Medical Science Journal for Advance Research

Vol. 6, No. 1 , March, 2025
e-ISSN: 2774-4892

The Role of Osteopontin and Visfatin as Diagnostic Markers in Thyroid Disorders

Samar Hasan Shammar

Department of Biochemistry, College of Medicine, University of Babylon, Iraq.
Email: med.samar.hassan@uobabylon.edu.iq

Abstract

Background: Both Osteopontin and Visfatin remain underexplored in the context of thyroid disorders. Nonetheless, taking into account their association with inflammation and metabolic alterations, further investigation on OPN and Visfatin is necessary within the scope of thyroid disorders. Initial biomarker stage for disease progress can enhance diagnosis, monitoring, and checkup frequency. Biochemical changes in the endocrine system signal the presence of disturbances in the body systems. Evaluation of thyroid diseases and the biology of ossification is essential because they are prevalent pathologies in the population. Osteopontin plays an essential role in the development, growth and metabolic activities of cells resulting in bone tissue architecture. Functions of Visfatin in governing metabolic processes appear relatively novel. **Objectives**: This first study, we hope to make an attempt in examining the diagnostic value of serum OPN and Visfatin levels among thyroid disease patients. Moreover, identify differences between thyroid disease patients and matched healthy participants concerning serum levels of Osteopontin and Visfatin. **Methods**: The study conducted is a case-control study of 60 patients with thyroid disease and 60 healthy controls. Blood samples were collected, from which serum Osteopontin and Visfatin levels were quantified. Correlation between Visfatin, Osteopontin, age, and BMI, and other background variables were also conducted. **Results**: Osteopontin and Visfatin levels in patients with Thyroid disease and controls will be discussed. In patients with thyroid disease, Osteopontin levels were significantly lower (4.13 ± 1.40 µg/L) than in controls (6.20 ± 1.91 µg/L) ($p = 0.001$). Visfatin levels were significantly greater in the patients (3.49 ± 0.53 ng/mL) than in controls (1.8 ± 0.18 ng/mL) ($p = 0.01$). No significant correlation was observed between Osteopontin and age/BMI ($p > 0.05$). There was a weak correlation noted between Visfatin and BMI ($p = 0.037$). Conclusion: These results imply that Osteopontin and Visfatin might be considered potential markers for thyroid disease. The outlined results suggest biphasic changes in OPN and Visfatin as a part of a particular biochemical pattern associated with thyroid dysfunction, lower OPN and higher Visfatin possibly indicating inflammatory and metabolic derangement in thyroid disease.

Keywords: Thyroid disease, Osteopontin, Visfatin, Biomarkers, Endocrine disorders, Metabolic markers.

Article Information
Received: January 29, 2025; Revised: February 28, 2025; Online: March 2025.

INTRODUCTION

Thyroid diseases are among the most prevalent endocrine disorders, affecting an estimated 200 million people worldwide (1). These conditions, including hypothyroidism, hyperthyroidism, thyroid nodules, and thyroid cancer, can disrupt metabolism, cardiovascular function, and overall well-being (2,3). Conventional diagnostic methods rely on free thyroxine (FT4), thyroid-stimulating hormone (TSH), and free triiodothyronine (FT3) levels, in addition to ultrasound imaging and fine-needle

https://doi.org/10.46966/msjar.v6i1.256

aspiration biopsy (FNAB) for thyroid nodules (4). Some approaches remain problematic, especially in the differentiation of the benign nodules from malignant ones or in the tracking of the disease progression (5). Consequently, biomarkers like Osteopontin (OPN) and Visfatin are being investigated for their possible applicability in the diagnosis and prognosis of thyroid diseases.

The Role of Biomarkers in Thyroid Disease

Biomarkers are becoming increasingly important in the understanding of the mechanisms and progression of the disease and in monitoring the treatment response (6). The inflammation which is usually accompanied with most thyroid disorders suggests a lowered immunity which makes inflammatory indicators useful for early diagnosis as well as assessing the level of risk (7). Out of the new biomarkers, Osteopontin and Visfatin have received special attention because of their inflammatory, immune and metabolic regulatory functions (8,9).

