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Studying Periostin as a Diagnostic Marker in Sera of Iraqi Patients Hypothyroidism

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Abstract

Hypothyroidism is one of the most common thyroid diseases in adults. Hypothyroidism is a condition that results from a deficiency of thyroid hormone and can range from being asymptomatic to life-threatening. A decrease in thyroid hormone production in the thyroid gland, a shortage of pituitary thyroid stimulating hormone, or a hypothalamic Thyrotropin-releasing hormone deficiency can cause hypothyroidism. Thyrotropin-releasing hormone deficiency Periostin is classified as both an extracellular matrix protein and a matricellular protein that belongs to the fasciclin family. As a matricellular protein, Postn plays a crucial role in the growth and maintenance of tissues and organs. Due to the limited research on the effects of Postn on the thyroid gland, the aim of this study is to investigate the relationship between Postn and hypothyroidism. The 120 samples were divided into two groups: 80 patients with hypothyroidism and 40 healthy people. Postn levels significantly increased in the hypothyroidism group compared to the control group ($p < 0.001$). The results indicate that Postn can be a sensitive and accurate marker for diagnosing hypothyroidism in Iraqi patients.

Keywords: Hypothyroidism, thyroid stimulating hormone, tetraiodothyronin, tri iodothyronine, periostin.

1. Introduction

Periostin (Postn) is a matricellular protein that belongs to the fasciclin family, which is glutamate-containing and dependent on vitamin K. Initially discovered in murine osteoblasts and categorized as an osteoblast-specific factor, Postn is also found in the periosteum and collagen-rich fibrous connective tissues, such as ligaments, it is an osteoblast-specific factor [1-3].

The periosteum and collagen-rich fibrous connective tissues, such as ligaments, also contain it [4]. A 19-kD carboxylated matrix protein called Postn can be found in the lung and bone, as well as other extracellular matrices [5, 6]. A hydrophilic COOH-terminal domain, a region with internal homologous repeats, domains rich in cysteine, and a signal peptide sequence at the NH_2 end make up Postn. The Postn participates in the regulation of bone formation and the reaction to mechanical pressure in bone physiology by regulating the expression in the periosteum of

sclerostin. Additionally, Postn has been linked to the control of cell activity, energy metabolism, and cell-matrix interaction [7]. In addition to being implicated in inflammatory diseases, Postn also actively promotes carcinogenesis and metastasis. High levels of the protein Postn and mRNA are found in the majority of solid tumors, such as neuroblastoma, ovarian, gastric, breast, colon, head and neck, pancreatic, lung, papillary thyroid, stomach, and liver cancers [8, 9]. After establishing Postn's involvement in the etiology of bronchial asthma, researchers looked into Postn's potential involvement in other inflammatory diseases. Postn has been linked to several allergy disorders, including AD, Sclerosing sialadenitis associated with IgG4, and eosinophilic otitis media 38 [10], with chronic rhinosinusitis and allergic rhinitis [11].

Additionally, Postn was revealed to be involved in non-allergic inflammatory disorders such as scleroderma, drug-induced or idiopathic fibrosis of the lungs and bone marrow, and proliferative diabetic retinopathy. Additionally, Postn is highly expressed in a variety of malignant tissues. Since it is known that fibroblast growth is influenced by a number of cytokines besides IL-4 and IL-13-151 and 352 of the transforming growth factor, a number of substances, including factor 1, angiotensin II, BMP-2, platelet-derived growth factor, and others have been shown to increase the expression of Postn in non-allergic inflammatory conditions [12]. Since its discovery in 1993, Postn has been the subject of numerous scientific articles [13-15]. The fascinating general structure of these molecules is still poorly understood. There are still a number of illnesses for which the mode of operation is unknown [16-18].

Different splice forms might be connected to various roles in diverse tissues and diseases [3]. Postn performs at least two important roles, one in the matrix-based process of fibrillogenesis and the other in cell migration. In both Postn and hypothyroidism, there is a lack of research and studies on the effect of Postn on the thyroid gland. This study aims to investigate the relationship between the impact of Postn and hypothyroidism.

