in papillary thyroid carcinoma and comparison with HBME-1, galectin-3 and cytokeratin 19. *Polish Journal of Pathology: Official Journal of the Polish Society of Pathologists*, *68*(1), 1–10.

Nesreen, H. H., Manal, S. Z., & Mohamed, A. M. (2018). Diagnostic utility of trophoblastic cell surface antigen 2 immunohistochemical expression in papillary thyroid carcinoma. *Journal of Pathology of Nepal*, *8*(1), 1235–1243.

Raouf, S. M. A., Atia, H., Soliman, S. A., Elshahidy, T. M., & Mohamed, S. Y. (2020). Diagnostic Utility of Immunohistochemical Markers Trop2 and CD56 in Differentiating Follicular Derived Thyroid Lesions. *La Prensa Medica Argentina*, *106*(6), 2-6.

Saffar, H., Jahanbin, B., Ameli, F., Farhang, F., Tavangar, S. M., & Saffar, H. (2021). Diagnostic Value of TROP2 Expression in Papillary Thyroid Carcinoma. *Applied Immunohistochemistry & Molecular Morphology: AIMM*, *29*(3), 218–222.

Sun, H., Chen, Q., Liu, W., Liu, Y., Ruan, S., Zhu, C., Ruan, Y., Ying, S., & Lin, P. (2021). TROP2 modulates the progression in papillary thyroid carcinoma. *Journal of Cancer*, *12*(22), 6883.

Turan, Z., & Erkılıç, S. (2023). TROP2: a potential marker in diagnosis of thyroid neoplasms. *Irish Journal of Medical Science*, *192*(1), 99–103.

Vella, C., Baldacchino, S., Formosa, R., & Vassallo, J. (2022). The Utility of Galectin-3 and HBME-1 Immunohistochemical Expression in Thyroid Cancer in the Maltese Population. *Endocrines 2022, Vol. 3, Pages 225-239*, *3*(2), 225–239.

Yang, X., Hu, Y., Shi, H., Zhang, C., Wang, Z., Liu, X., Chen, H., Zhang, L., & Cui, D. (2018). The diagnostic value of TROP-2, SLP-2 and CD56 expression in papillary thyroid carcinoma. *European Archives of Oto-Rhino-Laryngology*, *275*(8), 2127–2134.