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Research Article

The Relationship between Functional Status and Insulin Resistance in Patients with Pituitary Adenoma

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Abstract

Objective: Pituitary adenomas (HA) are diagnosed by radiological imaging or by evaluating the hormonal activity of the pituitary incidentaloma in order to investigate the signs and symptoms that are thought to be related to the compression of a mass in the pituitary gland. The increase in the use of pituitary imaging modalities and the frequency of detection of pituitary incidentaloma have also increased. In this study, we aimed to investigate demographic features, functional status and insulin resistance of patients with pituitary adenoma.

Methods: The study included 88 patients (60 females, 28 males) who were followed for pituitary adenoma between the years of 2016 - 2018. Patients' physical examination, pituitary MR results, FSH, LH, estradiol, Testosterone, ACTH, cortisol, Growth hormone, Igf-1, prolactin results were recorded. 1 mg dexamethasone test was performed in appropriate patients. Insulin resistance was calculated according to the homeostatic model assessment- insulin resistance (HOMA-IR) formula of patients with fasting blood glucose and insulin values.

Results: The mean age of the patients was 36.2 (min: 18-max: 68). 54 patients had prolactinoma, 20 had nonfunctional adenoma and 11 had acromegaly and 3 had cushing. Of all patients, 41 had HOMA-IR < 2.5 and 47 had ≥ 2.5. The most frequent insulin resistance among the groups was found to be significantly higher in patients with acromegaly (81.8%).

Conclusion: Insulin resistance was high especially in acromegalic patients. This is probably due to the effect of Igf-1 on peripheral tissues. Acromegalic patients should be evaluated in this respect because they are risky for metabolic diseases.

Keywords: *Pituitary Adenoma; Insulin Resistance; Acromegaly*

Introduction

Pituitary adenomas are classified as microadenoma/macroadenoma according to their size or functional/nonfunctional according to hormone status. In functional adenomas (23%), prolactinoma was the most common (18%), somatotropinoma was the second (3%) and the others (2%) were rare. In recent years, it has been shown to be Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) positive adenoma as a result of immunohistochemical staining in adenomas which are hormone negative. Genetic factors, fetal malnutrition, physical inactivity, obesity, and progression of age cause insulin resistance. Insulin resistance is seen in 25% in healthy population, 60% in impaired glucose tolerance and 60 - 75% in patients with type 2 DM. The most commonly used method in clinical practice is the HOMA-IR formula. Insulin resistance and metabolic complications have been frequently reported in patients with cushing especially in pituitary diseases [1-7].

Aim of the Study

The aim of this study was to investigate the presence of insulin resistance in patients with pituitary adenoma.

Materials and Methods

The study included 88 patients (60 females, 28 males) who were followed for pituitary adenoma between the years of 2016 - 2018. Patients' physical examination, pituitary Magnetic Resonance Imaging (MRI) results, FSH, LH, estradiol, Testosterone, Adrenocorticotropic Hormone (ACTH), cortisol, Growth hormone, 'insulin-like growth factor 1 (Igf-1), prolactin results were recorded. 1 mg dexamethasone test was performed in appropriate patients. Insulin resistance was calculated according to the homeostatic model assessment- insulin resistance (HOMA-IR) formula of patients with fasting blood glucose and insulin values.

Results

The mean age of the all patients was 36.2 (min: 18-max: 68). The mean age of the patients with non-functional adenoma was 41.7 years (min: 18-max: 68); 7 (33.3%) were males and 13 (61.9%) were females. In 10 patients, homa-ir was < 2.5, while 10 patients had a homa-ir value of ≥ 2.5. The mean age of patients with acromegaly was 46.1 years (min: 33-max: 64); 6 (54.5%) were males and 5 (45.5%) were females. In 2 patients, homa-ir was < 2.5, while 9 patients had homa-ir value of ≥ 2.5. The mean age of the 3 female patients with Cushing disease was 33.3 years(min: 18-max: 48). The mean age of patients with prolactinoma was 32.3 years (min: 19-max: 60); 15 (33.3%) were males and 39 (61.9%) were females. In 27 patients, homa-ir was < 2.5, while 27 patients had homa-ir value of ≥ 2.5.

