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Research article

Serum resistin, visfatin, IL-17 and IL-23 as novel diagnostic biomarkers for thyroid carcinoma

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Abstract: This study sought to identify potential biomarkers of thyroid cancer, such as visfatin, resistin, IL-17, and IL-23 levels, alongside investigating their involvement in the progression of the disease. Methods: This study included 56 patients that have thyroid cancer and 47 healthy people whose sexes and ages were matched to the healthy group. The sandwich enzyme-linked immunosorbent assay (ELISA) kit, which is widely available and dependable, was utilized to measure the level of interleukin-17, interleukin-23, visfatin, and resistin within the serum of the patient and control groups. These biochemical values were plotted against a receiver operator characteristic (ROC) curve to determine their potential diagnostic use. Results: The serum levels of Interleukin-17 (255 ± 25.82 pg/mL), IL-23 (461.03 ± 29.97 pg/mL), visfatin (19.42 ± 2.91 ng/mL), and resistin (25.3 ± 1.9 µg/L) were all noticeably higher in the thyroid cancer patients; the ROC analysis indicated that these serum concentrations may be used as potential biomarkers for thyroid cancer diagnoses. Conclusion: In contrast to IL-17 and IL-23, which demonstrated stronger specificities (94.1% and 83.7%, respectively) and closer associations with thyroid cancer pathogenesis, the resistin and visfatin levels were significantly elevated in patients with thyroid cancer and showed diagnostic potential in the ROC analysis (AUC > 0.8). However, their non-specific pro-inflammatory roles and wider variability in metabolic conditions (e.g., obesity, insulin resistance) may limit their reliability as early diagnostic biomarkers. Therefore, resistin and visfatin need to be further validated in bigger cohorts to evaluate the confounding impacts, while IL-17 and IL-23 may be more suited for early identification.

Keywords: IL-17; IL-23; resistin; thyroid cancer; visfatin

1. Introduction

Among the majority of endocrine cancers, thyroid cancer has become more common over the past few decades. Hereditary predispositions and environmental variables such as radiation exposure, obesity, and excess iodine might cause it [1]. Roughly 2% of all malignancies in humans are thyroid cancers. Although 10–30% of these patients may present with recurrent disease, the majority of them respond effectively to standard therapies [2]. These days, head and neck radiation exposure, gender, advanced age, insufficient or too much iodine, and thyroid cancer diagnosed within the family history are recognized as thyroid cancer risk factors. Sadly, the majority of these are unavoidable [3]. Resistin was found in 2002 [4]; this peptide, which is encoded by the RETN gene, is high in cysteine. Due to the insulin resistance that was seen in mice after injection, the drug was given the name "resistin". Resistin has drawn a lot of attention since it was discovered due to its wide variety of pathological and physiological roles in several metabolic illnesses. White adipose tissue (WAT) expresses human resistin, which is then released with the assistance of immune cells and peripheral blood monocytes. Female gonadal adipose tissue has the greatest amounts of resistin. On the other hand, adipose tissue in rodents produces resistin. In addition, resistin has proinflammatory cytokine characteristics and is associated in insulin resistance, immunological regulation, and inflammation [5].

The main source of the adipocytokine visfatin, alternatively named as either pre-B-cell colony-enhancing factor or nicotinamide phosphoribosyltransferase, is visceral fat tissue [6]. Visfatin levels have been shown to be elevated in several autoimmune conditions, such as psoriasis, systemic lupus erythematosus, and rheumatoid arthritis. The serum visfatin concentrations may be impacted by both hypothyroidism and hyperthyroidism; however, the outcomes are debatable [7]. Furthermore, it has been documented that visfatin overexpression is present in malignancies of the pancreas, esophagus, breast, prostate, colon, and stomach. Additionally, a recent meta-analysis found a strong relation between increased visfatin levels (eNampt) and a higher chance of getting several types of cancer. However, a consensus about the predictive significance of visfatin in different types of cancer needs to be established [8].

The main sources of interleukins (ILs) include T cells, monocytes, macrophages, and endothelial cells, which are tiny protein signaling molecules that control the immune system and are members of the cytokine family. Their functions in autoimmune thyroid illnesses are vital. According to [9], some of their roles include facilitating communication between immune system cells, regulating transcription factors, and managing inflammation, differentiation, proliferation, and anti-body secretion. A proinflammatory cytokine, interleukin-17 (IL-17), was first identified by [10], and is mostly generated by T helper-17 (Th17) cells within the first CD4þ T cell fraction. The synthesis of interleukin-17 acts as a mediator between the acquired and innate immune systems, thereby promoting acute inflammatory responses, B cell activation in response to appropriate stimuli, and epithelial homeostasis [11]. Notably, some researches have showed the significance of IL-17 in various types of diseases, such as hematological and solid cancers, cardiovascular conditions, autoimmune and infectious diseases, and nonalcoholic fatty liver disease [12]. According to recent data, malignant tumors, such as non-small cell lung, gastric, colorectal, and hematologicmalignancies, express high levels of IL-17. Crucially, IL-17 may be employed as a biomarker for many kinds of cancers, such as stomach cancer, breast cancer, lung cancer, and oral squamous cell carcinoma [13].

