

## Serum Level of Resistin in Patients with Hyperthyroidism and Hypothyroidism

Mehdi Hedayati,<sup>\*1</sup> Sanaz Shabani,<sup>2</sup> Mahsa Frazndemehr,<sup>2</sup> Marjan Zarif-Yeganeh,<sup>1</sup> Laleh Hoghooghiri<sup>1</sup>

1. Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran

Article information	Abstract
<p>Article history: Received: 10 Jan 2012 Accepted: 15 Mar 2012 Available online: 2 Nov 2013 ZJRMS 2014; 16(11): 1-4</p> <p>Keywords: Resistin Hypothyroidism Hyperthyroidism Body Mass Index</p> <p>*Corresponding author at: Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. E-mail: Hedayati@endocrine.ac.ir</p>	<p><b>Background:</b> Resistin hormone is a polypeptide hormone belonging to the family of hormone-like resistin molecules. Controversial results have been reported between serum level of resistin and thyroid abnormalities, including hypothyroidism and hyperthyroidism. The purpose of this study was to evaluate the serum level of resistin hormone in patients with hypothyroidism and hyperthyroidism and its association with weight and body mass index.</p> <p><b>Materials and Methods:</b> In this case-control cross sectional study 48 patients with hypothyroidism, 34 patients with hyperthyroidism, and 82 individuals as control group were considered. BMI, fasting resistin, TSH, and T4 serum levels were measured by enzyme immunoassay methods. Data were compared using <i>t</i>-test, Pearson correlation coefficient, and ANOVA to evaluate correlation between variables. <math>p &lt; 0.05</math> was considered statistically significant.</p> <p><b>Results:</b> Resistin serum levels in hypothyroidism and hyperthyroidism patients was significantly higher than the control group. There was not any significant correlation between resistin serum levels, BMI, age, and thyroid hormones level. Also in hypothyroidism patients a positive correlation was observed between BMI and TSH level, and a negative correlation between BMI and T4 level.</p> <p><b>Conclusion:</b> The result of this study showed the increase in serum level of resistin in patients with thyroid dysfunction. This correlation was independent of BMI changes in patient. The findings suggest that changing in serum level of resistin may be considered as a criterion for diagnosis of thyroid dysfunction. Although, this hypothesis needs to be more study.</p>

Copyright © 2014 Zahedan University of Medical Sciences. All rights reserved.

## Introduction

Resistin is a hormone and adipokine which is produced and secreted from adipose tissue. The molecule was discovered by Stephen et al. [1]. Resistin as a hormone has the endocrine effects including effects on obesity, insulin resistance and also plays a role in energy homeostasis. Insulin consider as inhibitor of resistin, so mRNA level of resistin is increased in insulin resistance. Resistin likely is a hormone that linking obesity to diabetes. It is a serine and cysteine rich molecule which is secreted from adipose tissue in rats and epithelial and immune cells in dogs and pigs and primates. This hormone contains 108 amino acids with a molecular weight 12.5 KDa in human [1]. Resistin gene belongs with RELM (Resistin-Like Molecules) family in mouse and human. This gene family already was discovered as FIZZES (Found Inflammatory Zone). FIZZ3 family genes are similar to resistin gene. Also resistin is well known as ADSF (Adipose Tissue-Specific Secretory Factor) [2]. Resistin gene expression is mainly in white adipose tissue, and especially in abdominal fat [1, 3].

Studies have shown that serum resistin levels are increased in obese subjects, thus reducing resistin gene expression in obesity treatment has been proposed [4].

Furthermore, genetic variation in the resistin gene is not associated with obesity and type 2 diabetes in Italian population [5] and Japanese [6]. Also it has been observed that resistin levels are not associated with insulin resistance or obesity and it is not regulated by leptin [7].

Thyroid hormones regulate the body's energy balance and have effects on adipokine level [8]. Some studies with different results on resistin concentration in patients with hyperthyroidism and hypothyroidism have been reported [9]. The study showed that resistin levels in patients with thyrotoxicosis followed treated with radioactive iodine reduced [10].

