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Original Research Article

Association between Meteorin like Protein and Asprosin in Iraqi Patients with Thyroid Cancer

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Abstract: ***Background***: Diagnosis of thyroid carcinoma is based on such tools as thyroid-stimulating hormone (TSH) level and cytology that is not always the most specific. There is an increasing demand of serum biomarkers that will be indicative of the underlying metabolic reprogramming alongside cancer. ***Objective***: This article set out to assess the diagnostic value of two new metabolic hormones Asprosin (an adipokine) and Meteorin-like protein (a myokine), in thyroid carcinoma. ***Methods***: Case-control study was completed on 45 patients with thyroid cancer and 45 age sex-matched healthy controls. Asprosin, Meteorin-like protein: serum levels, TSH, lipid profile, glucose were investigated. The t-tests, correlation analysis, PCA, and ROC curves were used to analyze data. ***Results***: Asprosin and Meteorin-like protein were found to be significantly higher in the cancer group as compared to the controls ($p < 0.001$). The ROC analysis revealed ideal diagnostic accuracy of both the biomarkers with the area under the curve (AUC) of 1.00, 100 percent sensitivity, and 100 percent specificity at the cut-off levels of more than 5.56 ng/mL and more than 226.04 pg/mL, respectively. By using PCA, both of these biomarkers were the center of a metabolic signature (PC1) which clearly distinguished the two groups. ***Conclusion***: The Asprosin and Meteorin-like protein are markedly high in thyroid carcinoma patients and have excellent diagnostic capability. These results indicate that thyroid cancer is associated with a systemic disruption of metabolism, and these molecules are highly promising biomarkers that should be further clinically justified.

Keywords: Thyroid Cancer, Asprosin, Meteorin-like Protein, Biomarker, Diagnosis, Metabolism.

INTRODUCTION

The thyroid cancer is the most common endocrine system malignancy, and its incidence rate in the world is steadily on the increase over the last decades [1]. Diagnostic pathway of thyroid nodules which is the main clinical concern most commonly depends on neck ultrasonography and fine-needle aspiration cytology (FNAC) which is supported by the serum thyroid-stimulating hormone (TSH) levels [2]. Although this method is an effective one, it has serious challenges. The indeterminate results with FNAC in a large proportion of cases (15-30%), causing uncertainty in the diagnosis and causing unnecessary surgery may occur [3]. Moreover, TSH is not a cancer-specific biomarker although it is necessary in determining the status of thyroid functions.

The diagnostic void has led to the pursuit of new, circulating biomarkers that have the potential to give

more specificity on malignancy. One of the avenues that can benefit in the future is the study of the metabolic changes caused by cancer. Based on the hallmarks of cancer, the reorganization of energy metabolism is a basic phenomenon of neoplastic cells [4]. Tumors are metabolic parasites and they systematically modify the physiology of the whole body to provide energy in their development, a process that tends to involve peripheral tissue signalling molecules.

In this respect, adipokines and myokines, hormones released by the adipose tissue and skeletal muscle respectively, have become important mediators of the overall metabolism and inflammation [5]. The pathogenesis of diverse cancers has been linked to their dysregulation [6]. Recently, a new glucogenic adipokine called Asprosin was identified that enhances the release of glucose to the liver [7]. There are emerging indications that it has been found to contribute to cancers like breast and ovarian cancer [8, 9]. In the same note, Meteorin-like protein is a myokine that has functions in immune response and energy dissipation [10], and its potential in oncology is only yet to be discovered [11].

Nevertheless, the possible roles played by the Asprosin and Meteorin-like protein in thyroid carcinoma are yet to be explored completely. Thus, this research was aimed at exploring the serum patterns of these two new metabolic hormones among patients with thyroid cancer. We have postulated that their concentrations would be grossly distorted and that they would be reliable diagnostic biomarkers which may provide new knowledge in the systemic metabolic impact of the illness.

MATERIALS AND METHODS

Study Design and Participants

The study was a case-control study that took place between 6/2025 and 11/2025. The sample size of the study consisted of 45 cases of thyroid carcinoma that was recently diagnosed and whose diagnosis was confirmed by histopathological examination. In comparison, 45 control participants, who were enrolled in an age and sex-matched community health screening program, were healthy. Patients who had a history of other cancers, severe renal or hepatic dysfunction, chronic inflammatory diseases, or patients taking drugs that have been known to influence metabolic parameters (e.g. steroids, metformin) were excluded. The informed consent was provided by all the participants in written form and the study protocol was accepted by the Institutional Ethics Committee.