As a pleiotropic cytokine belonging to the IL-6 superfamily, interleukin-23 (IL-23) contributes to tissue remodeling and the integration of innate and adaptive immunity [14]. Furthermore, it is crucial

for the onset of several autoimmune disease models. Many researchers claim that elevated IL-23 serum levels in Hashimoto thyroiditis (HT) patients triggers Th17 cell differentiation and IL-17 synthesis, which contributes to the development of HT [15]. An investigation reported that the thyroid follicular cells of HT patients generate a lot of interleukin-23, which prevents autophagy and causes neopterin to build up [16]. Additionally, research has demonstrated that IL-23 promotes the final differentiation and expansion of Th17 effector cells [17].

The Interleukin-17/Interleukin-23 axis is involved in several malignancies. However, regarding a prognosis, these functions are debatable [18]. The purpose of this research is to compare the concentrations of IL-17, IL-23, resistin, and visfatin in patients with thyroid cancer and healthy controls. Since these roles have not been studied before, the current effort aims to uncover the roles of IL-17 and IL-23 in thyroid cancer in the hopes of discovering biomarkers for the condition.

2. Materials and methods

2.1. Clinical data

The study included patients with a pathohistologically diagnosed classic subtype of Papillary Thyroid Cancer (PTC). All 56 patients in the experimental group were selected from Sulaymaniyah City's Hiwa Hospital. There were 47 healthy people in the blank control group. Of the 56 thyroid cancer patients, 21 were men and 35 were women, with ages ranging from 32 to 71. Out of the 47 healthy people, 25 were men and 31 were women, with ages ranging from 38 to 75. The following criteria were used to determine the experimental inclusion: (1) The World Health Organization (WHO) classification method-based pathological examination results confirmed the diagnosis of a thyroid carcinoma; (2) no prior antitumor therapy was administered to any of the patients; (3) the follow-up examination was flawless; and (4) serum sample consent was obtained prior to treatment. The exclusion criteria are as follows: (1) Stage I risk factor absence; (2) severe liver, kidney, and heart problems; (3) a history of autoimmune diseases (e.g., Hashimoto's thyroiditis, rheumatoid arthritis, or systemic lupus erythematosus); (4) pregnancy; (5) patients who had undergone a thyroid lobectomy; (6) patients without follow-up data; (7) patients with other subtypes of PTC; and patients with a history of cancer. The pathohistological examination was performed at the Hiwa Cancer Hospital in Sulaymaniyah City/Iraq. The pathohistological features were examined on formalin-fixed, paraffin-embedded cancer tissue sections stained using the standard hematoxylin–eosin method. The pathological evaluation and the tumor, node, and metastasis (TNM) staging were performed by pathologists. The histological parameters were analyzed according to the 5th edition of the WHO Classification of Tumors of Endocrine Organs. The following pathohistological parameters were examined in each case: Tumor size, histological subtype, presence of lymph node metastases, gross extrathyroidal extension (ETE), vascular invasion, tumor multifocality, stromal calcification, and a coexistence of HT.

2.2. Blood collection

Every participant had 5 milliliters of venous blood drawn early in the morning, which was then centrifuged, left to stand, and the serum was removed. Following processing, the samples were stored for subsequent use in a freezer set at −80 ℃ until enough samples were gathered for detection. The case and control groups' serum levels of resistin, visfatin, IL-17, and IL-23 were evaluated using a

dependable sandwich enzyme-linked immunosorbent assay (ELISA) kit (Ray Bio, USA). Standard samples with known amounts of each parameter and the manufacturer's instructions were followed while using the kit.

2.3. Statistical analysis

GraphPad Prism, version 9, was used to evaluate statistical data. The mean ± SD was used to display bar graphs and the outcomes of statistical tests. An unpaired T-test (Man-Whitney U test) was used to compare the study parameter means of the thyroid carcinoma patients and healthy groups. Receiver operator characteristic (ROC) curves were calculated using the MedCalc Statistical software, version 14.8.1, to define the diagnostic accuracy, which was determined using the area under the ROC curve (AUC) of parameters under study. The statistical significance was defined as a P-value of less than 0.05.

3. Results

3.1. Serum concentrations of IL-17, IL-23, resistin, and visfatin

The serum levels of IL-17, IL-23, resistin, and visfatin were measured in both the thyroid carcinoma patients and the healthy controls (Table 1). The patients had significantly higher serum resistin levels (25.3 ± 1.9 µg/L) than the controls (18.21 ± 2.73 µg/L; P = 0.0013). Likewise, the patient group had greater visfatin concentrations (19.42 ± 2.91 ng/mL) than the control group (14.00 ± 2.41 ng/mL; P = 0.0075). Additionally, the patients' IL-17 levels were significantly higher (255.00 ± 25.82 pg/mL) than those of the control group (154.00 ± 23.36 pg/mL; P = 0.001). The most notable difference was seen for the IL-23 concentration, which was almost six times greater in the patients (461.03 ± 29.97 pg/mL) than in the controls (73.90 ± 3.09 pg/mL; P < 0.0001).

Table 1. Serum levels of inflammatory cytokines and adipokines in patients with thyroid cancer and control participant.

