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Research Article / Araştırma Makalesi

# *Investigation of Ghrelin and Leptin Value in Obese and Non-obese Cats*

*Obez ve Obez Olmayan Kedilerde Ghrelin ve Leptin Hormonlarının Araştırılması*

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**Abstract:** Obesity is the deterioration of metabolic and physiological functions due to excessive accumulation of fat in the body. Leptin and ghrelin are two hormones involved in energy balance. There is still not enough information about these two hormones and there is very little research investigating their connection with obesity. The aim of this study was to investigate of leptin and ghrelin hormones in obese and non-obese cats. In this study, 20 cats were evaluated with the body fat measurement system in cats. Those with body fat ratio above 30% were considered obese (Group 1, n=10), those below 30% were considered as the control group (Group 2, n=10). Serum leptin (p=0.05) and ghrelin (p=0.001) values were determined in cats in both groups, and statistically significant differences were observed. A statistical difference was determined in ALT and calcium values (p< 0.001). No statistical difference was found in BUN, creatinine, total bilirubin and hematological values between obese cats and the control group. As a result, it was determined that leptin and ghrelin hormones play an important role in obesity.

**Keywords:** Leptin, Ghrelin, Obesity, Cat.

**Öz:** Obezite, vücutta fazla miktarda yağ birikmesine bağlı olarak metabolik ve fizyolojik fonksiyonlarının bozulmasıdır. Leptin ve ghrelin enerji dengesini ile ilgili iki hormondur. Bu iki hormon hakkında hala yeterince bilgi yoktur ve obezite ile bağlantısını araştıran araştırmalar çok azdır. Bu çalışmanın amacı obez ve obez olmayan kedilerde leptin ve ghrelin hormonlarını araştırmaktır. Çalışmada kedilerde vücut yağ ölçüm sistemiyle 20 kedi değerlendirildi. Vücut yağ oranı, %30'un üzerinde olanlar obez (Grup 1, n=10) olarak değerlendirildi, %30'un altında olanlar ise kontrol grubu (Grup 2, n=10) olarak değerlendirildi. Her iki grupta olan kedilerde serum leptin (p=0,05) ve ghrelin p=0,001) değerleri belirlendi ve istatiksel olarak anlamlı farklılıklar gözlendi. ALT ve kalsiyum değerlerinde (p< 0,001) istatistiksel farklılık belirlendi. Obez kediler ile kontrol grubu arasında BUN, kreatinin, total bilirubin ve hematolojik değerler açısından istatistiksel bir fark bulunamadı. Sonuç olarak obezitede leptin ve ghrelin hormonları önemli rol oynadıkları saptandı.

**Anahtar Kelimeler:** Leptin, Ghrelin, Obezite, Kedi.

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## Introduction

Obesity is often the result of excessive dietary intake or inadequate energy use, resulting in a state of positive energy balance (German, 2006). Many factors can predispose a cat to obesity, including genetics, the amount of physical activity and the energy content of the diet (German, 2006). Obesity is generally defined as a body fat percentage above 30%, and normal cats are expected to have between 10% and 30% body fat percentage (Hoelmkjaer and Bjornvad, 2014).

In 1999, Japanese scientists discovered the gastrointestinal peptide hormone ghrelin as the endogenous ligand for growth hormone receptor (GHR)1a, which can stimulate the release of growth hormone (GH) from the anterior pituitary gland. Ghrelin was found to modulate systemic metabolism through activation of orexigenic neural circuits. It is a 28 amino acid lipopeptide



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hormone secreted from tissues and organs such as the hypothalamus, pituitary, thyroid gland, salivary gland, small intestine, kidney, heart, pancreas, lung, placenta, gonads, immune system, breast, mainly from the fundus of the stomach. Ghrelin is also known as the apetite hormone (Müller et al., 2015). In adult mammals, ghrelin is most densely released from gastric tissue (Bang et al., 2007). It is suggested that ghrelin acts as a meal initiation or hunger hormone, signaling gastrointestinal (GI) fuel status to the central nervous system (CNS) to regulate food intake and energy (Kojima and Kangawa, 2005).

