Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(4D):1487-1491 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2017.v05i04.050

Original Research Article

Study of Fasting Plasma Insulin Levels and Insulin Resistance Index in the Patients of Thyroid Disorders

Sharma Vanita*[1], Walia Harpreet Kaur[1], Sah Narendra Kumar[3], Singh Amandeep[1], Kaur Kiranjeet[2], Singh Kamaljit[2]

[1]Assistant Professor, Maharishi Markandeshwar Medical College & Hospital, Kumarhatti, Solan, H.P
[2] Professor, Maharishi Markandeshwar Medical College & Hospital, Kumarhatti, Solan, H.P.
[3]Demonstrator, Maharishi Markandeshwar Medical College & Hospital, Kumarhatti, Solan, H.P

***Corresponding author**
Vanita Sharma
Email: svanita35@gmail.com

Abstract: Thyroid disorder, second most common endocrine disorder after diabetes mellitus results from the alteration in Hypothalamic-Pituitary-thyroid gland axis, affecting intermediary metabolism, insulin resistance and lipid profile. The present study is designed to compare the fasting plasma insulin level among patients of thyroid disorders and to study the insulin resistance index among such patients. 50 diagnosed patients with thyroid disorders were included in the present study with 30 age and sex matched healthy controls. Serum thyroid - stimulating hormones (TSH), total tri iodo thyronine (T3), total thyroxine (T4), fasting plasma insulin were measured by Enzyme-linked immune sorbent assay (ELISA) techniques. The insulin resistance index was measured using the homeostasis model assessment (HOMA). Mean fasting plasma insulin levels in hypothyroid patients were found to be 10-40 µIU/ml as compared to control (2-9 µIU/ml). It indicated the significant increase of fasting plasma insulin levels in hypothyroid as compared to control group ($p < 0.001$). Insulin resistance index in hypothyroid patients ranged from 1.53-7.88 as compared to control group (0.43-2.08). Mean fasting plasma insulin levels in hyperthyroid patients were found to be 11-38 µIU/ml as compared to control (2-9 µIU/ml). It emphasized that the mean fasting plasma insulin levels in hyperthyroid patients were significantly increased as compared to control ($p<0.001$). The Insulin resistance index in hyperthyroid patients ranged from 2.11-7.50 as compared to control (0.43-2.08). It is concluded that hypothyroidism and hyperthyroidism have increased plasma insulin due to metabolic actions of thyroid hormones on insulin sensitive organs (skeletal muscle and adipose tissue) and also liver. Both hyper- and hypothyroidism are believed to cause insulin resistant states through insulin receptor and post-receptor defects. Therefore, all diabetic patients should be screened for thyroid dysfunction because correcting thyroid disorders can profoundly affect glucose homeostasis that will provide a better ideology towards the management of diabetes mellitus.

Keywords: Hypothyroidism, Hyperthyroidism, Plasma insulin, Insulin Resistance, Thyroid hormones

INTRODUCTION

Diseases of thyroid gland are amongst the most abundant endocrine disorder in the world second only to diabetes mellitus [1]. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment and the relative visibility that even a small swelling of the thyroid offers to the treating physician. Early diagnosis and treatment remains the cornerstone of management [2]. Imbalance in production of thyroid hormones arises from dysfunction of the Hypothalamo-pituitary-thyroid gland axis. [3]. Insulin resistance **(**IR) indicates the presence of an impaired peripheral tissue response to endogenously secreted insulin. It is typically manifested as both decreased insulin-mediated glucose uptake (IMGU) at the level of adipose and skeletal muscle (SM) tissue and as an impaired suppression of hepatic glucose output [4-6]. Thus, impaired glucose utilization by insulin sensitive tissues and increase hepatic glucose output, contribute to hyperglycemia. Insulin resistance is relative, since supernormal levels of circulating insulin will normalize the plasma glucose. Increased hepatic glucose output predominantly accounts for increased

fasting plasma glucose levels, whereas decrease peripheral glucose usage results in postprandial hyperglycemia [7]. Thyroid hormones (TH) play an important role in regulating energy balance, metabolism of glucose and lipids [8]. Thyroid abnormalities (hyperthyroid and hypothyroid) are accompanied by changes in intermediary metabolism including alterations in body weight, insulin resistance and lipid profile [9,10]. The present study was conducted with an aim to estimate the plasma insulin levels in patients of thyroid disorders, to study the insulin resistance index in such patients and to compare the parameters with healthy controls.

