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# Serum Leptin Concentrations in Patients with Intestinal Parasites

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**SUMMARY**: Leptin is a protein hormone controlling food intake and energy expenditure. In all infections icluding parasitic infections there is loss of appetite and anorexia. The aim of the present study was to clarify the relationship between intestinal parasites and serum leptin concentrations in children and adults. Forty patients with intestinal parasites and 34 healthy subjects took part in this study. Body weight, height and body mass index (BMI) were measured for all patients and controls. Patients were grouped according to age and parasitic infections (*Giardia intestinalis*, *Blastocystis hominis, Enterobius vermicularis, Entamoeba histolytica/Entamoeba dispar, Entamoeba coli*). Serum leptin concentrations were detected by immunoenzymometric assay using the Biosource Leptin EASIA kit. Statistical analysis was made by Mann-Whitney–U test using SPSS version 10.0. In children, the serum leptin levels were not statistically significant (patient: 1.49±1.97ng/ml, control: 3.48±4.97; p = 0.854) But for adults, although the BMI of patients were similar to that of the control group; the leptin levels of patients were low. These levels were not significant (patients: 9.06±10.34; controls: 4.7 ± 9.02 ng/ml; p =0.271). There was no statistical difference for leptin levels in patient groups, children and adults due to intestinal parasitic infections. Further investigations are needed.

**Key words**: Leptin, intestinal parasite, body mass index (BMI)

### Bağırsak Paraziti Olan Hastalarda Serum Leptin Düzeyleri

**ÖZET**: Leptin enerji kullanımını ve beslenme davranışını etkileyen protein yapıda bir hormondur. Paraziter infeksiyonlar dahil olmak üzere tüm infeksiyonlarda iştahsızlık ve anoreksi görülür. Bu çalışmada erişkinlerde ve çocuklarda bağırsak parazitlerinin leptinle ilişkisi araştırılmıştır. Bağırsak paraziti saptanan toplam 40 hasta ve 34 sağlıklı birey çalışmaya alındı. Tüm hasta ve kontrollerin boyu, kilosu ve vücut kitle indeksleri (VKİ) ölçüldü. Hastalar yaşlarına ve etken parazitlere göre gruplandırıldı (*Giardia intestinalis, Blastocystis hominis, Enterobius vermicularis, Entamoeba histolytica, Entamoeba coli*). Serum leptin düzeyleri Biosource firmasına ait olan Leptin EASİA kiti ile immünoenzimatik olarak ölçüldü. İstatistiksel analizler için SPSS istatistiksel programının 10.0 versiyonu kullanıldı ve Mannn-Whitney-U testi uygulandı. Çocuklarda tüm parazitler için serum leptin düzeyleri açısından anlamlı bir fark saptanmadı (hasta: 1,49±1,97ng/ml, kontrol: 3,48±4,97; p = 0,854). Fakat erişkinlerde VKİ kontrol grubuna yakın olmasına rağmen leptin düzeyleri kontrol grubuna göre düşük olarak bulunmuştur. Fakat bu düşüş istatistksel olarak anlamlı bulunmadı (hasta: 9,06±10,34; kontrol: 4,7 ± 9,02 ng/ml; p = 0,271). Bağırsak paraziti olan çocuk ve erişkin hastaların leptin düzeylerinde kontrol gruplarına göre istatistiksel olarak anlamlı bir fark saptanamamıştır. Daha geniş kapsamlı araştırılmasının yapılması gerektiği kanaatine varılmıştır.

**Anahtar Sözcükler**: Leptin, bağırsak paraziti, Vücut Kitle İndeksi (VKI)

## INTRODUCTION

Leptin, the 16-kDa product of the obese (ob) gene was originally described as a regulator of food intake and energy expenditure. Leptin is constitutively produced by adipocytes but may also be expressed in stomach, muscles, placenta and mammary epithelial cells (20, 31).

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A broader role for leptin than regulation of adipose tissue mass has been suggested because this hormone seems to be involved in fertility control in the onset of puberty and in the regulation of immune response. Leptin is a protein hormone synthesized by adipose tissue mass (2, 30). Leptin concentrations parallel changes in nutritional status and energy storage across a broad range of nutritional states, from starvation to obesity. Serum leptin concentration reflect the total body fat content in children as well as adults (2). Up to now, we couldn't find any study in human concerning serum leptin concentration in parasitic infections. But some studies were performed on experimental animal models (9-11, 17-19, 21, 24, 26, 28, 29, 30).