Some studies have also shown that resistin levels are increased in patients with hyperthyroidism and its concentration decreased with normalizing thyroid hormone status following treatment [11]. In one study, sera resistin levels in patients with Graves' disease decreased and on the other hand it increased in Hashimoto's and simple goiter patients [12].

In recent years the role of resistin in thyroid function has been noticed and considered by researchers. So far disagreements relation studies have been reported about resistin and thyroid disorders. This study aimed to evaluate serum resistin levels in patients with hypo and

hyperthyroidism and relation the results to weight and body mass index.

## Materials and Methods

This study was done as a cross sectional case-control study which performed on selected patients with thyroid disorders who came to endocrine clinic of Endocrinology and Metabolism Research Center, Shahid Beheshti University of Medical Sciences. The study included 82 patients, 48 persons with hypothyroidism and 34 persons with hyperthyroidism and totally 82 subjects as the control group, because of clinical and biochemical criteria for inclusion were evaluated. The sample size was based on the similar study and sample size determination formula, at least 32 patients in each group was determined. TSH levels greater than 10 mIU/L, consider as hypothyroidism criteria, and its levels less than 0.2 mIU/L was considered as hyperthyroidism status. To confirm the thyroid function status based on TSH, the amount of thyroxine determined in all subjects. In the first group T4 was less than 4 µg/dL and in the second group; it was higher than 13.5 µg/dL. All patients before entering the study were signed the informed consent form. Demographic data collection form for each of the participants in the study was completed. Anthropometric characteristics included measurement of weight and height, with a sensitivity of 100 g and 0.5 cm were obtained respectively. BMI by dividing weight (kg) by the square of height (m) was calculated too.

### Laboratory determinations

In the fasting state 3 mL of venous blood was took from the volunteers in seated position from antecubital vein of left hand. After 5 min, incubation time for coagulation, the samples were centrifuged at 3000 rpm for 10 min and the obtained sera were kept at -80°C until testing. Serum samples for measurement of serum TSH, T4 and resistin concentrations were considered.

In this study TSH levels were measured using Immuno Radio Metric Assay (IRMA) method (Turbo TSH [125 I] kit, Isotope, Hungary) and T4 concentration was determined using Radio Immuno Assay (RIA) method using the same company product (T4 RIA kit [125I] Isotope, Hungary). Serum resistin level was determined by Enzyme Linked Immuno Sorbent Assay (ELISA)

method using an ELISA kit of human resistin, (Cusabio Biotech, and Wuhan, China); the assay sensitivity was 0.16 ng/mL.

In this study, data analysis was performed by SPSS-18 software. Normal distribution of data was tested by Kolmogorov-Smirnov test. For descriptive presentations, the data are expressed as mean±standard error. Independent *t*-test for comparison among groups and Pearson's test was used for examination of relationship among groups. Simultaneous comparison of three groups' data including hyper, hypo and control subjects was done using one-way ANOVA test. Significance level was considered less than 0.05.

## Results

In this study, as mentioned before, 82 patients with thyroid disorders, 48 patients in hypothyroid group and 34 patients in hyperthyroidism participated. BMI and serum levels of hormones including resistin, TSH and T4 separately for controls and patients are shown in table 1. The obtained results showed that BMI and resistin levels in patients with hypothyroidism was significantly ( $p<0.05$ ) greater than the control group.

Data presented in table 1 showed that no significant correlation between resistin, BMI, TSH and T4 in the hypothyroid group and also control group subjects.

Mean serum level of resistin, TSH, T4 levels and body mass index were compared between cases and controls (Table 2).

The results showed that the mean BMI in patients with hyperthyroidism ( $25.11\pm 0.15$ ) was significantly lower than control ( $25.98\pm 0.18$ ) group ( $p<0.05$ ). The resistin serum levels in patients with hyperthyroidism ( $7.93\pm 0.86$ ) was significantly higher than the control ( $3.15\pm 0.16$ ) group ( $p<0.05$ ). In patients with hyperthyroidism significant correlation between serum resistin levels, BMI, serum levels of TSH and T4 were not observed. The results are shown in table 2.

## Discussion

The obtained results showed that serum resistin levels in patients with thyroid disorders including hypothyroidism and hyperthyroidism are higher than the control group.