MATERIAL AND METHODS

The present study was conducted on 50 clinically confirmed cases of thyroid diseases attending the OPD and indoor of Department of Medicine of Rajindra Hospital, Patiala. Patients in study group were divided into two groups according to diagnosis: 50 patients with thyroid disorders (Hyper- and Hypothyroidism) and 30 age and sex matched healthy controls. Subsequent investigations were carried out in Biochemistry Department of Government Medical College, Patiala. Written consent was obtained from all patients and controls and approval of Institutional Ethics Committee was also obtained. Known cases of diabetes mellitus, obese patients, patients with history of steroid use and patients with any infection/illness were excluded in the study.

All the patients were subjected to routine investigations like Hemoglobin, Total leukocyte count(TLC), Differential leukocyte count (DLC), Blood urea, Serum Creatinine, Aspartate transaminase (AST), Alanine transaminase (ALT), Fasting plasma glucose and special investigations like Plasma insulin, Serum TSH, total T_3 & T_4 by ELISA technique [11-14]. Evaluation of insulin resistance index was done using the homeostasis model assessment (HOMA). HOMA was first described by Matthews *et al.;* in 1985 [15].

$$\text{Insulin Resistance index} = \frac{\text{Fasting plasma glucose (mmol/L)}}{\text{Fasting plasma insulin (}\mu\text{IU/ml)}} \times 22.5$$

RESULTS AND DISCUSSION:

In the present study, the sex-wise distribution in study group is as: 44(88%) were females and 6(12%) were males. This preponderance could be explained on the basis of more prevalence of thyroid disorders in female. Maximum number of patients i.e., 25 (50%) had history of duration of thyroid disorders as 1-4 years. According to the diagnosis basis, patients were divided into two groups –Hypothyroidism and Hyperthyroidism [Table 1] Majority were hypothyroid (80%) patients as there is more prevalence of hypothyroidism.

Table 1: Showing distribution of patients according to diagnosis.

Diagnosis	No. of Patients	% age
Hypothyroidism	40	80
Hyperthyroidism	10	20

Mean value of fasting plasma glucose was 80.4 ± 8.3 (mg %) and 82.7 ± 9.9 (mg %) in the hypothyroid patients and control group respectively. Also, Mean value of fasting plasma glucose was 86.0 ± 6.3 (mg %) and 82.7 ± 9.9 (mg %) in the hyperthyroid patients and control group respectively. [Table 2 & 3]

Table 2: Comparison of fasting plasma glucose in hypothyroid patients and control group

Parameter	Group	Range (mg %)	Mean ± SD	P Value
Fasting plasma glucose	Hypothyroid	62-98	80.4±8.3	0.298 Non-Significant
	Control	62-98	82.7±9.9	

Table 3: Comparison of fasting plasma glucose in hyperthyroid patients and control group

Parameter	Group	Range (mg %)	Mean ± SD (mg %)	P Value
Fasting plasma glucose	Hyperthyroid	78-98	86.0±6.3	0.331 Non-Significant
	Control	62-98	82.7±9.9	

The mean value of fasting plasma insulin in hypothyroid patients was 21.07 ± 8.4 μIU/ml, whereas in control group, the mean was 6.26 ± 1.76 μIU/ml. Thus, the increase in plasma insulin in patients group was highly significant ($p<0.001$) as compared to control. Mean value of Insulin resistance index in hypothyroid patients was 4.15 ±1.61, whereas in control group the mean was 1.26 ± 0.38. [Table 4]