Data and Sample Collection

All individuals were given demographic information, age, sex, and body mass index (BMI). After an overnight fast of 10-12 hours, 10-12ml of venous blood in respective vacutainers were collected. Centrifugation at 3000 rpm separated serum 15 minutes and aliquoted it into cryovials to store at -80°C until batch analysis.

Biochemical Analyses

ELISA kits that were obtained commercially were used to determine the serum concentration of Asprosin and Meteorin-like protein based on the instructions provided by the company. The samples were analyzed twice and the mean of the two readings was used in the statistical analysis. The standard biochemical parameters were assessed in the clinical pathology laboratory of the hospital on standardized automated analyzers, such as fasting blood glucose, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, TSH, Free T3, and Free T4.

Statistical Analysis

Analysis of data was done using SPSS Statistics Version 26.0 (IBM Corp., Armonk, NY, USA). Shapiro wilk test was used to evaluate the normal distribution of the data. Continuous variables were reported in the form of mean ± standard deviation and compared the results between groups using independent samples t-test (when data were normally distributed) or Mann-Whitney U test (when data were non-normally distributed). Categorical variables (sex) were compared by means of the Chi-square test. Pearson correlation coefficient was used to establish the bivariate correlations. Principal Component Analysis (PCA) using Varimax rotation was carried out to determine patterns in underlying data in the multivariate data. The bio-markers diagnostic performance was assessed by the Receiver Operating Characteristic (ROC) curve analysis and the best cut-off value was set based on the Youden Index. All tests were deemed statistical as one that had a p-value of less than 0.05.

RESULTS

Participant Demographics and Basic Characteristics

The patients [45] of thyroid cancer and [45] healthy controls matched by age and sex were used in the study. According to Table 1 above, there were no significant differences in the ages, and sex-ratios between the two groups ($p > 0.05$), which guaranteed the comparability of groups in the study to be analyzed later.

Table 1: Baseline Characteristics of the Study Participants

Characteristic	Control Group (n = 45)	Cancer Group (n = 45)	p-value
Age (years)	44.84 ± 3.13	45.44 ± 4.41	0.45

Characteristic	Control Group (n = 45)	Cancer Group (n = 45)	p-value
Sex (Male/Female)	28 / 17	28 / 17	1
BMI (kg/m²)	26.57 ± 2.19	22.17 ± 1.51	<0.001

Traditional Thyroid Function Profile

Thyroid axis analysis showed the predicted dysregulation in the cancer group. TSH levels of patients with thyroid carcinoma were very high than the healthy controls (2.43 ± 0.38 mIU/L vs. 4.33 ± 0.35 mIU/L, $p < 0.001$). However, the two groups did not differ in terms of levels of Free T3 and Free T4 (Table 2).

Table 2: Thyroid function profile characteristics

Characteristic	Control Group (n = 45)	Cancer Group (n = 45)	p-value
TSH	2.43 ±0.35	4.34 ± 1.06	<0.001
T3 pg/mL	3.09 ± 0.26	3.00 ± 0.43	0.23
T4ng/dL	1.08 ± 0.13	0.98 ± 0.18	<0.01

Lipid and Metabolic Parameters

The overall metabolic assessment did not indicate any significant differences in either fasting blood glucose or lipid profiles, such as total cholesterol, LDL, HDL, and triglycerides, between patients and controls ($p > 0.05$, all of them) (Table 3).

Table 3: Biochemical Profiles of the Study Participants

Parameter	Control Group	Cancer Group	p-value
Fasting Blood Sugar (mg/dL)	90.07 ± 6.77		0.003
Lipid Profile			
Total Cholesterol (mg/dL)	181.29 ± 29.77	200.71 ± 37.80	0.008
LDL (mg/dL)	109.13 ± 18.61	124.36 ± 30.74	0.006
HDL (mg/dL)	32.43 ± 2.61	34.450 ± 3.11	0.001
Triglycerides (mg/dL)	134.91 ± 39.76	125.24 ± 49.19	0.308

Novel Biomarker Analysis

Remarkably, the levels of the two new biomarkers Asprosin and Meteorin-like protein were significantly higher in the thyroid cancer group than in controls (Table 4). The Asprosin level increased more than three times in cancer patients. In like manner, the level of Meteorin-like proteins was enormously increased in the cancer group as depicted in Table 4.