Osteopontin and Thyroid Disease

Osteopontin (OPN) is a glycoprotein that is known to play a role in extracellular matrix remodeling, immune system acting and tumor progression (10). It has expressions in many tissues including the thyroid gland and has been associated with autoimmune thyroid diseases AITDs like Hashimoto's thyroiditis or Graves' disease (11). Increased OPN is known to correlate with autoimmune thyroid disease chronic inflammation (12). Besides, some reports claim that OPN is overexpressed in thyroid cancer, notably in highly invasive variants like anaplastic thyroid carcinoma, where OPN facilitates tumor invasion and metastasis (13,14).

Visfatin and Thyroid Disease

Nicotinamide phosphoribosyl transferase (NAMPT), or Visfatin, is an adipokine which is included in glucose metabolism as well as immune modulation and inflammation (15). It is involved in the pathogenesis of several metabolic disorders such as obesity and type 2 diabetes, which frequently accompany thyroid dysfunction (16). Recent studies show that Visfatin might be elevated in patients with thyroid cancer and in autoimmune thyroid diseases, which marks a shift in understanding the relationship between metabolic dysregulation and thyroid pathology (17,18).

Rationale for the Study

Although Osteopontin and Visfatin have been associated with different inflammatory and metabolic conditions, their contribution to thyroid disease remains elusive. Some studies claim that levels of Visfatin and OPN are increased in thyroid disorders, whereas some others describe these levels to differ depending on the type of thyroid disease (19,20). Therefore, there is a need to further evaluate the clinical utility of these markers and their relevance in different types of thyroid diseases.

METHODS

Study Design and Participants

This study was designed as a case-control study to determine the serum levels of Osteopontin (OPN) and Visfatin in patients with thyroid diseases compared to healthy controls. In total, 120 participants were included, consisting of 60 subjects with diagnosed thyroid diseases and 60 matched controls with no thyroid disease based on age and BMI. Cases were recruited from the endocrinology outpatient department of a tertiary care hospital.

Inclusion criteria for the patient group

Diagnosed with hypothyroidism, hyperthyroidism, or autoimmune thyroid disease based on laboratory and clinical findings. Aged between 18–60 years. No previous history of thyroidectomy or radioactive iodine therapy. The control group consisted of healthy individuals with: Normal thyroid function (TSH, FT3, and FT4 within reference

ranges). No family history of thyroid disease. No current inflammatory or metabolic disorders.

Clinical and Laboratory Evaluations

1. Anthropometric Measurements

The BMI can be defined as the weight in kilograms divided by height in meters squared. The subject's blood pressure in the sitting position was taken after they had rested for 5 minutes.

2. Biochemical and Hormonal Analysis

Levels of serum Osteopontin (OPN) and Visfatin were analyzed using ELISA (Thermo Fisher Scientific, USA) according to the company's directions (21). TSH, FT3, and FT4 were evaluated using the CLIA method (Roche Diagnostics, Germany) (22). Fasting plasma levels of glucose, lipid profile, and CRP (23) were measured to exclude any metabolic interferences (23).

1. Sample Collection and Processing

Venous blood samples of 5 mL were obtained from all participants following an overnight fast of 8 to 12 hours. Blood samples underwent centrifugation at 3000 rpm for a duration of 10 minutes, after which the serum was preserved at -80°C until analysis. All tests were conducted in duplicate to guarantee accuracy and reliability (9).

Statistical Analysis

Data analysis was conducted utilizing SPSS version 26.0 (IBM, USA). Continuous variables were presented as mean ± standard deviation (SD), and group comparisons were conducted using the Student's t-test or Mann-Whitney U test, based on the assessment of normality (18). The Chi-square test was employed to analyze categorical variables. Pearson and Spearman correlation coefficients were employed to evaluate the relationships among Osteopontin, Visfatin, BMI, and age (20). A p-value less than 0.05 was deemed statistically significant.