2. Materials and Methods

2.1 Study subjects

The researchers worked in cooperation with the Al-Amal National Hospital Department in the Republic of Iraq to investigate 120 individuals. The 80 patients with hypothyroidism and 40 healthy people aged 30–60 years participated in the study. Exclusion criteria: Type 1 and type 2 diabetes mellitus; thyroid cancer; patients with pregnancy. Different splice forms might be connected to various roles in diverse tissues and diseases [3]. Postn performs at least two important roles, one in the matrix-based process of fibrillogenesis and the other in cell migration. Between Postn and hypothyroidism, there is a lack of research and studies on the effect of Postn on the thyroid gland. This study aims to investigate the relationship between the impact of Postn and hypothyroidism.

2.2 Blood sample collection

Blood samples (10 mL) were collected ten to twelve hours after fasting from 80 patients with hypothyroidism and 40 healthy subjects. Blood samples were taken from hypothyroidism patients and the control group under aseptic conditions and centrifuged for 15 minutes at 1000g. Next, samples of serum were separated into tiny aliquots for storage at −20 °C until a portion of the acquired serum was used for lipid profile measurement. Each person's weight and height were measured in kilograms/m2. By dividing the weight (in kg) by the square of the height (in m^2), the body mass index (BMI) was determined [19]. The Kenza (240TX) equipment (Biolabo) and kit (Biolabo) were used to measure biochemistry, fasting blood glucose (FBG), triglyceride

(TG), total cholesterol (TC), and high-density lipoprotein (HDL). A commercially available ELISA kit was used to measure the level of Postn analytes according to the manufacturer's instructions (MyBiosource, America). The triiodothyronine (T3), thyroxin (T4), and thyroid stimulating hormone TSH hormones were measured automatically by the Vidas Instrument for each patient.

2.3 Statistical analysis

The median (25^{th} and 75^{th} percentiles) for irregularly distributed numerical variables: The (Mann-Whitney) tests were employed to describe numerical variables that were not regularly distributed. The significance level was set at a *p*-value of 0.05. Pearson's correlation was used to test the significance of correlation for the relationship between two quantitative variables. Through the use of receiver operating characteristic (ROC) curve analysis, the Postn cut-off value was established.

3. Results and Discussion

The age and BMI of hypothyroidism patients and healthy subjects are listed in **Table 1** by the median (25^{th} and 75^{th} percentiles).

Table 1. Demographic characteristics of hypothyroidism and healthy subjects.

Variables	Hypothyroidism (n= 80)	Healthy subjects (n= 40)	*p*-value
Age (Year)	40.00(32.35 -47.10)	39.10 (30.20 – 44.35)	N.S
BMI (kg/m^2)	40.00 (33.22 – 39.50)	25.87 (23.85 – 29.95)	0.05*

There was a significant difference between the two independent means when the gathered data were examined by median (25^{th} and 75^{th} percentiles) using the Mann-Whitney test at the $p < 0.05$ level.

The median (25^{th} and 75^{th} percentiles) of the age distribution of the hypothyroidism group was 40.00 (32.35–47.10) years, and the healthy subjects group was 39.10 (30.20– 44.35). The data on the BMI distribution of the hypothyroidism 40.00 (33.22–39.50) patients and the healthy subjects group 25.87 (23.85–29.95), respectively.

Table 2 shows the serum levels of cholesterol, T.G., HDL, VLDL, and LDL in hypothyroidism and Healthy subjects. Highly significant differences appeared in the levels of cholesterol, T.G., HDL, VLDL, and LDL when comparing two groups of hypothyroidism patients and a control group with $p < 0.001$. The Cholesterol levels were increased significantly in hypothyroidism patients group 299.85 (269.35-355.55). When compared with the control group, 155.55 (150.55–160.50) $p < 0.001$. The T.G., LDL, and VLDL levels increased significantly in hypothyroidism patients group 199.50 (169.35–239.10), 217.60 (195.55-267.98), 39.88 (33.95–47.88), when compared with control group 120.50 (98.55–169.50), 81.55 (71.50–89.00), 25.80 (20.80–34.50), respectively, $p < 0.001$, while there was a low significant difference in HDL when we compared Hypothyroidism patients group 41.35 (40.55–47.85) with control 48.50 (46.97–49.50), $p < 0.001$.