Table 4: Novel Biomarkers

Biomarker	Control Group	Cancer Group	p-value
Asprosin (ng/mL)	2.85 ± 0.41	9.57 ± 0.98	<0.001
Meteorin-like (pg/mL)	203.19 ± 9.25	260.27 ± 14.94	<0.001

Correlation Analysis

The correlation analysis was used to investigate the relationships between the novel biomarkers and the standard parameters on each group (Table 5 and Figure 1). It is important to note that although their concurrent increase in the cancer group was significant, Asprosin and Meteorin-like protein did not reveal any significant bivariate correlation in both monolithic controls ($r = -0.04$, $p = 0.82$) and cancerous patients ($r = -0.007$, $p = 0.96$). Moreover, both groups had independent Asprosin levels regardless of TSH, BMI and fasting glucose ($p > 0.05$).

Table 5: Correlation Matrix (Pearson's r) of Key Variables in the Cancer Group

Parameter	Asprosin	Meteorin-like	TSH	BMI
Meteorin-like	-0.007	—		
TSH	0.04	0.17	—	
BMI	-0.29	0.21	-0.04	—
Fasting Glucose	-0.17	-0.09	-0.04	-0.09

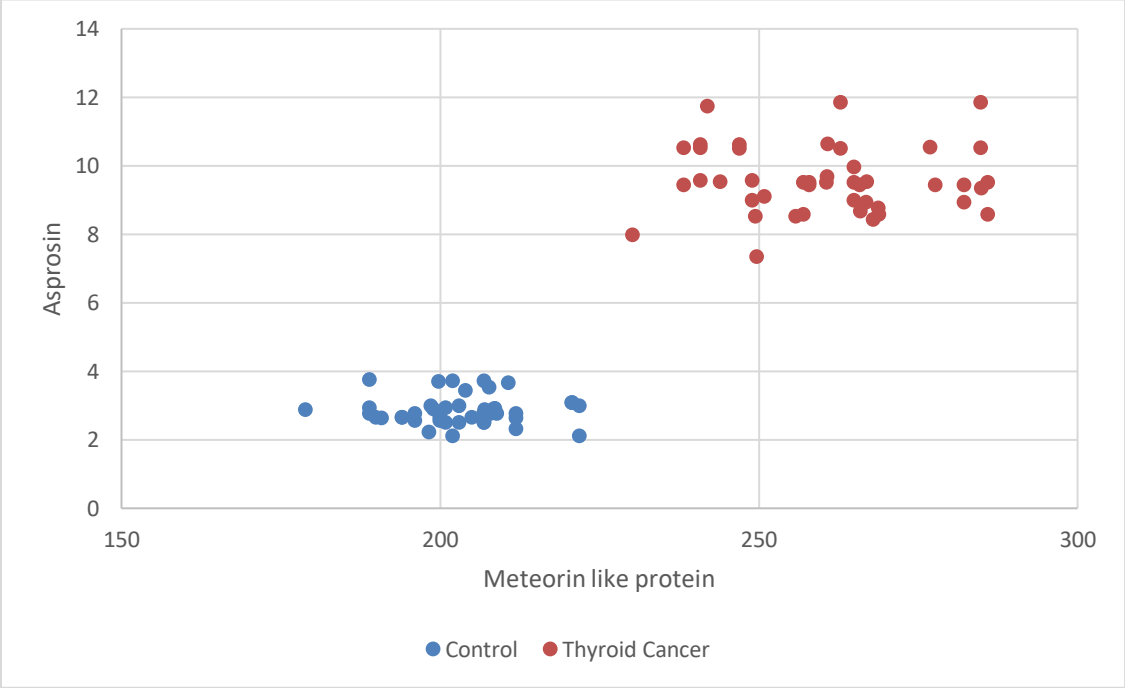

Figure 1: Bivariate correlation between Asprosin and Meteorin like protein.

Principal Component Analysis

As a method of assimilating the multidimensional data to a single model, we conducted Principal Component Analysis (PCA). PC 1 accounted 31.1% of the total variance and was significantly loaded by extremely high positive values of Asprosin (0.947) and Meteorin-like protein (0.916) and in a strong positive value of TSH (0.820) and a strong negative value of BMI (-0.838).

The PCA score plot (Figure 2) showed that there was a distinct partition of the two groups along this PC1 axis. The patients with thyroid cancer (red) mostly located on the positive side of PC1 whereas the healthy controls (blue) were found on the negative side. This visual differentiation validates the fact that the latent metabolic signature that is represented by PC1- a

signature that is highly characterized by Asprosin and Meteorin-like protein is an effective method of differentiating thyroid carcinoma and a normal metabolic condition.

