

## Vitamin D Levels in Cats Infected with Feline Herpesvirus Type-1

*Feline Herpesvirüs Tip-1 ile Enfekte Kedilerde Vitamin D Düzeyleri*

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**Abstract:** In this study, it was aimed to measure vitamin D levels in Feline Herpesvirus Type-1 (FeHV-1) infected cats and thus to determine its relationship with the disease activity. The animal material of this study was composed of 20 cats of different breeds, ages and genders, which showed clinical symptoms of the disease and were diagnosed with Feline Herpesvirus infection by rapid test. The control group of the study consisted of 10 cats of different breeds, ages and genders, which were healthy according to the results of routine physical examination, laboratory works, which were brought for the purpose of vaccination, and which were determined to be Feline Herpesvirus Type-1 antigen negative with the rapid test. Blood samples were taken from cats in both groups and 25-hydroxy vitamin D3 levels were determined by the fluorescent immunoassay method. The mean standard deviation values of 25 hydroxyvitamin D3 levels in FeHV-1 infected cats and healthy cats were found to be 33.30 and 64.70 ng/ml, respectively. FeHV-1 infected cats showed a significant decrease in serum vitamin D levels compared to healthy cats in the control group. As a result, vitamin D deficiency may have an effect on the formation of the disease.

**Keywords:** Cat, Feline Herpesvirus Typr-1, Vitamin D.

**Öz:** Bu çalışmada, Feline Herpesvirüs Tip-1 (FeHV-1) ile enfekte kedilerde D vitamini düzeylerinin ölçülmesi ve böylelikle hastalık aktivitesi ile olan ilişkisinin belirlenmesi amaçlandı. Bu çalışmanın hayvan materyalini hastalığa ait klinik semptom gösteren ve yapılan hızlı test ile Feline Herpes Virus enfeksiyonu tanısı konulan değişik ırk, yaş ve cinsiyette 20 adet kedi oluşturdu. Çalışmanın kontrol grubunu ise aşılama amacı ile getirilen rutin fizik muayene ile laboratuvar muayenesi sonuçlarına göre sağlıklı olan ve yapılan hızlı test ile Feline Herpesvirüs Tip-1 antijen negatif olarak belirlenen değişik ırk, yaş ve cinsiyette 10 adet kedi oluşturdu. Her iki gruptaki kedilerden alınan kan örneklerinden florösan immunoassay yöntemi ile 25 hidroksivitamin D3 düzeyleri belirlendi. FeHV-1 ile enfekte kediler ve sağlıklı kedilerde 25 hidroksivitamin D3 seviyelerine ait ortalama standart sapma değerleri gruplara göre sırası ile 33,30 ve 64,70 ng/ml olarak saptandı. FeHV-1 ile enfekte kedilerde, serum vitamin D düzeylerinde kontrol grubundaki kedilere göre önemli oranda düşme şekillenmiştir. Sonuç olarak D vitamini eksikliğinin hastalığın oluşumu üzerine etkisi olabilir.

**Anahtar Kelimeler:** Kedi, Feline Herpesvirüs Tip-1, D vitamini.

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### Introduction

Feline Herpesvirus Type-1 (FeHV-1) is a highly contagious infectious agent affecting the upper respiratory tract and eyes in cats (Stiles, 2003; Maggs, 2005). The virus causes intense infection in the conjunctiva and cornea, as well as upper respiratory tract problems. Animals that survive the primary infection usually become latently

infected in their trigeminal ganglia. Most recovered animals carry the agent throughout their lives and continue to shed it (Gaskell et al., 2007; Townsend et al., 2013; Jubb et al., 2016; Thomasy et al., 2016). It is suggested that the cause of 50-75% of upper respiratory tract diseases in cats is FeHV-1 (Townsend et al., 2013).

FeHV-1 infections have a multifactorial character. The occurrence and severity of the disease depend on many factors such as virulence, the transmission route of the infection, the susceptibility of the animal, the dose of the virus, the secondary infections that may develop, the age of the animal, and the stress and environmental conditions (Kawaguchi et al., 1995; Stiles, 2003; Maggs, 2005).