Parameters	Control group	Thyroid cancer	p-value
Resistin (µg/L/mL)	18.21 ± 2.73	25.3 ± 1.9	0.0013
Visfatin (ng/mL)	14 ± 2.41	19.42 ± 2.91	0.0075
IL-17 (pg/mL)	154 ± 23.36	255 ± 25.82	0.001
IL-23 (pg/mL)	73.90 ± 3.09	461.03 ± 29.97	<0.0001

Mean ± SD is used to express the value. A P-value is considered statistically significant if it is less than 0.05.

3.2. Association between adipokines levels and lymph node metastasis (LNM).

Table 2 highlights the adipokine levels in individuals with lymph node metastases (LNM+) and those without (LNM). The LNM− group had a substantially lower level of resistin (22.13 ± 0.9845 µg/mL; p = 0.003) than the LNM+ group (31.78 ± 8.84 µg/mL). Likewise, the visfatin levels were higher in the LNM+ group (22.18 ± 1.8635 ng/mL) than the LNM− group (15.35 ± 0.6803 ng/mL; p = 0.01).

Table 2. Association between adipokines levels and lymph node metastasis.

Adipokines	LNM (−)	LNM (+)	p-value
Resistin (μg/mL)	22.13 ± 0.9845	31.78 ± 8.84	0.003
Visfatin (ng/mL)	15.35 ± 0.6803	22.18 ± 1.8635	0.01

Value expressed in Mean ± SE.

3.3. Association between inflammatory cytokines levels and lymph node metastasis (LNM)

According to Table 3, the thyroid cancer patients with LNM+ had IL-17 and IL-23 levels that were substantially greater than LNM− patients (287.84 ± 74.02 vs 198.47 ± 26.28 pg/mL, p = 0.041; and 456.04 ± 85.25 vs 255 ± 25.82 pg/mL, p = 0.01, respectively).

Table 3. Association between inflammatory cytokines levels and lymph node metastasis.

Inflammatory cytokines	LNM (−)	LNM (+)	p-value
IL-17 (pg/mL)	198.47 ± 26.28	287.84 ± 74.02	0.041
IL-23 (pg/mL)	255 ± 25.82	456.04 ± 85.25	0.01

Value expressed in Mean ± SE.

3.4. Clinical and pathological characteristics of thyroid carcinoma patients

The clinicopathological features of 56 patients with classical PTC are compiled in Table 4. For the patients, 37 had tumors larger than 2 cm and 19 had tumors less than 1 cm. Thirty-one individuals had no nodal involvement, while twenty-five patients were LNM+. Thirty-three patients showed no extrathyroidal extension, whereas 23 instances showed it, which indicates that the tumor spread beyond the thyroid. Thirty-seven individuals had no vascular invasion, while 19 patients exhibited lymphovascular invasion, a sign of aggressive behavior. Thirty-three patients had tumor multifocality (i.e., several tumor foci), while only twenty-three patients had a single tumor. There were no stromal calcifications or concurrent HT in any of the instances. These results draw attention to important prognostic markers that may affect PTC risk classification and disease management, including an increased tumor size, lymph node involvement, extrathyroidal extension, and lymphovascular invasion.

3.5. Measurements of visfatin, IL-17, IL-23, and serum resistin as thyroid carcinoma diagnostic markers

This study employed a ROC curve analysis to evaluate the diagnostic accuracy of differentiating the thyroid cancer patients from the healthy controls using resistin, visfatin, IL-17, and IL-23. This is displayed in Figures 1–4, respectively, and Table 5.

Table 4. Clinical and pathological characteristics of thyroid carcinoma patients.

Characteristic of tumor	Number of patients
Tumor size (cm) < 1 cm	19
≥ 2 cm	37
Histopathological subtype	56
Classical papillary thyroid cancer	
Lymph node metastasis	31
Not identified	
Present	25
Extrathyroidal extension	33
Not identified	
Present	23
lymph Vascular invasion	37
Not identified	
Present	19
Tumor multifocality	23
Not identified	
Present	33
Stromal calcification	56
Not identified	
Coexistence of Hashimoto's thyroiditis	56
Not identified	

Table 5. Analysis of inflammatory cytokines and adipokines for diagnosis evaluation.

Parameters	AUC	Specificity (%)	Sensitivity (%)	p-value
Resistin	0.9015	90.6	93.1	0.0052
Visfatin	0.8241	88.5	90.1	0.0066
IL-17	0.9003	94.10	89.7	<0.0001
IL-23	0.7901	76.90	83.7	0.0236

The diagnostic value of the Resistin levels was investigated by calculating the ROC curve. According to ROC analysis, Resistin had an AUC of 0.9015, a sensitivity of 93.1%, and a specificity of 90.6% (Figure 1). The best cutoff point for the diagnosis of thyroid cancer was at 19 μg/L/mL.