Infections including intestinal parasites causes anorexia (6). Infection-induced anorexia is an acute phase response to infection. The evidence suggests that food restriction is one of the important behavioral strategies that organisms have evolved for the fight against pathogenic invasion (6, 15). Anorectic response to infection is produced by similiar mechanisms as other acute phase responses. Infectious agents trigger the release of number of interacting cytokines by peripheral immunocompetant cells as well as from neural sources in the Central Nervous System (CNS). Such cytokines can act directly or via the activation n of prostoglandin release, on glucose sensitive neurons in hypothalamic nuclei such as the lateral hypothalamic area or ventromedial hypothalamus, thus driving the supression of food intake (6). In mice, leptin production is increased by stimuli such as TNF, IL-1 and lipopolysaccharide (7, 10, 23*).*

When administered exogenously, these cytokines induce anorexia and weight loss in rodents, and IL-1 and TNF and plasma leptin levels increase**.** These data have led to the suggestion that the anorexia of infection may be mediated via cytokine induction of leptin synthesis (10).

In most experimental studies, leptin levels increase during parasitic infections (21, 29, 30). Their results suggested that, leptin is not responsible alone for the parasite-induced anorexia (29, 30).

In children, serum leptin concentrations are low in many forms of malnutrition, including intrauterine growth retardation, untreated anorexia nervosa, the results of these studies are contradictory about the effects of parasitic infections on the growth status of children (2). There is no information about relation of leptin levels in parasitic diseases of adults.

The present study was undertaken in order to investigate the relationship between serum leptin concentrations in children and adults which have parasitic infections

## MATERIAL AND METHODS

**Patients and Controls:** 40 patients with intestinal parasite and 36 healty subject were selected which admitted to Adnan Menderes University Faculty of Medicine, Parasitology Department. Serum samples were collected and stored –20 $^{o}$C before use. Body weight and height were measured for all patients. The weight for height, body mass index (BMI) were calculated.

**Measurement of serum leptin concentrations:** Fasting serum leptin concentration was measured using Biosource Leptin EASIA kit (Cat. No: KAP2281; Biosource Europe S.A.; Nivelles, Belgium), a solid phase enzyme amplified sensitivity immunoassay (EASIA) on microtiter plate. This assay uses monoclonal anti- human leptin antibodies (9).

**Statistical analysis:** Statistical analysis were done with the SPSS software program (version 10.0). Results were presented as mean ± SD. Significance was determined at %0,5 level. Correlations between parameters were evaluated using Pearson's rank correlation analysis. Data of study groups were compared by Mann-Whitney-U test.

**Table 1.** Features and leptin levels in parasitic infections and controls.

| | Patient child (n=33) | Control child (n =18) | Child (p) | Adult patient (n=17) | Adult control (n=18) | Adult (p) |
|---|---|---|---|---|---|---|
| **Age** | 10,33± 4,4 | 7,73± ,89 | 0,786 | 43,61±13,06 | 31,40±7,61 | 0,000 |
| **Height** | 134,80±23,75 | 120±32,16 | 0,175 | 168,83±9,14 | 167,50±9,76 | 0,997 |
| **Weight** | 33,28±13,33 | 28,60±16,10 | 0,763 | 69,55±14,60 | 66,10±13,17 | 0,877 |
| **Body Mass Index (BMI)** | 17,62±2,81 | 18,13±3,67 | 0,978 | 24,37±4,80 | 23,45±3,50 | 0,870 |
| **Leptin (ng/ml)** | 1,49±1,97 | 3,48±4,97 | 0,854 | 9,06±10,34 | 4,70±9,02 | 0,271 |

**Table 2.** The number and ages of patients regarding to parasites

| Parasite | Female | | Male | | Total |
|---|---|---|---|---|---|
| | Age | | | | |
| | 1-20 | >20 | 1-20 | >20 | |
| ***Giardia intestinalis*** | 3 | 2 | 5 | 3 | 13 |
| ***Blastocystis hominis*** | 3 | 4 | 1 | 4 | 12 |
| ***Entamoeba histolytica/ Entamoeba dispar*** | 1 | - | - | - | 1 |
| ***Entamoeba coli*** | - | 3 | - | 1 | 4 |
| ***Enterobius vermicularis*** | 4 | - | 6 | - | 10 |
| **Total** | 11 | 9 | 12 | 8 | 40 |

## RESULTS

The ranges of ages, heights and weights of patients were measured between 2-64 years old, 77-184 cm, 10-95 kg respectively (Table 1). The number of patients included this study was 40. Out of 40 patients 20 of them were men and 20 of them were women (Table 2). *Giardia intestinalis, Blastocystis hominis, Entamoeba histolytica/Entamoeba dispar, Entamoeba coli, Enterobius vermicularis* were detected. The serum leptin levels were measured between 0,01- 33,07 ng/ml (Table 3).

The features of patients and controls was summarized in table 1, the number of patients regarding to parasites were shown in table 2 and leptin levels regarding to parasites was shown in table 3.

Positive significant correlations were found between leptin levels and age (p = 0,006; r = 0,315), weight (p=0,000; r= 0,402), and BMI (p = 0,000; r = 0,608).