Ghrelin in metabolism, food intake and body weight plays an important role in regulation. Therefore, ghrelin may be a potential drug target for body weight regulation. Ghrelin levels are inversely proportional to energy stores and increase with weight loss in response to body weight changes and decrease with weight gain. Circulating ghrelin levels decrease with obesity, but when obese individuals lose weight, ghrelin levels increase to tolerate this weight loss (İlhan and Erdost, 2009).

The peptide hormone leptin plays a role in regulating food intake, body mass, reproductive function, fetal growth, proinflammatory immune responses, angigonesis, and lipolysis. Leptin is a product of the obese gene. Following the synthesis and secretion of fat cells in white adipose tissue, it binds to and activates the leptin receptor (LEP-R) (Obradovic et al., 2021). Feline leptin is partially protein bound in the circulation. As with other species, circulating leptin primarily reflects body fat mass in cats, and weight loss is associated with decreased peripheral blood leptin levels. Leptin levels are slightly increased during feeding compared to the fasting state (Backus et al., 2000).

The aim of this study is to determine the changes in the values of leptin and ghrelin hormones in obese and non-obese cats.

## Materials and Methods

### *Animal Material*

The research material consisted of 20 cats of both sexes and different breeds, aged between 1 and 11 years. The groups were divided into two as control (10) and obese (10). Ten of the blood samples were collected from obese cats with a body fat percentage above 30% (obese) and 10 from non-obese cats with a body fat percentage below 30% (control) according to the body fat measurement system. There are cats of different breeds, 4 of which are infertile females and 6 of which are male sterile, with ages ranging from 5 to 10 years in the obese group. The control group consisted of 10 cats with ideal weight over 1 year old. According to the body fat measurement system, the groups were divided into two as obese cats with a body fat percentage above 30% (Group 1, n=10) and as control non-obese cats with a body fat percentage below 30% (Group 2, n=10).

### *Methods*

During the study, the weight, chest circumference and leg lengths of all cats were measured and their body mass indexes were calculated. Those with a body mass index greater than 7 were considered obese. A total of 5 cc blood was collected from all cats for haematological and biochemical examination. The collected blood was centrifuged at 4000 rpm for 10 minutes. The obtained sera were separated and stored in a -20°C freezer until used as aliquots.

### *Body Fat Measurement System*

.Rib cage value: 9. Rib cage circumference passing over rib

.Leg index value: Distance between patella and calcaneal rump

.The body fat ratio of cats with ideal weight is between 15%-30%,

.Those who are considered extremely thin and have less than 20% fat,



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Those who are overweight or obese are considered as cats with a body fat ratio of 30% or more.

***Ghrelin and Leptin Test Protocol***

Ghrelin enzyme was measured by ELISA (Enzyme-Linked Immunosorbent Assay) method. Cat Ghrelin ELISA kit (Bioassay Technology Laboratory Cat Ghrelin BT-LAB Kit Cat. NO. E0117CAT LOT 202202009) and cat Leptin ELISA kit (Bioassay Technology LaboratoryCat Leptin BT-LAB Kit Cat. No. E0079Cat LOT 202202009) were used in the study. Procedures were performed according to the kits procedure. In this study, all samples were taken in the morning after a 2-hour fast to minimize the effects of daily ghrelin dynamics.

***Statistical analysis:*** IBM SPSS 26.0 for Windows package program was used to evaluate the study data. The normal distribution of the groups in the analyzes was evaluated using the Shapiro-Wilk test. Due to the normal distribution of the data, between measurements Paired t-test was used for comparisons. Pearson Correlation analysis was used to determine the relationship between variables. p value <0.05 was considered statistically significant.

**Results**

In obese cats (Group1), compared to the control group (Group2), decreased leptin value (p< 0,05), increased ghrelin, glucose, ALT, calcium values (p< 0.001) and statistical difference was determined. No statistical difference was found between the obese cats and the control group in terms of BUN, creatinine, and total bilirubin values (Table 1).

No statistically significant difference was found between obese cats and control group in terms of WBC, RBC, PLT, NEU, HGB, HCT values in hematological findings (Table 2).