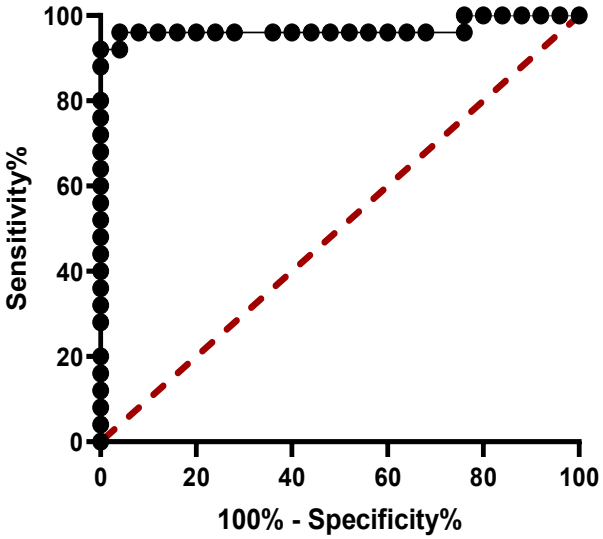

Figure 1. ROC curve of resistin.

When calculating the ROC curve of the Visfatin levels, the specificity and sensitivity of serum visfatin were 90.1% and 88.5%, respectively, with a significant AUC of 0.8241and P = 0.0066 (Figure 2). The best cutoff point for the diagnosis of thyroid cancer was at 12 ng/mL.

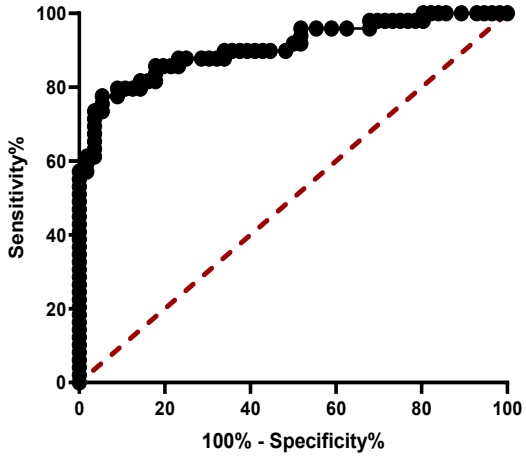

Figure 2. ROC curve of visfatin.

When calculating the ROC curve of the IL-17 levels, the serum IL-17 showed a sensitivity of 89.7%, a specificity of 94.10%, and a significant AUC (0.9003; P < 0.0001) (Figure 3). The best cutoff point for the diagnosis of thyroid cancer was at 179 pg/mL.

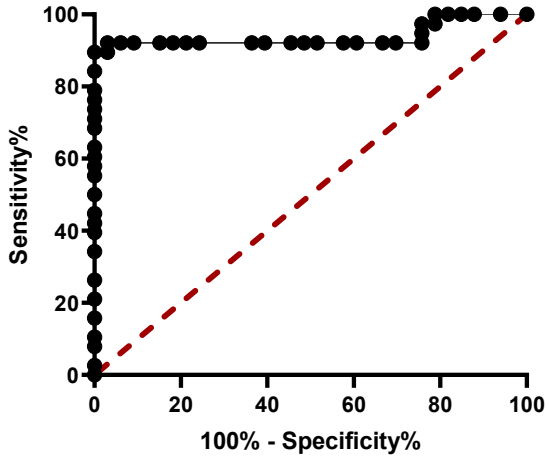

Figure 3. ROC curve of IL-17.

When calculating the ROC curve of the IL-23 levels, the serum IL-23 demonstrated a significant AUC (0.7901; P = 0.0236), a specificity of 76.90%, and a sensitivity of 83.7% (Figure 4). The best cutoff point for the diagnosis of thyroid cancer was at 283 pg/mL.

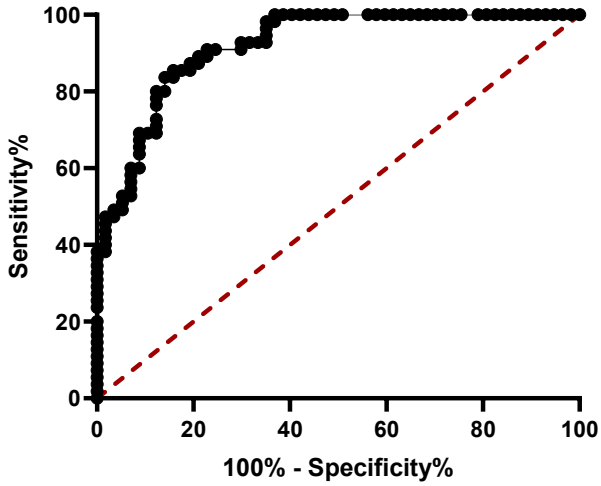

Figure 4. ROC curve of IL-23.

4. Discussion

According to a recent study, the serum level of resistin may be able to predict lymph node metastases. Elevating the level of the resistin concentration was an independent risk factor for metastases to lymph nodes. Resistin and visfatin, two adipokines generated from adipose tissue, have been shown in prior research to be important in the development and spread of cancer [19]. Increased serum resistin levels are associated with cytokine-driven inflammation in thyroid cancer, and resistin stimulates endothelial cell proliferation, differentiation, and migration, which, in turn, promotes

tumorigenesis and angiogenesis [20]. According to [21], resistin mechanistically promotes the spread of cancer by upregulating adhesion molecules (such as ICAM-1 and VCAM-1) in endothelial cells, which is associated with an advanced stage of the disease and a poor prognosis. Interestingly, our results show that serum resistin levels > 25.3 μg/L is a predictor of LNM on its own, thus indicating that it plays a part in lymphatic dissemination.