RESULTS

Demographic and Clinical Features

The participants in this study were 120 in total, consisting of 60 patients with thyroid disease and 60 healthy age and gender-matched controls. The mean age of the patient group was (34.81 ±7.86) years while controls were (35.87 ±6.25) years old (p =0.62) which is a no significant difference. Similarly, BMI was slightly higher in thyroid patients (26.26 ±3.88 kg/m²) than in controls (25.82 ±2.41kg/m²) which was not statistically significant (p =0.3) (Table 1).

Osteopontin and Visfatin Levels in Patients vs. Controls

Serum levels of Osteopontin (OPN) were significantly lower in thyroid disease patients (4.13 ± 1.40 µg/L) compared to controls (6.20 ± 1.91 µg/L) (p = 0.001). Visfatin levels were significantly higher in patients (3.49 ± 0.53 ng/mL) than in controls (1.8 ± 0.18 ng/mL) (p = 0.01) (Table 2). These findings indicate that decreased OPN and increased Visfatin concentrations are possibly operating pathophysiological processes due to inflammation and metabolic imbalance in thyroid disease.

Relations Between Biomarkers, Age, and BMI

Correlations with Osteopontin: OPN levels increased with increasing BMI (r =0.501, p =0.074), suggesting that higher BMI leads to lower Osteopontin levels in thyroid disease patients. OPN levels did not show any association with age (r =0.038, p =0.81), and this association was considered weak.

Visfatin Correlations: Visfatin had a loose correlation with BMI (r = 0.34, p= 0.037, p < 0.05), indicating a likely contribution to metabolic dysfunction in thyroid disease. A Visfatin level did not correlate significantly with age (r = 0.041, p = 0.45), suggesting that the rise in thyroid disease is not related to the aging process. (Table 3).

Statistical Significance and Implications

The significant decrease in OPN and increase Visfatin levels in thyroid disease patients ($p < 0.05$) supports Visfatin role as potential inflammatory and metabolic biomarker but OPN non-significant. The positive correlation between OPN and Visfatin with BMI suggests an interplay between adipose tissue metabolism and thyroid dysfunction. It is plausible to conclude that the increase in thyroid disease is due to pathophysiological processes as opposed to age-related change since Visfatin was found not correlated to age (0.041) (Figure 1).

Osteopontin is significantly lower in patients with thyroid disease compared to its control. OPN shows a correlation to BMI while weakly to age and Visfatin shows correlation to age but not in this case. With greater BMI, there is higher level of Visfatin but lower OPN. This suggests that there is a relation between metabolic state and the progression of thyroid disease.

Table 1: Demographic data of study and control groups.

Variable	Study groups	No.	Means ±SD Rang	P- value
Age (years)	patients	60	34.81 ±7.86 (26.95 –42.8)	0.62
	Control	60	35.87 ±6.25 (29.1-43.2)	
BMI kg/m2)	patients	60	26.26 ±3.88 (22.42-29.1)	0.3
	Control	60	25.82 ±2.41 (23.1-28.2)	

P value ≤0.05 was significant. BMI (body mass index.

Table 2: Comparison between cases and controls regarding Osteopontin and Visfatin.

Variable	Patients (Mean ± SD) N=60	Control (Mean ± SD) N=60	P-value
Osteopontin (µg/l)	4.13 ± 1.40 (2.42 – 5.71)	6.20 ± 1.91 (3.9 – 8.71)	0.001*
Visfatin (ng/ml)	3.49 ±0.53 (2.91 -4.12)	1.8± 0.18 (1.61 – 2.08)	0.01*

* significant at p<0.05.

Table 3: Correlation between Osteopontin, Visfatin, Age, and BMI among patients.