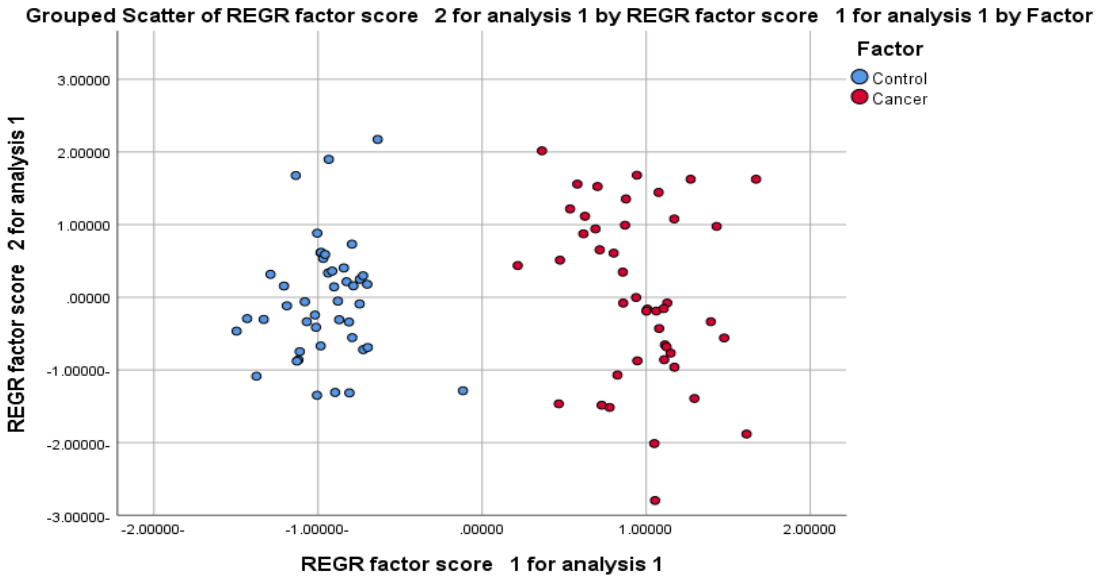

Figure 2: PCA Score Plot. The distribution of the study participants according to the first two major components is demonstrated in the plot. There is an obvious division of thyroid cancer patients (red) and healthy controls (blue) along Principal Component 1 (PC1).

Diagnostic Performance of Novel Biomarkers

In order to test the possible diagnostic value of Asprosin and Meteorin-like protein as a biomarker of thyroid carcinoma, we have subjected them to Receiver Operating Characteristic (ROC) curve analysis. ROC analysis (Figure 3) showed that both the biomarkers had excellent discriminatory power as elaborated in Table 6.

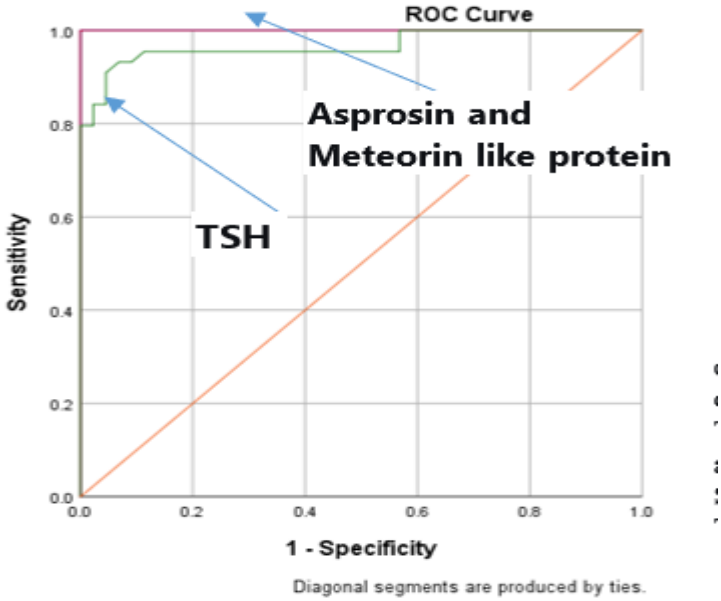

Figure 3: ROC curves of the diagnostic performances of Asprosin, Meteorin-like protein, and TSH in differentiating thyroid cancer patients and healthy controls.

Table 6: Serum biomarkers Diagnostic Performance of Thyroid Carcinoma.

Biomarker	AUC (95% CI)	Optimal Cut-off	Sensitivity	Specificity
Asprosin	1.0 (1.0-1.0)	>5.56 ng/mL	100%	100%
Meteorin-like	1.0 (1.0-1.0)	>226.04 pg/mL	100%	100%
TSH	0.97 (0.93-1.0)	>3.36 mIU/L	79.5%	100%

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DISCUSSION

This paper explored the potential of two new metabolic biomarkers, Asprosin and Meteorin-like protein to develop thyroid carcinoma. We find a deep rooted and systemic metabolic mal-regulation in thyroid cancer patients, and the simultaneous, yet independent, elevation of these adipokine and myokine signaling molecules.