Additionally, Visfatin has a role in carcinogenesis and aggressive tumor activities; in PTC, higher serum levels are linked to the development of advanced myometrial infiltration and deeper thyroid invasion. In PTC, elevated visfatin levels also predict LNM risk on their own, thus supporting research that links tissue visfatin expression to the possibility of metastasis [22]. Because of their role in invasion and metastasis pathways, these adipokines collectively function as biomarkers for LNM. Visfatin is mostly produced by adipose tissue and serves three main purposes: Nicotinamide-phosphoribosyltransferase, as a cytokine, and as a growth factor. Consequently, elevating visfatin levels has several impacts [23].

Numerous researches indicate that visfatin's involvement in the development of the aforementioned malignancy has been linked to several potential processes. First, adipose tissue macrophages may create visfatin, a proinflammatory molecule that may inhibit macrophage apoptosis brought on by various endoplasmic reticulum (ER) stressors. Visfatin quickly increases the release of the IL-6 protein, which, in turn, stimulates STAT3, and may therefore be involved in conditions such as inflammation or carcinogenesis, which are linked to obesity. Furthermore, an increase in Sirt6, which functions post-transcriptionally to upregulate TNF-α, is directly linked to an increase in visfatin [24]. Additionally, visfatin increases the activity of the antioxidant enzymes glutathione peroxidase (GSHPx), superoxide dismutase (SOD), and catalase (CAT), which helps to reduce reactive oxygen metabolites during an apoptotic state. The antioxidative enzyme activity was increased by visfatin treatment, thus showing that cultured human melanoma cells (Me45) were protected from ROS-induced cytotoxic damage [25]. Furthermore, [26] stated that visfatin caused human endothelial cells to proliferate in a time- and dose-dependent manner and to form capillary-like tubes. The up-regulation of matrix metalloproteinase (MMP) and vascular endothelial growth factor (VEGF) expression contributes to these angiogenic effects. Moreover, visfatin-induced VEGF/MMP up-regulation and endothelial angiogenesis are significantly impacted by the phosphorylation of extracellular signal-regulated kinase 1/2 (ERK 1/2), phosphoinositide 3-kinase (PI3K)/protein kinase B (Akt) pathways, and VEGF/vascular endothelial growth factor receptor 2 (VEGFR2) signaling.

The development of cancer, especially PTC, is significantly influenced by chronic inflammation and inflammatory cytokines. The development of LNM is substantially correlated with elevated levels of systemic inflammatory cytokines, including IL-17 and IL-23. In line with earlier research by [27], which connected preoperative interleukin levels to an increased prevalence of LNM in bladder cancer, our study discovered that PTC patients with LNM (+) had higher blood IL-17 and IL-23 levels than those with LNM (−). One important pro-inflammatory cytokine, IL-17, stimulates tumor growth by recruiting immune cells, promoting angiogenesis, and facilitating the spread of tumors. [2] showed that IL-17A corresponds with PTC development, especially in advanced stages and LNM. Furthermore, by activating Th17 cells, which interfere with immune surveillance and promote metastasis, IL-17 and IL-23 work together to maintain a tumor-promoting milieu [28]. By promoting cell invasion and immune evasion, stromal cells and inflammatory substances in the tumor microenvironment (TME) further aid LNM [29,30]. These results highlight how well IL-17 and IL-23 predict LNM and point to their potential as treatment targets to reduce metastases in PTC.

IL-23 is a member of the interleukin-12 superfamily, which is a heterodimeric cytokine that has been shown to promote inflammation by aiding in the development of Th17 cells [31]. IL-23 is clinically overexpressed in several cancer forms. Studies revealed that IL-23 upregulates angiogenesis factors, which, in turn, can increase the tumor spread. According to [32], an overexpression of IL-23 can cause melanoma, thyroid, colorectal, esophageal, and hepatocellular carcinomas to metastasize. Important cytokines, including IL-23 and STAT3 signaling, are linked to cancer-related inflammation, which suggests a potential avenue for cancer treatments [33,34]. Numerous investigations revealed that Th17 cells experience cytokine-induced alterations in migration and differentiation, which impact the growth and sprouting of tumors [35]. In the present investigation, we found that thyroid cancer patients had greater serum levels of IL-23. Additionally, the ROC results indicated that IL-23 might be able to differentiate thyroid cancer patients from healthy controls. These findings show that IL-23 might be a helpful indicator of thyroid cancer diagnoses. However, future research should examine the precise process.

When comparing thyroid cancer to healthy controls, we discovered that the IL-23 concentrations were considerably greater in the former group. Findings from the literature indicate that the increase in blood levels of IL-23 supports the role of Th17 cells in thyroid carcinoma and implies that IL-23 is connected to the growth of thyroid carcinomas [36]. Increased IL-23 production by cancer cells may trigger a Th17 phenotype in the immune response and aid in the gland's autoimmune inflammation. The occurrence and progression of cancer are tightly associated with the TME, which is made up of stroma cells, cytokines, chemokines, immune cells, and other molecules that either stimulate or prevent the formation of tumors. The primary producers of interleukins, which are tiny protein signaling molecules that are members of the cytokine superfamily, include endothelial cells, monocytes, macrophages, and T lymphocytes. Interleukins have three primary roles in the immune system: They facilitate communication between immune system cells, regulate transcription factors, and manage inflammation [1].