**Table 1. Leptin, ghrelin and some other biochemical findings in obese and control groups.**

| | **Group 1** ***(n=10)*** $\bar{x} \pm ss$ | **Group 2** ***(n=10)*** $\bar{x} \pm ss$ | ***p*** |
|---|---|---|---|
| **Leptin (ng/ml)** | 2,03±,45 | 4,54±2,46 | 0,05 |
| **Ghrelin (ng/L)** | 440,49±305,12 | 35,07±20,05 | 0,001 |
| **Glucose (mg/dl)** | 215,00±34,18 | 165,70±21,17 | <0,001 |
| **ALT (U/L)** | 168,00±53,53 | 52,20±7,29 | <0,001 |
| **ALP (U/L)** | 41,20± 5,11 | 37,20±2,29 | 0,43 |
| **BUN (mg/dl)** | 20,50±3,53 | 19,50±3,56 | 0,470 |
| **Creatinine (mg/dl)** | 1,02±15 | 1,02±,0.96 | 1,00 |
| **Ca (mg/ml)** | 15,47±3,51 | 9,71±0,85 | <0,001 |
| **T.Bil (mg/dl)** | 20±,02 | 20±,01 | 0.108 |

**Table 2. Hematological findings in cats in the obese and control groups.**

| | **Group 1** ***(n=10)*** $\bar{x} \pm ss$ | **Group 2** ***(n=10)*** $\bar{x} \pm ss$ | ***p*** |
|---|---|---|---|
| **WBC (0^9/L)** | 12,06±2,41 | 11,70±3,82 | 0,805 |
| **RBC (0^12/L)** | 9,08±2,07 | 9,02±3,10 | 0,963 |
| **PLT (0^9/L)** | 154,80±63,42 | 153,10±70,70 | 0,955 |
| **NEU (10^9/L)** | 7,34±1,34 | 7,55±2,46 | 0,813 |
| **HGB (g/dl)** | 11,51±,2,87 | 10,59±,1,36 | 0,375 |
| **HCT (%)** | 0,399±0,41 | 0,399±0,47 | 0,680 |



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**Discussion**

Obesity is multifactorial nutritional disorder in pets. Many factors can predispose a cat to obesity, including genetics, the amount of physical activity and the energy content of the diet (German, 2006). The causes of obesity are not clear as there are many different variables that play a role in its development (Speakman, 2004).

Leptin and ghrelin are two hormones that maintain energy homeostasis. As an anorexigenic hormone, leptin is a means of long-term regulation of energy balance (Yalçın et al., 2017). Ghrelin and cholecystokinin in the short-term hormonal regulation of eating; Insulin, leptin and peptide YY are effective in long-term hormonal regulation. Leptin, a prototypical adipoquinolan, is the best-characterized of the adipokines for cats and dogs (Zoran, 2019). Leptin is an important regulator of fat mass, and its concentration in serum is positively correlated with fat mass (Hoenig et al., 2007).

In this study, in the serum analyzes collected after a 2-hour fasting in the morning in obese and normal body condition cats of different ages and genders, were decrease in leptin levels in obese cats, while in levels of ghrelin, glucose, alt and calcium an increase was observed. Leptin is positively correlated with body fat mass. It is a strong marker in obese cats. In parallel with the increase and decrease in leptin in the development and recovery phases of obesity, physiological increases and decreases in the vascularity of adipose tissue have been determined. This suggested that leptin acts as a local regulator of angiogenesis. (Crandall et al., 1997). Obesity occurs in the absence of leptin and high leptin levels(Auwerx and Staels, 1998). Decreased leptin production in adipocytes leads to the development of obesity (Friedman and Halaas, 1998). It has been known since 1997 that congenital leptin deficiency causes obesity in humans (Montague et al., 1997). The decrease in leptin in our study suggests that obese cats' congenital leptin deficiency and preference for diet food may be associated with weight loss processes and exercise before coming to the clinic. Appleton et al (2000) reported in their study that weight loss was associated with a decrease in leptin levels (Fried et al., 2000). In addition, it should be kept in mind that leptin secretion peaks between 00:00 and 4:00 hours due to its diurnal rhythm and is lowest between 8:00 and 12:00 hours, decreases in prolonged fasting and increases in overfeeding (Wallace, 2000). Ghrelin, an orexigenic hormone plays a role in the initiation of food intake (Yalçın et al., 2017). Orexigenic activation of ghrelin is regulated by neurons in the hypothalamus that harbor specific receptors. Ghrelin is a versatile metabolism regulator (Öztürk and Arpacı, 2008).