**Table 3.** Serum leptin levels regarding to parasitic infections

| Parasitic infection | Serum Leptin Level (ng/ml) | |
|---|---|---|
| | Child (n=33) | Adult (n= 17) |
| ***Giardia intestinalis*** | 1,30 ± 1,6 | 6,46 ±7,86 |
| ***Enterobius.vermicularis*** | 1,6 ± 2,23 | |
| ***Blastocystis hominis*** | 0,6 ± 0,62 | 8,72 ± 10,97 |
| ***Entamoeba coli*** | - | 12,2 ± 12,7 |
| ***Entamoeba histolytica/ Entamoeba dispar*** | 5,59 ± 0,2 | - |
| **Mean (Patient)** | 1,49 ± 1,97 | 9,06 ± 10,34 |
| **Mean (Control)** | 3,26 ± 4,88 | 4,70±9,02 |
| **p** | 0,854 | 0,271 |

## DISCUSSION

Including parasitic infections, generally all infections cause anorexia. Anorexia is a disease coping-strategy, part of the mechanism of recognition of parasite invasion by the immune system, which leeds to a modification of the host's feding behaviour (15). Because there is a little energy in anorexia, serum leptin concentrations rise via cytokines (6, 13, 18). The cytokines considered to be the most relevant to inflammatory anorexia include IL-1β, IL-6, and TNF-α. Leptin, a member of cytokines, induces a strong T helper1 response and is regarded as a proinflammatory inducer. Leptin's actions on food intake are controlled, in part, by an increase in the level of IL-1β in the hypothalamus. Similarly, anorectic effects of IL-1 are mediated via increasing leptin levels (4). Leptin interacts with neuronal leptin receptors in brain areas that are involved in the control of ingestive behaviour. Administration of relatively low doses of leptin into the CNS causes a reduction of food intake and body weight without production incapatication or malasie. Central leptin administration reduces gastic emptying. Leptin may normally serve to inhibit gastrointestinal motility (15).

In our study, no stastistical significance was found in leptin concentrations between neighter adults and nor children groups.

However mean concentrations of leptin of children was low, adult leptin levels of patient group was contradictory high. This contradictory result can be related to the ages of adult controls and patients.

There are limited studies in human concerning leptin levels and parasite-induced anorexia but most of the studies are about children(2, 25).The experimental studies demonstrated that anorexia frequently accompanies parasitic infections (6, 9, 21, 23). In a model of systemic infection, lipopolysaccharide (LPS) administration causes release of proinflamatory cytokines (IL-1, IL-6, TNF) , which induce leptin production (7, 10, 28). Serum leptin levels increase in infected rats with N. brasiliensis. (21). When administered exogenously, IL-1, IL-6 and TNF induce anorexia and plasma leptin levels increase in rodents (11). Leptin plays an important role in parasite-induced anorexia in general. In lambs, however, it is not the only factor (29, 30).

Serum leptin values were found higher in *malaria* and in *Heligmosomoides bakeri* a gastrointestinal nematode infected mice (17, 24).

Studies on parasitic infections of children focused on nutritional and growth status. The effect of helminth and protozoa infections on the nutrition, growth and physiology of the host is still poorly understood. The results of these studies are contradictory about the effects of parasitic infections on the growth status of children. Some authors found that these infections are related to growth retardation while others reported no relationship (5, 8, 12, 25).

Büyükgebiz et al. were found that low leptin concentration in mild-to-moderate Protein-energy malnutrition (PEM) and PEM without chronic disease. During recovery from malnutrition, leptin concentrations increase in relation to fat mass. Leptin might trigger catch-up growth with its regulator effects on growth, if the fat mass reaches a critical point (2).

In children malnutrition contributes to an increase in the risk of enteroparasite infections which are causally associated with a chain of events involving anorexia, digestive problems, malabsorption and losses of nutrients and inflammatory reaction (22, 27). Intestinal parasitic infections may cause damage in intestinal mucosa such as inflamation, ulceration, and pathological changes in the villi of epitelhial cells in the acute period of infection. During the chronic period of the pathology, epithelial cell damage and intestinal abcesses have also been reported (16). Kurpad et al. reported that intestinal infection with parasites increases the requirement for lysine and that this may be one factor responsible for the higher lysine requirement observed in persons with chronic undernutrition (14).

*Giardia intestinalis* trophozoites attach to the intestinal mucosa through the suction generated by a ventral disk and

cause diarrhea and malabsorbstion (1). There are contradictory results published about the effects of giardiasis on the nutritional and growth status of children. Some authors found that giardiasis is related to growth retardation while others reported no relationship (19). Anorexia is also seen in giardiasis (8, 16, 19, 25).

Dağcı et al showed that *intestinal parasites* were more common in patients with *G. intestinalis* and *B.hominis.* These finding supported that *B. hominis* can be a pathogenic protozoon (3). Most of the patient with *B.hominis* have anorexia and growth retardation (5, 32).

This is the first study concerning leptin levels of human parasitic infections. We couldn't find any study for leptin levels in human parasitic infections. Interestingly, although statistically not significant, the leptin levels were lower in children patients, whereas they were higher in adult patients, compared to their age-matched control groups. In conclusion; we need further investigations with the different parasites in bigger groups for elucidade the role of leptin in parasitic infections.

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