Vitamin D belongs to the group of fat-soluble vitamins. Vitamin D has 2 different functions:

1. It has paracrine or autocrine effects as a local cytokine in some tissues. Vitamin D, which protects the organism from infectious agents, is also synthesized from monocytes and macrophages.

2. Another function of Vitamin D is to exert a hormone-like effect on the circulation as a result of further development. In case of insufficient amount in the circulation, it stimulates the kidneys through PTH, and as a result, the production of 1,25(OH)<sub>2</sub> increases and its normal levels in the circulation are achieved (Özkan et al., 2009). Vitamin D deficiency may occur due to insufficient exposure to sunlight, insufficient dietary intake, and malabsorption. In vitamin D deficiency, problems such as cardiovascular diseases, chronic musculoskeletal pain, rickets, osteoporosis, obesity, Type I and Type II Diabetes Mellitus (DM), microalbuminuria, some cancer types and autoimmune diseases occur (Autier et al., 2014). While most animals synthesize vitamin D in the skin with sunlight; This event rarely occurs in cats and dogs. Direct sunlight contact with the skin is required for synthesis (Mc Dowell, 2000).

In this study, it was aimed to investigate the vitamin D levels in naturally infected cats with FeHV-1, to compare the amounts in sick animals and healthy animals and to evaluate the possible role of deficiency of this vitamin in the formation of the disease.

## Materials and Methods

This research was carried out based on the permission of Mehmet Akif Ersoy University Experimental Animals Local Ethics Committee, dated 16.01.2019 and numbered 484.

Owned cats brought to private veterinary clinics in Antalya were included in the study. Kittens and adult cats that were not vaccinated with FeHV-1 within 21 days were used in the study. Informed consent form was obtained from the cat owners. The anamnesis, age, gender, breed, and the number of days they have been sick for the cats brought to the clinic with suspected FeHV-1 clinical findings were recorded.

FHV Ag (Feline Herpesvirus) and FCV Ag (Feline Calicivirus) rapid test kits were used in cats suspected of FeHV-1 (wheezing in the upper respiratory tract, weight loss, weakness, stagnation, fever, cough, ocular discharge, salivation) in accordance with the recommended procedures and only those positive for FHV Ag and negative for FCV Ag were included in the study (Diseased group n: 20 cats). The control group (n:10) consisted of cats that were negative in all tests. Cats that did not show any suspicious clinical symptoms of FHV and were positive for FCV Ag together with FHV Ag were not included in the study.

During the study, test kits (Savant, Beijing Savant Biotechnology Co, Ltd 25-OH-D) were used for the quantitative determination of 25(OH)D levels in serum plasma or whole blood samples. Measurements were performed with a Savant fluorescent immunoassay device using the chromatographic method.

## Statistical analysis

Statistical package software (Minitab 16.1.1, 2011) was used for statistical comparison of the data. Since the data did not show normal distribution as a result of the normality test, non-parametric Mann-Whitney statistical analysis method was applied.

**Table 1.** Vitamin D levels in the Diseased and Control Group.

Groups	Number of cats	Median	
Control	10	64.70	P<0.005
Diseased	20	33.30	

## Results

The age of the FeHV-1 infected cats used in the study was minimum 1.5 months and maximum 3 months, and this group consisted of 11 female and 9 male cats. While the age of the cats in the control group was minimum 1.5 months and maximum 7 months, this group consisted of 3 male and 7 female cats.

Swap samples were taken from cats with classical rhinotracheitis, rhinitis, chronic sinusitis, corneal ulcer, stromal keratitis, keratoconjunctivitis sicca and applied in accordance with the high fever, stagnation, anorexia, depression, sneezing and conjunctivitis were determined in all FeHV-1 positive cats.

Vitamin D levels in the diseased and control group was given in Table 1. When compared with the control group Vitamin D levels in diseased group was significantly lower (P<0.005).