**Table1.** Anthropometric and biochemical parameters of hypo, hyper and control groups

	Patients with hypothyroidism Mean±SD	<i>p</i> -Value	Patients with hyperthyroidism Mean±SD	<i>p</i> -Value	Control group Mean±SD
BMI (kg/m <sup>2</sup> )	27.40±0.17	0.008	25.11±0.15	0.008	25.98±0.18
TSH (µIU/mL)	14.26±1.92	0.54	0.02±0.003	0.94	2.42±0.13
T4 (µg/dL)	3.49±0.14	0.032	14.59±0.71	0.021	8.82±0.24
Resistin (ng/mL)	6.24±0.63	0.000	7.93±0.86	0.000	3.15±0.16

*t*-test used for mean comparison and statistical significant level was considered  $p<0.05$

**Table2.** Pearson's correlation coefficient of resistin, BMI, TSH and T4 among hypo, hyper thyroid and control groups

	Patients with hypothyroidism	Patients with hyperthyroidism	Control group
BMI (kg/m <sup>2</sup> )	0.15	0.22	0.08
TSH (µIU/mL)	0.07	0.04	-0.13
T4 (µg/dL)	-0.17	0.03	0.04

In this study, a significant relationship between hormones including TSH, T4, and resistin and body mass index in patients with hypothyroidism and hyperthyroidism were not observed. In general, few studies assessed the resistin levels in patients with thyroid disorders but the results of those studies differed with the present study.

A study on 43 patients with hypothyroidism showed that resistin levels are increased in these patients. After treatment with thyroid hormone and normalization of thyroid hormones level, resistin levels are also reduced. In mentioned study, there was no relation among resistin levels with weight, fat mass, and waist circumference and body mass index before and after treatment [11].

Other research suggested resistin levels positively correlated with FT4 and FT3 but TSH levels were negatively correlated [13]. In a study mentioned that resistin level regulated by thyroid hormone, it was shown that resistin levels in patients with hypothyroidism increased and conversely, in patients with hyperthyroidism resistin levels decreased. Also an increased resistin level in obese patients has been reported. In animal studies, injection of antibodies against to resistin decreases insulin resistance in obese mice and improved blood sugar and insulin function [14].

However, another report on 76 patients and 30 controls showed that serum resistin levels are no different in patients with hyperthyroidism and controls [15]. This result is similar to our study, no significant correlation between levels of thyroid hormones and resistin in patients with hyperthyroidism has been reported.

Also another report titled resistin levels in patients with hypothyroidism showed that resistin concentrations in the control group were similar to hypothyroidism group and the thyroid hormone and resistin had not relationship [16]. In this study, the correlation between resistin level and

thyroid hormones in patients with hypothyroid was not seen.

Little information on the effects of weight reduction on the regulation of resistin levels is achieved. Recent studies have shown that energy restriction and weight loss has no associated with changes in resistin levels in healthy individuals with normal weight [17]. These results are similar to results of studies in obese subjects with insulin resistance who participated in a behavior modification program for weight loss [18].

In summary, the results of this study suggests that serum resistin is likely to be consider as a confirmation extra test for the diagnosis of thyroid disorders including hypothyroidism and hyperthyroidism in patients probably. Thus, the measurement of resistin, possibly can prevent the false diagnosis of thyroid assessment and maybe offer more effective interventions to improve patient care and the economy aspect.

### Acknowledgements

We are indebted to kind collaboration of several endocrinology specialists. We express our gratitude to the staff of research laboratory at Endocrine Research Center, for their skillful technical assistance.

### Authors' Contributions

All authors had almost equal role in design, work, statistical analysis and manuscript writing.

### Conflict of Interest

The authors declare no conflict of interest.

### Funding/Support

This study was supported by the authors and performed in Research institute for endocrine sciences, Shahid Beheshti University of Medical Sciences.