Body composition and thyroid hormones appear to be related. Thermogenesis, lipid and glucose metabolism, hunger, and other metabolic processes are all significantly influenced by thyroid hormones and fat oxidation, regardless of physical activity. Changes in body weight and composition, core body temperature, and total and resting energy consumption are all correlated

with thyroid dysfunction (REE) [20]. Hypothyroidism has been associated with a higher body mass index (BMI), a higher prevalence of obesity, and decreased thermogenesis and metabolic rate. According to clinical research, subclinical hypothyroidism, a mild form of thyroid dysfunction, is linked to significant weight fluctuations and is a risk factor for obesity and overweight people [21].

The source of T.G. is exogenous or free fatty acids (FFAs), which are created by fat and glycolysis. Thyroid hormone may reduce the liver's ability to synthesize VLDL-TG (T.H.). The current pace of lipolysis will result in lower rates of lipid oxidation and higher T.G. levels in hypothyroidism [22, 23]. According to numerous studies, thyroid hormones affect how lipids are processed, which causes lipid levels to increase when TSH levels do [24, 25]. The production, transport, and breakdown of fat are all impacted by T.H. Lipoprotein activity dropped, apolipoprotein carrying capacity for LDL and T.G. was affected, and people with hypothyroidism had lower levels of cholesterol transport than the general population. The T.G. and LDL levels in the blood rose. as a result of less cholesterol being removed and broken down [26]. By advancing the development of controlling the expression of LDL and oxidative stress disease in vivo, receptors, and liver cells have lipoprotein lipase on their surface. Hypothyroidism can impair the mechanism by which cholesterol is carried backward in liver epithelial cells. This results in a decrease in LDL cholesterol, LDL receptor sensitivity, the number of LDL receptors, and their activation on the surface of liver cells. Hypothyroidism will cause significant amounts of free fatty acids to enter the liver, increasing the formation of LDL there and ultimately elevating T.G. and LDL levels [27].

Table 2. Serum lipid profile of hypothyroidism and healthy subjects.

Variables	Hypothyroidism (n= 80)	Healthy subjects (n= 40)	*p*-value
Cholesterol (mg/dL)	299.85(269.35-355.55)	155.55(150.55-160.50)	0.00
T.G (mg/dL)	199.50(169.35-239.10)	120.50(98.55-169.50)	0.00
HDL (mg/dL)	41.35 (40.55-47.85)	48.50(46.97-49.50)	0.00
LDL (mg/dL)	217.60(195.55-267.98)	81.55(71.50-89.00)	0.00
VLDL (mg/dL)	39.88(33.95-47.88)	25.80(20.80-34.50)	0.00

The collected data were analyzed by median ($25^{th}$and 75^{th} percentiles) via the Mann-Whitney test at the $p < 0.05$ level, there was a significant difference between the two independent means.

The median of T3 revealed a no significant increase in the hypothyroidism group 1.61(1.32-1.82), compared to that of the healthy subject groups 1.71 (1.32-2.20) $p > 0.05$, while T4 revealed a significant decrease in the hypothyroidism group 94.50 (88.52-105.50) compared to that of the healthy subject groups 99.20 (89.50-111.50) $p > 0.128$, and TSH revealed a significant increase in the hypothyroidism group 17.50 (8.50-36.50) compared to that of the healthy subject groups 1.69 (1.25-2.18) $p < 0.001$. The result showed a significant increase in Postn level when compared the hypothyroidism group 1151.44(1074.36–1384.34) with the healthy subject 36. 483.45 (434.57–563.84), $p < 0.001$, as shown in **Table 3**.

Food intake and energy storage are significantly regulated by TSH and thyroid hormones (THs). They control the balance between lipogenesis and lipolysis, adipogenesis, and thermogenesis. A greater TSH could bring on low-grade chronic inflammation. Many mechanisms exist by which adipose tissue can affect thyroid function, and it is well known that even little variations in

thyroid function have a significant impact on changes in body weight. The release of adipocytokines, chronic inflammation, and lipotoxicity are involved. Humans can develop body fat even with modest thyroid dysfunction, and obese people may have subclinical hypothyroidism, which is why their TSH levels are slightly elevated. Determining the cause of hypothyroidism is crucial for understanding how TSH tests should be interpreted. However, the hypothalamic-pituitary-thyroid axis is probably becoming activated, causing hyperthyro-tropinemia. Measuring the T3 concentration may help differentiate between several causes of elevated TSH levels. It is believed that thyroid gland dysfunction may be caused by obesity, an inflammatory condition, and lipotoxicity [28].