Table 4: Comparison of fasting plasma insulin in hypothyroid patients and control group

Hormone/Parameter	Group	Mean ± SD (IU/ml)	P Value
Plasma Insulin	Hypothyroid	21.07 ± 8.4	<0.001 Highly Significant
	Control	6.26 ± 1.76	
Insulin Resistance Index	Hypothyroid	4.15 ± 1.61	<0.001 Highly Significant
	Control	1.26 ± 0.38	

Thus, the increase in insulin resistance index in hypothyroid patients was highly significant ($p<0.001$) as compared to control. This is due to the fact that thyroid hormones exert both insulin agonistic and antagonistic actions in different organs. Thyroid hormones have insulin antagonistic action on the liver [16]. At peripheral tissues, thyroid hormones have been shown to exert some of their actions synergistically with insulin. Thyroid hormones up regulate the expression of genes such as GLUT-4 and phosphoglycerate kinase, involving glucose transport and glycolysis respectively, and act synergistically with insulin in facilitating glucose disposal and utilization in peripheral tissues. In hypothyroidism, insulin resistance in peripheral tissues cause increase demand of β-cells implying a hyperinsulinemia state. In some study, it was found that IR also causes the diminished blood flow in adipose tissue and skeletal muscle in hypothyroidism [17-19]. There are some predisposing factors like role of adipokines, increased expressions of carnitine palmitoyl transferases on skeletal muscles, decreased plasma NEFA levels of muscle and adipose tissue that contribute to insulin resistance state in hypothyroidism [20]. Also, the decreased insulin responsiveness in hypothyroidism includes a dysregulation of leptin action at the hypothalamus as indicated in the study [21].

Mean value of fasting plasma insulin in the hyperthyroid patients was 22.9 ±7.5 μIU/ml, whereas in control group the mean was 6.26 ± 1.76 μIU/ml. The increase in plasma insulin was highly significant ($p<0.001$) as compared to control. The mean value of Insulin resistance index in hyperthyroid patients was 4.85 ±1.54, whereas in control group the mean was 1.26±0.38 [Table 5].

Table 5: Comparison of fasting plasma insulin in hyperthyroid patients and control group

Hormone/Parameter	Group	Mean±SD (μIU/ml)	P Value
Plasma Insulin	Hyperthyroid	22.9±7.5	<0.001 Highly Significant
	Control	6.26±1.76	
Insulin Resistance Index	Hyperthyroid	4.85 ±1.54	<0.001 Highly Significant
	Control	1.26±0.38	

Thyroid hormones oppose the action of insulin and stimulate hepatic gluconeogenesis and glycogenolysis. Therefore, there is hyperinsulinemia in hyperthyroidism. The increase in peripheral insulin resistance in hyperthyroidism may be explained due to increased secretion of bioactive mediators (adipokines) such as interleukin 6 (IL6) and tumor necrosis factor a (TNFα) from adipose tissue. Therefore, in hyperthyroidism, insulin resistance ultimately leads to hyperinsulinemia [22].

CONCLUSIONS

It is concluded from the present study that fasting plasma insulin and insulin resistance index are significantly increased in hypothyroid and hyperthyroid patients. Thyroid disorders, including both hypothyroidism and hyperthyroidism have been associated with altered glucose homeostasis and insulin metabolism, involving defective insulin secretion in response to glucose, hyperinsulinemia, altered glucose disposal and insulin resistance. The thyroid disorders, Hypo- and hyperthyroidism cause to affect metabolic functions of insulin-sensitive target tissues like skeletal muscles, adipose tissue and liver itself, thus increasing plasma insulin, and through alteration in receptor and post-receptor signaling corresponds to insulin resistance states.

In the light of above findings, it is strongly advised to screen for thyroid dysfunction in clinical practice and hormone mediated glucose homeostasis so that it would help the clinicians for better management of the patients of thyroid disorders and diabetes mellitus also.

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