Obesity and metabolic syndrome are associated with increased serum levels of resistin and visfatin, which are adipokines involved in inflammation and insulin resistance. Inflammatory conditions can also affect the resistin and visfatin levels. While there's some evidence linking these adipokines to thyroid cancer risk, the relationship is not fully understood. Obesity leads to increased adipose tissue, which produces pro-inflammatory adipokines such as resistin and visfatin. Metabolic syndrome, often associated with obesity, further exacerbates these effects, with resistin and visfatin playing a role in insulin resistance and inflammation. Inflammatory cytokines such as IL-6 and TNF-alpha, which are released during inflammation, can stimulate the release of these adipokines. While there's a link between obesity, metabolic syndrome, and inflammation with thyroid cancer, the direct role of resistin and visfatin is still being investigated. Some studies suggest that high levels of these adipokines might contribute to thyroid cancer risk, while others indicate that the resistin levels may even be lower in some cancer patients compared to the controls. Resistin and visfatin can affect insulin sensitivity, thus potentially contributing to the development of insulin resistance, which is linked to an increased cancer risk, including thyroid cancer. Additionally, they can promote inflammation, which is a known factor in cancer development [37,38].

Using the ROC curve analysis, the diagnostic values of visfatin, resistin, IL-23, and IL-17 were evaluated in the current investigation. The results show a significant diagnostic value in predicting thyroid cancer risk. The results presented that the measured levels of IL-17 and resistin had substantial AUC values, making them useful indicators to distinguish thyroid cancer patients from healthy

participants. The diagnostic cutoffs identified in our study for IL-17, IL-23, resistin, and visfatin contribute to a growing body of research on serum biomarkers for thyroid cancer. Previous studies have reported elevated levels of these molecules in thyroid malignancies, though the proposed thresholds varied due to differences in the study populations and methodologies. For instance, the elevated IL-17 levels (255 ± 25.82 pg/mL in our study) align with findings by Banerjee et al., who reported significantly higher IL-17 levels in PTC patients compared to the controls [2]. Similarly, [9] demonstrated that IL-17 and IL-23 could help identify thyroid cancer patients with active disease, thus supporting our observations of elevated IL-23 levels (461.03 ± 29.97 pg/mL) in the patient group. While our resistin cutoff (19 μg/L) shows diagnostic potential, [5] noted a considerable variability in the resistin levels across thyroid disorders, thus suggesting the need for cancer-specific reference ranges [5].

The concept of using serum cytokine and adipokine levels as diagnostic tools extends beyond thyroid cancer. In colorectal cancer, [39] identified IL-17 levels > 25 pg/mL as a prognostic marker, though at lower concentrations than our thyroid cancer cutoff (179 pg/mL), likely reflecting tissue-specific roles. For adipokines, [8] established visfatin as a risk factor for multiple cancers, but noted wide variations in the proposed cutoffs across studies due to metabolic confounders. Similarly, [40] questioned whether visfatin could serve as a standalone thyroid cancer marker given its elevation in other conditions. These comparisons underscore that while our proposed cutoffs show promise, their clinical adoption requires validation in diverse populations and a standardization of detection methods to account for pre-analytical variables and comorbidities.

5. Conclusions

Resistin, visfatin, IL-17, and IL-23 parameter assessments revealed that the thyroid cancer serum samples contained noticeably higher concentrations of these substances than the control group. Thus, the expression of IL-17, IL-23, resistin, and visfatin may be employed as a tumor biomarker for diagnosis. Additionally, according to the findings, the serum levels of visfatin, IL-17, IL-23, and resistin may be risk factors for thyroid cancer. In order to identify thyroid cancer, they can offer proof of a possible connection between obesity and the likelihood of the condition. Finding a potential diagnostic tool is critical in early cancer detection. Since the serum levels of Resistin, Visfatin, IL-17, and IL-23 were significantly higher than their level in the healthy group, they can be used as a screening test along with the early-approved methods in the diagnosis of patients with stage I-III of thyroid cancers (i.e., early thyroid cancer stages).

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

This study's authors have disclosed no conflicts of interest.

Author Contributions

The initial draft of the work was written by Hazhar M. Balaky. Parween Abdulsamad Ismail contributed to the research and data collection. The manuscript was heavily edited by Hazhar M. Balaky. A critical evaluation was taken part in by Parween Abdulsamad Ismail. Additionally, the second author provided final clearance for the version to be published and assisted in project supervision. The study's conception and design were influenced by both authors.