Table 3. The median ($25^{th}$and 75^{th} percentiles) of thyroid hormones and Postn of hypothyroidism and healthy subjects.

Variables	Hypothyroidism (n= 80)	Healthy subjects (n= 40)	*p*- value
T3 (ng/mL)	1.61(1.32-1.82)	1.71(1.32-2.20)	0.050
T4 (ng/mL)	94.50(88.52-105.50)	99.20(89.50-111.50)	0.128
TSH (ulU/mL)	17.50(8.50-36.50)	1.69(1.25-2.18)	0.000
Postn (ng/mL)	1151.44(1074.36-1384.34)	483.45(434.57-563.84)	0.000

The collected data were analyzed by the mean ± standard deviation and median ($25^{th}$and 75^{th} percentiles) via the Mann-Whitney test at the $p < 0.05$ level, there was a significant difference between the two independent means.

The capacity of serum Postn levels to distinguish patients with hypothyroidism from healthy individuals was evaluated using the ROC curve analysis, as shown in **Table 4** and **Figure 1**. The high sensitivity (96.9) and specificity (97.5) of the ROC curve over the hypothyroidism diagnostic test indicated improved validity. The AUC of the ROC curve for the presence of a hypothyroidism diagnosis revealed that the best level of accurate hypothyroidism prediction was 0.996 ($p < 0.001$). In this study, patients with hypothyroidism had their serum levels of Postn evaluated. According to the study's findings, serum Postn levels were higher in hypothyroidism patients than in healthy people.

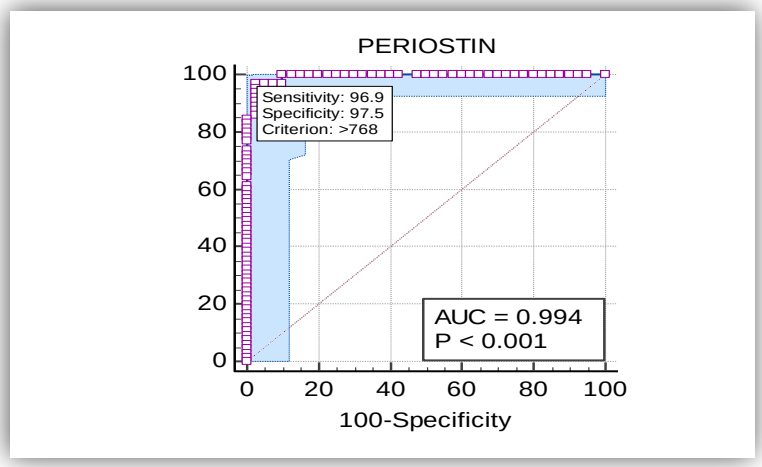

Figure 1. The ROC curve analysis of serum Postn concentration in hypothyroidism patients.

Table 4. Periostion AUC and validity in distinguishing between hypothyroidism and healthy subjects.

Variable	AUC	*p*-Value	Cutoff value	Sensitivity	Specificity	Accuracy	PPV	NPV
Postn (ng/mL)	0.994	0.001	768	96.9	97.5	0.9442	98.4	95.1

Postn is widely expressed, with the most significant amounts found in the thyroid tissue, breast, placenta, third uterus, aorta, stomach, and lower gastrointestinal tract, despite the fact that its current name comes from the production of this protein in the long bones' periosteum. Ongoing mechanical stimulation (stretch) in adult connective tissues, such as heart valves, skin, periodontal ligaments, tendons, and bones, causes it to express itself more prominently during ontogenesis [29,30].

4. Conclusion

To summarize, serum Postn levels were higher in hypothyroidism Iraqi patients. Hypothyroidism can be diagnosed most accurately and sensitively with a cut-off value of 768. Thyroid dysfunction can strongly influence the lipid profile.

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Conflict of Interest

The authors declare there is no conflict of interest.

Ethical Clearance

The project was approved by the local ethical committee at the College of Science for Women on 5/12/2022, in accordance with Ministry of Health approval No. 51413.

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