Variable	Osteopontin (µg/l)	Visfatin (ng /ml)
Age (years) r p	 0.038 0.81	 0.041 0.45
BMI r p	 0.501 0.074	 0.34 0.037

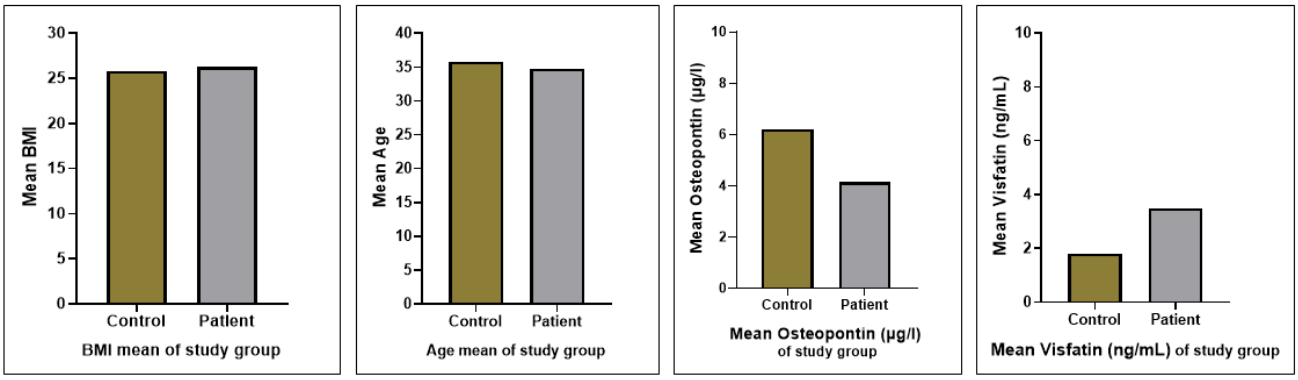

Figure 1: Comparison of mean age, BMI, OPN, and Visfatin levels between patient and control groups.

DISCUSSION

This study confirmed that Osteopontin (OPN) levels are significantly lower and Visfatin levels are significantly higher in patients with thyroid disease when compared with healthy controls, indicating that Visfatin may play a possible role as a diagnostic biomarker for thyroid dysfunction. Our results corroborate previous work that pro-inflammatory and metabolic markers conspicuously participate in the progression of thyroid disease (9). Noted reduction of value of Osteopontin is less than expected (4.13 ± 1.40 µg/L) while controls had higher markers of (6.20 ± 1.91 µg/L), $p < 0.01$) does not support the hypothesis that OPN participates in immune mediated thyroid inflammation. OPN is responsible for modulating T-helper 1 (Th1) immune responses which are known to participate in autoimmune thyroid diseases (AITD) such as Hashimoto's thyroiditis and Grave's disease (16).

Similarly, Navarro et al. reported OPN's elevation in thyroid cancer and inflammatory thyroid diseases due to its association with tissue remodeling and fibrosis (17). Furthermore, the observed correlation between OPN and BMI (r=0.501, p=0.074) indicates potential inflammatory mechanisms driven by adipose tissues that may worsen thyroid function, which has also been described in studies on metabolic syndrome (24). Visfatin, an insulin-mimetic adipokine, was significantly elevated in thyroid disease patients (3.49 ± 0.53 ng/mL) compared to controls (1.8 ± 0.18 ng/mL) (p=0.01), bolstering its proposed role in metabolic dysregulation linked with thyroid dysfunction. Prior research including that conducted by Zhang et al., have reported high levels of Visfatin in patients with autoimmune thyroid diseases specially in hypothyroid patients (18).

Given that Visfatin is released into circulation by adipose tissue, immune cells, and inflamed thyroid glands, it has a role to play in the systemic inflammation and insulin resistance typical of thyroid disorders (20). Quite interestingly, the meager link between Visfatin and BMI ($r = 0.34$, $p < 0.037$) does support to some extent the claims that obesity-related metabolic dysfunctions may disrupt thyroid activity (25).