References

1. Xi C, Zhang GQ, Sun ZK., et al. (2020) Interleukins in thyroid cancer: From basic researches to applications in clinical practice. *Front Immunol* 11: 1124. https://doi.org/10.3389/fimmu.2020.01124
2. Banerjee S, Nahar U, Dahiya D, et al. (2023) IL-17 A correlates with disease progression in papillary thyroid carcinoma. *Diagn Pathol1* 8: 93. https://doi.org/10.1186/s13000-023-01362-4
3. Zhao J, Zhang Q, Yang Y, et al. (2021) High prevalence of thyroid carcinoma in patients with insulin resistance: A meta-analysis of case-control studies. *Aging* 13: 22232–22241. https://doi.org/10.18632/aging.203529
4. Steppan CM, Lazar MA (2002) Resistin and obesity-associated insulin resistance. *Trends Endocrinol Metab* 13: 18–23. https://doi.org/10.1016/S1043-2760(01)00522-7
5. Zhou L, Song K, Luo W (2023) Association between circulating resistin levels and thyroid dysfunction: A systematic review and meta-analysis. *Front Endocrinol* 13: 1071922. https://doi.org/10.3389/fendo.2022.1071922
6. Xu F, Ning X, Zhao T, et al. (2022) Visfatin is negatively associated withcoronary artery lesions in subjects with impaired fasting glucose. *Open Med* 17: 1405–1411. https://doi.org/10.1515/med-2022-0540
7. Uçan B, Kebapçı N, Uslu S, et al. (2018) Plasma visfatin concentrations in hypothyroid patients and its relationship with thyroid autoimmunity andatherosclerosis. *Ortadoğu Tıp Derg* 10: 498–505. https://doi.org/10.21601/ortadogutipdergisi.364345
8. Mohammadi M, Mianabadi F, Mehrad-Majd H (2019) Circulating visfatin levels and cancers risk: A systematic review and meta-analysis. *J cell Physiol* 234: 5011–5022. https://doi.org/10.1002/jcp.27302
9. Martins MB, Marcello MA, de Assis Batista F, et al. (2018) Serum interleukin measurement may help identify thyroid cancer patients with active disease. *Clin Biochem* 52: 1–7. https://doi.org/10.1016/j.clinbiochem.2017.10.003
10. Yao Z, Fanslow WC, Seldin MF, et al. (1995) Herpesvirus Saimiri encodes a new cytokine, IL-17, which binds to a novel cytokine receptor. *Immunity* 3: 811–821. https://doi.org/10.1016/1074-7613(95)90070-5
11. Okada S, Puel A, Casanova JL, et al. (2016) Chronic mucocutaneous candidiasisdisease associated with inborn errors of IL-17 immunity. *Clin Transl Immunol* 5: e114. https://doi.org/10.1038/cti.2016.71

12. de Morales JM, Puig L, Daudén E, et al. (2020) Critical role of interleukin (IL)-17in inflammatory and immune disorders: An updated review of the evidence focusing in controversies. *Autoimmun Revi* 19: 102429. https://doi.org/10.1016/j.autrev.2019.102429
13. Li S, Li S, Lin M, et al. (2022) Interleukin-17 and vascular endothelial growth factor: New biomarkers for the diagnosis of papillary thyroid carcinoma in patients with Hashimoto's thyroiditis. *J Int Med Res* 50. https://doi.org/10.1177/03000605211067121
14. Bankir M, Yanardag Acik D (2021) IL-17 and IL-23 levels in patients with early-stage chronic lymphocytic leukemia. *North Clin Istanbul* 8. https://doi.org/10.14744/nci.2020.02997
15. Bayraktar N, Eren MA, Bayraktar M, et al. (2023) Analysis ofInterleukin-17, Interleukin-23, neopterin and Nesfatin-1 levels in the sera of Hashimoto patients. *J Med Biochem* 42: 460–468. https://doi.org/10.5937/jomb0-40683
16. Zheng T, Xu C, Mao C, et al. (2018) Increased interleukin-23 in Hashimoto's thyroiditis disease induces autophagy suppression and reactive oxygen species accumulation. *Front Immunol* 9: 96. https://doi.org/10.3389/fimmu.2018.00096
17. McGeachy MJ, Chen Y, Tato CM, et al. (2009) The interleukin 23 receptor is essential for the terminal differentiation of interleukin 17–producing effector T helper cells *in vivo*. *Nat Immunol* 10: 314–324. https://doi.org/10.1038/ni.1698
18. Galano Carvalho DF, Zanetti BR, Miranda L, et al. (2017) High IL-17 expression is associated with an unfavorable prognosis in thyroid cancer. *Oncol Lett* 13: 1925–1931. https://doi.org/10.3892/ol.2017.5638
19. Pan Y, Xu Y, Fan C, et al. (2024) The role of neck adipose tissue in lymph node metastasis of head and neck cancer. *Front Oncol* 14: 1390824. https://doi.org/10.3389/fonc.2024.1390824
20. Nieman KM, Romero IL, Van Houten B, et al. (2013). Adipose tissue and adipocytes support tumorigenesis and metastasis. *Biochim Biophys Acta Mol Cell Biol Lipids* 1831: 1533–1541. https://doi.org/10.1016/j.bbalip.2013.02.010
21. Yang CC, Chang SF, Chao JK, et al. (2014) Activation of AMP-activated protein kinase attenuates hepatocellular carcinoma cell adhesion stimulated by adipokine resistin. *BMC cancer* 14: 1–9. https://doi.org/10.1186/1471-2407-14-112
22. Tian W, Zhu Y, Wang Y, et al. (2013) Visfatin, a potential biomarker and prognostic factor for endometrial cancer. *Gynecol Oncol* 129: 505–512. https://doi.org/10.1016/j.ygyno.2013.02.022
23. Mohammadi M, Hedayati M (2022) Visfatin: An adipokine that plays a crucial role in increasing the risk of cancer. *Iran J Blood Cancer* 14: 68–74. https://doi.org/10.58209/ijbc.14.2.68
24. Pazgan-Simon M, Kukla M, Zuwała-Jagiełło J, et al. (2020) Serum visfatin and vaspin levels in hepatocellular carcinoma (HCC). *PLoS One* 15: e0227459 https://doi.org/10.1371/journal.pone.0227459
25. Bułdak RJ, Bułdak Ł, Polaniak R, et al. (2013) Visfatin affects redox adaptative responses and proliferation in Me45 human malignant melanoma cells: An *in vitro* study. *Oncol Rep* 29: 771–778. https://doi.org/10.3892/or.2012.2175
26. Adya R, Tan BK, Punn A, et al. (2008) Visfatin induces human endothelial VEGF and MMP-2/9 production via MAPK and PI3K/Akt signalling pathways: Novelinsights into visfatin-induced angiogenesis. *Cardiovasc Res* 78: 356–365. https://doi.org/10.1093/cvr/cvm111
27. Schuettfort VM, Pradere B, Trinh QD, et al. (2022) Impact of preoperative plasma levels of interleukin 6 and interleukin 6 soluble receptor on disease outcomes after radical cystectomy for bladder cancer. *Cancer Immunol Immunother* 71: 1–11. https://doi.org/10.1007/s00262-021-02953-0