## Discussion

It is suggested that the cause of 50-75% of upper respiratory tract diseases in cats is FeHV-1 (Townsend et al., 2013). Many studies conducted in the past years have shown the prevalence of FeHV-1 in domestic and wild cat populations (Di Martino et al., 2007). Although vaccination for FeHV-1 does not provide complete protection against infection, it is known that it reduces the shedding time of the virus and the amount of shed virus and positively affects the prognosis (Weigler et al., 1997; Maggs, 2005). For this reason, it is known that in areas where the cat population is high and cat births cannot be controlled, practices such as increasing the population immunity level with routine vaccination and disinfection may contribute to limiting the increase in the rate of transmission, although they do not completely

eliminate the infection (Berger et al., 2015). In addition, many previous studies have reported that FeHV-1 infection causes coinfection with other viral and bacterial agents (Burns et al., 2011; Filoni et al., 2012; Berger et al., 2015; Litster et al., 2015).

According to many studies in the past years, vitamin D is a group of sterols that enable hormonal functions to take place. Apart from vitamin metabolism, vitamin D has a very important place for vital functions in the body (Dusso et al., 2005; Holick, 2008; Jussila et al., 2013).

Vitamin D is also associated with many different diseases and inflammations. The presence of VDR in inflammatory cells may also explain the importance of vitamin D's effect on the immune system. In cases of vitamin D deficiency, a decrease in T cell response occurs (Nicholson et al., 2012). Vitamin D appears to have a direct effect on the response and development of T cells (Ulitsky et al., 2011) from T cells; Th1 (T1 helper) stimulates proinflammatory cytokine production and provides a strong immune response. Th2 (T2 helper) is involved in the release of anti-inflammatory cytokines (Özkan et al., 2011; Raman et al., 2011). Vitamin D inhibits the proliferation of Th1 cells and, together with interferon gamma, suppresses the formation of proinflammatory cytokines such as interleukin-2 (Lim et al., 2005; Nerich et al., 2011). Proinflammatory cytokines play a major role in the pathogenesis of many diseases (Hassan et al., 2013; Özkan et al., 2011).

Possible causes of low vitamin D in cats include; low or decreased dietary intake and the effects of some drugs. While some drugs, such as glucocorticoids, affect vitamin D metabolism in humans, it has been shown not to alter vitamin D metabolism in dogs. However, it is unclear

whether many commonly used drugs affect vitamin D metabolism in cats, and more research is needed on this subject (Kovalik et al., 2012a). In addition, some studies have suggested that vitamin D may be a negative acute phase reactant (Waldron et al., 2013).

Although studies in cats show low serum 25(OH)D levels in diseases such as inflammatory bowel disease, gastrointestinal lymphoma, and mycobacterial infection, little is known about the relationship between vitamin D level and disease prognosis in cats (Lalor et al., 2012, 2014). Low serum concentrations of 25(OH)D have been shown to be associated with an increased risk of death in sick cats (Titmarsh et al., 2015). In addition, low vitamin D level has been shown to be associated with a weaker response to prednisolone treatment in atopic skin disease in dogs (Kovalik et al., 2012b).

It has been reported that FIV-infected cats have significantly lower vitamin D levels than cats in the healthy control group. However, further investigation of the relationship between vitamin D levels and long-term prognosis in FIV-infected cats has been recommended (Titmarsh et al., 2015). In this study, it was determined that the vitamin D levels of cats infected with FeHV-1 were statistically significantly lower than those of healthy cats. Considering the known immunomodulatory effects of vitamin D metabolites, a relationship between Feline Herpesvirus Type-1 infection and possible low vitamin D levels is possible. However, more studies are needed on this subject and the effects of Vitamin D level on the prognosis of the disease.

FeHV-1 infected cats showed a significant decrease in serum vitamin D levels compared to healthy cats in the control group. As a result, vitamin D deficiency may have an effect on the formation of the disease. It can be said that by measuring vitamin D levels in FeHV-1 infected cats or healthy cats, adding the necessary supplements for protection and treatment in sick ones in case of deficiency will be beneficial.

More studies are needed to investigate the effects of vitamin D levels on susceptibility to diseases and treatment outcomes.

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