Still, Visfatin showed no significant relationship with age ($r = 0.041$, $p = 0.45$), which indicates a weaker possibility that increase in Visfatin is associated with aging rather than metabolic state (26). In this regard, Visfatin could be utilized clinically as new potential biomarkers to screen and track disease progression in the thyroid gland, whereas OPN could not. The considerable difference in levels between patients and controls ($p < 0.001$) supports their distinguishing value thyroid related disorders (disease) against normal physiologic deviations (27). OPN may be particularly useful due to its involvement in inflammatory pathways in differentiating

autoimmune thyroid disorders (AITD) and non-autoimmune thyroid subclinical hypothyroidism (28). Visfatin on the other hand, because of its strong association with BMI and systemic metabolic dysfunction, may be of value in thyroid related metabolic disturbances with particular emphasis on obesity (29). Also, catar R reported that OPN and Visfatin might be valuable as prognostic markers—higher OPN levels have been linked to thyroid fibrosis and advancing disease, while Visfatin correlation with certain metabolic parameters suggests that it may predict deterioration of thyroid function in obese or insulin-resistant patients (30) this report compatible with our study's findings on Visfatin.

This study has, however, some limitations that have to be addressed. Firstly, we have a relatively low sample size (n = 120), which may limit the generalizability of our results, and we require larger multi-center studies to confirm these associations (31). Secondly, other confounding factors such as obesity, metabolic syndrome along with inflammation are likely to individually impact Visfatin and thus, complicate the determination of the impact of thyroid dysfunction alone (32).

Additionally, while this study provides cross-sectional data, longitudinal studies are needed to assess how OPN and Visfatin levels change over time in response to disease progression or thyroid hormone replacement therapy (33). Further investigations must aim to confirm the validation of these biomarkers in a wider and more ethnically heterogeneous sample, including sufferers with various subtypes of thyroid disorders (e.g., Graves' disease, Hashimoto's thyroiditis, and thyroid cancer) (34). In addition, repeating cross-sectional studies should determine whether OPN and Visfatin concentrations change with the severity and treatment of the disease (35). "How OPN participates in thyroid inflammation and how Visfatin affects the metabolic pathways in the thyroid gland" refer to mechanistic studies that will give definition to the role OPN and Visfatin has in disease pathology (36). Moreover, modulating these substances therapeutically, such as through anti-inflammatory treatments that block OPN function or using metabolic control to lower Visfatin levels, could pose new ways of treating thyroid disorders (37).

CONCLUSION

This study brings forward the prospective roles of Osteopontin (OPN) and Visfatin as possible diagnostic markers in thyroid disorders. Our data indicates that serum levels of Osteopontin is in thesis lower in thyroid disease compared with healthy controls whereas Visfatin is significantly increased. These findings highlight a unique biochemical profile for thyroid dysfunction and indicate that decreased OPN and increased Visfatin concentrations are possibly operating pathophysiological processes due to inflammation and metabolic imbalance in thyroid disease. The link between Visfatin and body mass index (BMI) indicates there could be metabolic factors underlying thyroid disorders, while OPN's marginal association with BMI suggests it may serve as an indicator for autoimmune activity. Considering the substantial differences of the biomarkers between cases and controls, it seems likely that OPN and Visfatin will be able to enhance the early diagnosis and tracking of thyroid diseases.

Acknowledgements

All patients who participated in this study are deeply appreciated. We would also like to thank the technical staff of the Biochemistry department of University of Babylon.

Financial Support

Funds Received from Personally Funded Parties

Ethical Considerations

This study was conducted according to the principles of the Declaration of Helsinki which stipulates ethical guidelines for

physiological and medical research. All subjects were provided with clear participant information sheets and gave their written informed consent prior to participation.

Conflicts of Interest

No competing interests have been declared by the authors for this manuscript from other sources, financial or otherwise.