Leptin is known to have an effect on circulating ghrelin levels. Tschop et al. (2001) showed that fasting plasma ghrelin levels were negatively correlated with fasting plasma leptin levels in obese humans. However, in another study, fasting plasma leptin and ghrelin concentrations were not negatively correlated in obese children and adolescents (Ikezaki et al., 2002). Diabetes can be predicted to develop when the liver finally becomes insulin resistant and/or insulin secretion is too low to handle the increased glucose production (Hoenig, 2012). It can be difficult to discern possible causes of hyperglycemia in the cat.

Opitz (1990) found transient hyperglycemia in 320 cats in his study. The frequency and degree of stress hyperglycemia has been proven to be associated with different types of primary disease. Including animals with diabetes mellitus or pancreatic disease in this study; A glucose concentration equal to or greater than 140mg/dl (7.77mmol/l) in fasted animals was defined as hyperglycemia. Martin et al. (2010) showed that obese cats have higher glucose concentrations than lean cats in a study they conducted. In our study, the serum glucose levels of obese cats were found to be significantly higher than those of non-obese cats.

Hepatic circulatory disorders have been associated with obesity and fatty liver in humans. However, there is limited information in the veterinary literature regarding the effects of different body



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condition scores (BCS) on liver hemodynamic indices in dogs. Belotta et al. (2018), in the liver sonographic examination of 3 groups of dogs, which they separated according to body condition score; obese dogs found a higher percentage of abnormal hepatic vein spectral waves than ideal weight dogs. Accordingly, obesity was associated with changes in portal vein indices and hepatic vein spectral wave. These changes were accompanied by significant differences in some liver enzyme activities and may be a sign of early liver disease. In another study conducted on obese people, 29% of the patients had an elevated ALT enzyme (Engelmann et al., 2014). In another study, it was stated that adolescent obese people showed an increase in ALT levels compared to normal people (Man et al., 2017). In contrast, AST and GGT levels of the healthy group were higher in goats with liver metabolic dysfunction compared to the sick goats on day 15 of lactation (Kaya and Bozkurt, 2022). In our study, while an increase in ALT level was detected, there was no significant difference in ALP level between the two groups.

Obesity is largely caused by an imbalance in energy intake and expenditure. On the other hand, several studies have revealed that obese or diabetic patients are more likely to have micronutrient deficiencies such as vitamins and minerals. In addition to their effects on bone metabolism, vitamin D and calcium may contribute to the metabolic disorder associated with obesity (Karima et al. 2016). Obesity is associated with vitamin D deficiency, hyperparathyroidism, and secondary hypercalcemia (Shah and Chauhan, 2016). Morbidly obese patients are known to have abnormal calcium metabolism compared to non-obese patients, but the clinical significance of this is unknown (Hamoui et al., 2004). In our study, significant differences were found in calcium levels in obese cats compared to non-obese cats (<0.001). No significant hematological difference was detected between the obese and non-obese two cat groups, and it is in line with previous studies (Moura de Lima et al., 2021).

## Conclusion

Obesity is an increasingly common health problem in cats and can predispose cats to many diseases. The obesity development process is affected by many factors. Leptin and Ghrelin seem to play a key role in the appetite center. In this study, Leptin and Ghrelin levels were examined in obese cats without a pathological disease. In the study, it was observed that these two hormones were negatively correlated with each other. While negative correlation was found with leptin in obese individuals, positive correlation was found with ghrelin. For drug studies targeting obesity and indirectly diabetes mellitus, further investigation of the effects of these two hormones would be meaningful.

## Ethics Approval

This research was carried out on the basis of the permission of Mehmet Akif Ersoy University Local Animal Ethics Committee dated 17.03.2021 and numbered 744.

## Conflict of Interest

The authors declare that there have no conflict of interests.

## Author Contributions

The design of the study and evaluation of the results were executed by the contribution of Ş. AKGÜN and Ş. ŞAHİNDURAN. All authors also contributed to the preparation of the manuscript.

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