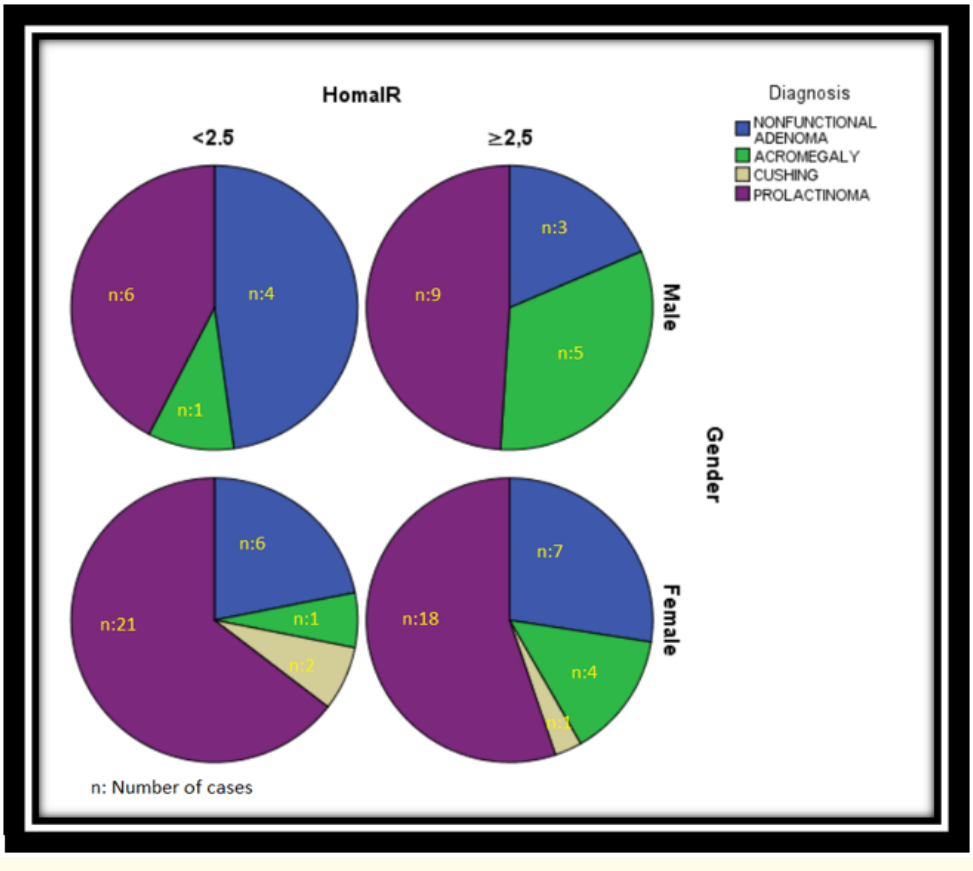

Figure 1: *Insulin resistance by gender in pituitary adenoma cases.*

Diagnosis	HOMA-IR	
	< 2.5 (n)	≥ 2.5 (n)
Nonfunctional adenoma	10	10
Acromegaly	2	9
Cushing	2	1
Prolactinoma	27	27

Table 1: *Insulin resistance in patients with pituitary adenoma.*

Discussion

Insulin resistance; defined as reduced response to insulin at normal concentration in the circulation. The term insulin resistance was introduced in 1922 by the introduction of insulin in some patients when hypersensitivity was required to correct hyperglycemia in some patients. For the first time, Himsworth and Carr used the term insulin insensitivity in 1936 to identify this condition in obese diabetics, which is characterized by insufficient glycemic response to exogenous insulin. Numerous studies to date have increased the importance of insulin resistance in terms of investigating the relationship with metabolic diseases [8]. The hypothalamic-pituitary-adrenal (HPA) axis is an important center of response to stress. In stress situations, glucocorticoid production occurs from the adrenal cortex by activation of this axis. The prolonged glucocorticoid excess is associated with insulin resistance (IR), leading to metabolic disorders [9,10]. In this study, insulin resistance was found in 33% of patients with chronic glucocorticoid exposure. However, patients with acromegaly had significantly higher insulin resistance than other pituitary adenomas. It also increases cardiovascular risk which is the most important cause of mortality as a result of disorders of glucose metabolism in patients with acromegaly. While growth hormone (GH) excess causes insulin resistance, deficiency can lead to an increase in insulin sensitivity. While acute exposure to GH may lead to insulin-like effects, excess of chronic GH causes insulin resistance. Acromegaly patients develop insulin resistance in the liver and peripheral tissues as a result of exposure to chronic growth hormone. Previous studies have shown that metabolic disorders are ameliorated by surgical removal of GH-secreting pituitary adenomas [11,12]. However, even though growth hormone is suppressed with peripheral insulin resistance after chronic GH exposure in acromegalic patients, insulin secretion does not improve on the basis of increased pancreas beta cell mass hypothesis [13].

Sonksen*., et al.* [11] observed that they were hyperinsulinemic in patients with acromegaly in the early period, and they observed normal glucose levels with rapid and higher insulin peaks in the glucose tolerance test. After this period, insulin response is reduced in those who are exposed to growth hormone (GH) exposure in the next stage. At the end of this period, impaired insulin response begins in patients with acromegaly. Muggeo., *et al*. [14,15] reported that when it examined insulin receptors on monocytes in acromegalic patients, they decreased in proportion to hyperinsulinemia.. Acromegalic patients were found to have down regulation in insulin receptors despite hyperinsulinemia. Some authors have explained the decrease in the use of glucose in peripheral tissues despite the hyperinsulin by post-receptor defect of insulin [16,17].

Conclusions

In acromegalic patients, an increased exacerbation of fasting insulin concentrations and an exaggerated insulin response to glucose overload are prominent. Insulin levels decrease and fasting hyperglycemia can occur in untreated cases and may cause metabolic disorders. Therefore, in patients with acromegaly, glucose metabolism should be carefully evaluated and treated.

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