### References

1. Steppan CM, Bailey ST, Bhat S, et al. The hormone resistin links obesity to diabetes. *Nature*. 2001; 409(6818): 307-12.
2. Degawa-Yamauchi M, Bovenkerk JE, Juliar BE, et al. Serum resistin (FIZZ3) protein is increased in obese humans. *J Clin Endocrinol Metab*. 2003; 88(11): 5452-5.
3. McTernan CL, McTernan PG, Harte AL, et al. Resistin, central obesity, and type 2 diabetes. *Lancet*. 2002; 359(9300): 46-7.
4. Ukkola O. Resistin-a mediator of obesity-associated insulin resistance or an innocent bystander? *Eur J Endocrinol*. 2002; 147(5): 571-4.
5. Sentinelli F, Romeo S, Arca M, et al. Human resistin gene, obesity, and type 2 diabetes: Mutation analysis and population study. *Diabetes*. 2002; 51(3): 860-2.
6. Osawa H, Onuma H, Murakami A, et al. Systematic search for single nucleotide polymorphisms in the resistin gene: The absence of evidence for the association of three identified single nucleotide polymorphisms with Japanese type 2 diabetes. *Diabetes*. 2002; 51(3): 863-6.
7. Lee JH, Chan JL, Yiannakouris N, et al. Circulating resistin levels are not associated with obesity or insulin resistance in humans and are not regulated by fasting or leptin administration: Cross-sectional and interventional studies in normal, insulin resistant, and diabetic subjects. *J Clin Endocrinol Metab*. 2003; 88(10): 4848-56.
8. Luvizotto RA, Sfibio MT, Olímpio RM, et al. Supraphysiological triiodothyronine doses diminish leptin and adiponectin gene expression, but do not alter resistin expression in calorie restricted obese rats. *Horm Metab Res*. 2011; 43(7): 452-7.
9. Iglesias P, Alvarez-Fidalgo P, Codoceo R and Diez JJ. Serum concentrations of adipocytokines in patients with hyperthyroidism and hypothyroidism before and after control of thyroid function. *Clin Endocrinol (Oxf)*. 2003; 59(5): 621-9.
10. Yatura S, Prado S, Grimes SR. Changes in adipocyte hormones leptin, resistin, and adiponectin in thyroid dysfunction. *J Cell Biochem*. 2004; 93(3): 491-6.
11. Krassas GE, Pontikides N, Loustis K, et al. Resistin level in hyperthyroid patients before and after restoration of thyroid function. *Eur J Endocrinol*. 2005; 153(2): 217-21.
12. Bossowski A, Sawicka B, Szalecki M, et al. Analysis of serum adiponectin, resistin and leptin levels in children and adolescents with autoimmune thyroid disorders. *J Pediatr Endocrinol Metab*. 2010; 23(4): 369-77.

13. Yaturu S, Prado S, Grimes SR. Changes in adipocyte hormones leptin, resistin, and adiponectin in thyroid dysfunction. *J Cell Biochem.* 2004; 93(3): 491-6.
14. Monzillo LU, Hamdy O, Horton ES, et al. Effect of lifestyle modification on adipokine level in obese subjects with insulin resistance. *Obes Res.* 2003; 11(9): 1048-1054.
15. Sieminska L, Niedziolka D, Pillich A, et al. Serum concentrations of adiponectin and resistin in hyperthyroid Graves' disease patients. *J Endocrinol Invest.* 2008; 31(9): 745-9.
16. Guldiken S, Demir M, Arıkan E, editors. Adipokines in patients with overt hypothyroidism and subclinical hypothyroidism. Philadelphia: Lippincott Williams and Wilkins; 2008.
17. Nogueiras R, Gualillo O, Caminos JE, et al. Regulation of resistin by gonadal, thyroid hormone, and nutritional status. *Obes Res.* 2003; 11(3): 408-14.
18. Wolfe BE, Jimerson DC, Orlova C and Mantzoros CS. Effect of dieting on plasma leptin, soluble leptin receptor, adiponectin and resistin level in healthy volunteers. *Clin Endocrinol (Oxf).* 2004; 61(3): 332-8.

**Please cite this article as:** Hedayati M, Shabani S, Frazndemehr M, Zarif-Yeganeh M, Hoghooghırad L. Serum level of resistin in patients with hyperthyroidism and hypothyroidism. *Zahedan J Res Med Sci.* 2014; 16(11): 1-4.