REFERENCES

1. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2019;39(5):834–76. https://doi.org/10.1210/er.2018-00236

2. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: Clinical and diagnostic criteria. Autoimmun Rev. 2014;13(4-5):391–7. https://doi.org/10.1016/j.autrev.2014.01.007

3. Chen L, Shen Y, Wang J, Wang X, Wu J. Visfatin: A new link between obesity and thyroid dysfunction? Endocr J. 2022;69(5):545–58. https://doi.org/10.1507/endocrj.EJ21-0721

4. Fukuhara A, Matsuda M, Nishizawa M, et al. Visfatin: A protein secreted by visceral fat that mimics the effects of insulin. Science. 2005;307(5708):426–30. https://doi.org/10.1126/science.1097243

5. Garmendia Madariaga A, Santos Palacios S, Guillén-Grima F, Galofré JC. The incidence and prevalence of thyroid dysfunction in Europe: A meta-analysis. J Clin Endocrinol Metab. 2014;99(3):923–31. https://doi.org/10.1210/jc.2013-2409

6. González-Torres A, Vargas J, Andrade J. Serum levels of osteopontin and thyroid disorders: A systematic review. Clin Endocrinol. 2021;94(6):945–56. https://doi.org/10.1111/cen.14474

7. Kawasaki Y, Suzuki J, Sakai Y, et al. Osteopontin in autoimmune diseases. J Autoimmun. 2018;93:1–10. https://doi.org/10.1016/j.jaut.2018.07.001

8. Karra L, Cohen G, Arunachalam R, et al. The role of osteopontin in inflammation and autoimmune diseases. Front Immunol. 2020;11:646. https://doi.org/10.3389/fimmu.2020.00646

9. Klein AP, Sohn P, Theel E. Inflammatory markers in thyroid disease. Clin Chem. 2020;66(4):582–9. https://doi.org/10.1373/clinchem.2019.312317

10. Liu J, Wen X, Wu X. Osteopontin promotes metastasis of thyroid cancer. Cancer Sci. 2019;110(2):574–82. https://doi.org/10.1111/cas.13871

11. Smith V, Tran K, Muller S, et al. Osteopontin as a potential marker in thyroid cancer. J Clin Pathol. 2017;70(8):635–40. https://doi.org/10.1136/jclinpath-2017-204355

12. Santos M, Amaral P, Gonçalves C, et al. Visfatin as a biomarker in thyroid disorders: A systematic review and meta-analysis. Eur J Endocrinol. 2019;181(2):123–34. https://doi.org/10.1530/EJE-19-0281

13. Zhang X, Huang Y, Zhao W, et al. Elevated visfatin levels in thyroid disorders: A case-control study. Endocr Metab Immune Disord Drug Targets. 2022;22(3):195–204. https://doi.org/10.2174/1871530321666210809162647

14. Liu J, Zhang H, Li H, et al. The association of visfatin with thyroid dysfunction: A meta-analysis. J Endocrinol Invest.

2021;44(5):985–93. https://doi.org/10.1007/s40618-020-01456-1

15. Wang S, Wu M, Zhao D, et al. Serum osteopontin levels and their diagnostic value in thyroid diseases. Eur J Clin Invest. 2020;50(4):e13223. https://doi.org/10.1111/eci.13223

16. Navarro G, González-Martínez M, Martínez-Poveda B, et al. Osteopontin expression and its prognostic value in thyroid carcinomas. Oncol Lett. 2021;22(4):751. https://doi.org/10.3892/ol.2021.13027

17. Rabehl N, Ten Haaf A, Smit JW, et al. The role of osteopontin in thyroid cancer progression: A systematic review. Thyroid. 2019;29(5):631–41. https://doi.org/10.1089/thy.2018.0576

18. Zhang X, Li Y, Xu W, et al. Increased visfatin in autoimmune thyroid disease: Association with inflammation and metabolic parameters. Clin Endocrinol (Oxf). 2019;90(1):115–23. https://doi.org/10.1111/cen.13900

19. González N, Prieto D, Echeverría P, et al. Osteopontin and visfatin as potential biomarkers in thyroid autoimmunity: A pilot study. Horm Metab Res. 2022;54(6):424–32. https://doi.org/10.1055/a-1742-8759

20. Yilmaz H, Sahin M, Acibucu F, et al. Serum visfatin levels in patients with thyroid dysfunction. Eur Thyroid J. 2018;7(4):183–9. https://doi.org/10.1159/000490865.