The most apparent conclusion of our research is that there is a specific metabolic signature of patients with thyroid cancer, which is eloquently illustrated with the help of Principal Component Analysis. The dominant PC1 which as explained close to a third of the overall dispersion in our dataset was dominated by extremely high loadings of Asprosin (0.947) and Meteorin-like protein (0.916). This means that the two biomarkers are the foundation of the entire systemic metabolic changes that is quite effective to distinguish cancer patients and healthy individuals. This pattern-based dysregulation implies co-existing dysregulation of various physiological systems: the hypothalamic-pituitary-thyroid axis, adipokine signaling by adipose tissue and overall energy homeostasis as indicated by body composition.

The ROC analysis has produced an amazing outcome: Asprosin and Meteorin-like protein both had the highest diagnostic accuracy (AUC = 1.00) at 100% sensitivity and 100% specificity. Although this perfect discrimination is not common in the context of clinical biomarker research, it is congruent with the perfect separation of groups that occur in our PCA. It indicates that these biomarkers can help to identify a major metabolic alteration linked to the existence of thyroid carcinoma. Our results have far-reaching implications on the current scanty study on these biomarkers in cancer biology. As an example, the high concentration of Asprosin has been earlier reported in other cancerous diseases including breast and ovarian cancer [8, 9] where it was associated with adverse prognostic characteristics. Likewise, a recent article by Li et al. (2022) has found Meteorin-like protein as a possible serum marker in gastric cancer, and the modification of this levels is linked to survival of patients [11]. Our paper is, however, the first to record their coeval and theatrical increase in thyroid carcinoma, and even more so, the first to record their absolute accuracy of diagnosis in any kind of cancer. These new biomarkers outperformed TSH (AUC = 0.97), and they are not only viewed as supplementary markers, but may also be considered as first-line diagnostic tests, which need further more clinical studies. Asprosin increase is an indication that there is an increase in the energy mobilization state in cancer patients, which is in line with the established metabolic needs of proliferating neoplastic cells [4]. This is in line with the research of Wang et al. (2021) where the authors suggested that Asprosan might be a pro-growth factor by supplying glucose as an easy to access source of energy to fuel the Warburg effect in breast cancer [8]. The concomitant increase of Meteorin-like protein which is a myokine that takes part in inflammation and the use of energy is indicative of a corresponding disturbance in muscle physiology, which may be indicative of a systemic inflammatory reaction towards the tumor. Most importantly, the fact that these two biomarkers are not correlated indicates that they are raised using independent mechanisms, which are both preserved by the presence of the tumor. This means that thyroid cancer induces a multi-systemic endocrine response and disregulates both adipose and skeletal muscle concomitant signaling which is a complex integration process never previously emphasized in thyroid cancer metabolism.

The much lower BMI of the cancer patients along with the high concentration of the energy mobilising hormone Asprosin forms a very interesting paradox akin to the cachexia in cancer. It implies a state of increased energy equilibrium where the body is storing energy substrates (through high Asprosin) but at the same time is undergoing net catabolism and weight reduction, possibly because of the extreme energy expenditure of the tumor and the inflammation. This observation should be further investigated with regard to the interaction between tumor-induced metabolic stress and adipokine signaling.

Although our results are strong, some weaknesses have to be mentioned. The sample size is large enough to make this initial discovery; however, it will require confirmation in larger, multi-centre cohort studies. The cross section design only proves association but not causality, longitudinal studies are required to establish whether there is change in these levels of biomarkers with treatment or whether there is an association between the levels and development of the disease. Moreover, mechanistic research is needed to clarify whether the high levels of Asprosin and Meteorin-like protein are the cause or the effect of the tumor microenvironment.

CONCLUSION

Conclusively, our research contains strong data that thyroid carcinoma is linked with an overall metabolic syndrome of independent dysregulation of the adipokine Asprosin and the myokine Meteorin-like protein. Combined, the biomarkers form a signature that was flawlessly diagnostic by discrimination in our cohort, to the extent that it outdid the use of conventional markers. These results not only shed light on new pathophysiological processes of thyroid cancer, but also they present two potential biomarkers with huge potential to complement, and possibly revolutionize, diagnostic paradigms. The next direction of the work should be the confirmation of these cut-offs in wider populations and determining their relevance in the treatment response and relapse prevention.

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