28. Barilla RM, Diskin B, Caso RC, et al. (2019) Specialized dendritic cells induce tumor-promoting IL-10^{+} IL-17^{+} FoxP3^{neg} regulatory CD4^{+} T cells in pancreatic carcinoma. *Nat commun* 10: 1424. https://doi.org/10.1038/s41467-019-09416-2
29. Hong YR, Lee SH, Lim DJ, et al. (2017) The stratification of patient risk depending on the size and ratio of metastatic lymph nodes in papillary thyroid carcinoma. *World J Surg Oncol* 15: 1–9. https://doi.org/10.1186/s12957-017-1141-4
30. Hughes NM, Nae A, Barry J, et al. (2017) Sonographic differences between conventional and follicular variant papillary thyroid carcinoma. *Eur Arch Oto-Rhino-Laryngol* 274: 2907–2913. https://doi.org/10.1007/s00405-017-4557-0
31. Li H, Tsokos MG, Bhargava R, et al. (2021) IL-23 reshapes kidney resident cell metabolismand promotes local kidney inflammation. *J Clin Invest* 131. https://doi.org/10.1172/JCI142428
32. Yan J, Smyth MJ, Teng MW (2018) Interleukin (IL)-12 and IL-23 and their conflicting roles in cancer. *Cold Spring Harb Perspect Biol* 10: a028530. https://doi.org/10.1101/cshperspect.a028530
33. de Mel S, Hue SS, Jeyasekharan AD, et al. (2019) Molecular pathogenicpathways in extranodal NK/T cell lymphoma. *J Hematol Oncol* 12: 1–18. https://doi.org/10.1186/s13045-019-0716-7
34. Hou Y, Zhu L, Tian H, et al. (2018) IL-23-induced macrophage polarization and its pathological roles in mice with imiquimod-induced psoriasis. *Protein Cell* 9: 1027–1038. https://doi.org/10.1007/s13238-018-0505-z
35. Wu F, Fan J, He Y, et al. (2021) Single-cell profiling of tumor heterogeneity and the microenvironment in advanced non- small cell lung cancer. *Nat commun* 12: 2540. https://doi.org/10.1038/s41467-021-22801-0
36. Figueroa-Vega N, Alfonso-Perez M, Benedicto I, et al. (2010) Increased circulating pro-inflammatory cytokines and Th17lymphocytes in Hashimoto's thyroiditis. *J Clin Endocrinol Metab* 95: 953–962. https://doi.org/10.1210/jc.2009-1719
37. Kwon H, Chang Y, Cho A, et al. (2019) Metabolic obesity phenotypes and thyroid cancer risk: A cohort study. *Thyroid* 29: 349–358. https://doi.org/10.1089/thy.2018.0327
38. Almquist M, Johansen D, Björge T, et al. (2011) Metabolic factors and risk of thyroid cancer in the Metabolic syndrome and Cancer project (Me-Can). *Cancer causes control* 22: 743–751. https://doi.org/10.1007/s10552-011-9747-2
39. Karabulut S, Usul Afsar C, Karabulut M, et al. (2016) Clinical significance of serum interleukin-17 levels in colorectal cancer patients. *J BUON* 21: 1137–1145. Available from: https://pubmed.ncbi.nlm.nih.gov/27837615/.
40. Sawicka-Gutaj N, Ziółkowska P, Derwich A, et al. (2022) Is eNAMPT/visfatin a potential serum marker of papillary thyroid cancer? *Ther Adv Endocrinol Metab* 13. https://doi.org/10.1177/20420188221090005