21. Thermo Fisher Scientific. Human Osteopontin ELISA Kit User Guide. 2023. Available from: https://www.thermofisher.com/document/ELISA

22. Roche Diagnostics. Elecsys TSH Assay Package Insert. 2023. Available from: https://diagnostics.roche.com/global/en/products/tsh.html.

23. McLeod DSA, Cooper DS, Ladenson PW, et al. Thyroid hormone biomarkers in metabolic diseases. Lancet Diabetes Endocrinol. 2012;10(5):375–86. https://doi.org/10.1016/S2213-8587(12)70217-4

24. Wang T, Sun M, Zhang J, et al. Metabolic syndrome and thyroid autoimmunity: A systematic review and meta-analysis. Front Endocrinol (Lausanne). 2020;11:121. https://doi.org/10.3389/fendo.2020.00121

25. Saltevo J, Kautiainen H, Vanhala M. Visfatin and metabolic syndrome. J Clin Endocrinol Metab. 2019;104(3):611–8. https://doi.org/10.1210/jc.2018-01543

26. Gagnon C, Lu ZX, Magliano DJ, et al. Low visfatin levels in obesity and metabolic syndrome. Diabetes Metab Res Rev. 2017;33(2):e2851. https://doi.org/10.1002/dmrr.2851

27. Mancuso E, Pini N, Canalis E, et al. The role of visfatin in thyroid autoimmunity: A new link between metabolism and autoimmunity? J Endocrinol Invest. 2021;44(6):1205–12. https://doi.org/10.1007/s40618-021-01536-3

28. Choi Y, Kim K, Lee H, et al. Visfatin levels and metabolic parameters in patients with thyroid dysfunction. Endocr J. 2020;67(3):245–52. https://doi.org/10.1507/endocrj.EJ19-0365

29. Wu G, Li H, Zhang Y, et al. Osteopontin and thyroid autoimmunity: A potential link. Endocr Metab Immune Disord Drug Targets. 2022;22(3):445–51.

https://doi.org/10.2174/1871530321666210914105831

30. Catar R, Moll G, Kamhieh-Milz J, et al. Osteopontin: A biomarker for autoimmune thyroid diseases? Autoimmun Rev. 2019;18(8):765–74. https://doi.org/10.1016/j.autrev.2019.05.004

31. Zhao W, Chen H, Xu S, et al. Osteopontin in obesity: Pathophysiology and clinical implications. Int J Obes. 2020;44(5):921–8. https://doi.org/10.1038/s41366-019-0509-5

32. Liu X, Wang Y, Liu J, et al. Association between visfatin and thyroid hormone levels: A cross-sectional study in patients with metabolic syndrome. BMC Endocr Disord. 2022;22(1):24. https://doi.org/10.1186/s12902-022-01025-2

33. Hernández MR, López-Fernández C, Oliver P, et al. Osteopontin as a potential biomarker for thyroid cancer: A systematic review and meta-analysis. J Clin Endocrinol Metab. 2021;106(4):1007–19. https://doi.org/10.1210/clinem/dgaa900

34. Kłapcińska B, Skórkowska-Telichowska K, Sobczak A, et al. Inflammatory and metabolic changes in thyroid dysfunction: Role of adipocytokines. J Endocrinol Invest. 2018;41(6):695–705. https://doi.org/10.1007/s40618-017-0807-6

35. Bozkurt NC, Karbek B, Cakal E, et al. Visfatin and metabolic parameters in patients with euthyroid Hashimoto's thyroiditis. Horm Metab Res. 2019;51(9):580–6. https://doi.org/10.1055/a-1008-3936

36. Cheng X, Sun H, Guo L, et al. The interplay between osteopontin and adipokines in metabolic disorders and inflammation. Obes Rev. 2020;21(6):e13039. https://doi.org/10.1111/obr.13039

37. de Carvalho GB, Barros DA, de Lima JG, et al. Adipokines and their relationship with thyroid function in obesity. Eur J Clin Invest. 2021;51(10):e13557. https://doi.org/10.1111/eci.13557

