



## The Levels of Adenosine Deaminase (ADA) in the Serum of *Enterobius Vermicularis* Positive Patients

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### Abstract

*It has been reported that the parasites can make the free oxygen radicals such as superoxide and hydrogen peroxide and they contain enzymes which produce them. The cytokines play role in the regulation of immune response in living beings. The synthesizing of IL-10 is increased in Enterobius vermicularis, too. The adenosine deaminase (ADA) is also an aminohydrolase which plays role in the catabolism of purine nucleotides, inosines and deoxyinosine deamidates the adenosine and deoxyadenosine irreversibly. In the study, the comparison of ADA levels between the serums of the control group and the group of patients with E. vermicularis was aimed. In the study, the experimental group included 40 E. vermicularis positive patients. The average age of the patients is 35.2±5.4, 20 of them are men and 10 of them are women. The average age of 40 healthy Enterobius vermicularis negative people is 40.23±7.01, 31 of them are male and 9 of them are female. A significant decrease between the Enterobius vermicularis positive patients and the control group was detected in the level of ADA (p=0.0001). It can be considered that the ADA level of E. vermicularis positive patients in the study may be decreased because of increasing oxidative stress due to the parasitic infection.*

**Key words:** *E. vermicularis*, Adenosine deaminase, intestinal parasites

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## Introduction

The *Enterobius vermicularis* (*E. vermicularis*) which is a nematode, is a highly infectious parasitosis that directly transmits from person to person. It is the most common helminth infection in the world. It lives in the human intestine, especially in the cecum and rectum parts. It affects mostly the children (elementary school age), the household and the individuals living in such an environment as a nursing home. It is common in those with personal hygiene deficiency because of self-infection [1,2].

The parasitosis causes some complaints such as restlessness, insomnia, perianal itching especially occurring at nights, nocturnal enuresis, teeth grinding at night, nasal itching, mouth drooling to the pillow at nights, involuntary movements. The secondary infection may occur in the itchy areas. Less often pseudo-meningitis findings can be seen depending on meningeal irritation as a result of allergic reactions developing against the excretas of the parasite. Particularly in girls, depending on adults entering to the vagina the vulvar itching and vulvovaginitis may occur, depending on adults entering to the urethra the urethritis may occur. A limited number of acute appendicitis cases have also been reported [1,2]. The defense of the host immune system is made through the cells also against the parasites (adult and larval forms). In this mechanism, various cytotoxic agents which are produced by activated phagocytes cells, reactive oxygen, and nitrogen intermediates take parts. These products are oxidative molecules in the free radical nature and they affect the parasite viability negatively [3-5].

The cytokines play role in the regulation of immune response for the living beings. While the Th1 cells are strengthening the defense mechanism of the host by secreting the IL-2, IFN- $\gamma$  and lymphotoxin, the Th2 cells make it susceptible against the infections by synthesizing IL-4, IL-5, IL-6, IL-10. The synthesizing of IL-10 increases in the *E. vermicularis*, too [6-8]. Also, the Adenosine deaminase is an aminohydrolase which plays role in the catabolism of the purine nucleotide [8,9]. The Adenosine deaminase (ADA) is an essential enzyme in the monocyte - macrophage system and in the proliferation and differentiation of lymphocytes [10]. The structural gene of the adenosine deaminase is in the twentieth chromosome, it is located in the form of multiple molecular in human tissue and it has a broad distribution [8-11]. In mammals it catalyzes the adenosine, deoxyadenosine and the known ribosides [8,9]. When compared to the erythrocytes, the ADA activity is more than 10 times in the lymphocytic cells [8-12]. In the

study, the comparison of ADA levels between the serums of the control group and the patient group with *E. vermicularis* was aimed.

### Material and Method

For research ethics committee report was taken (Date: 02.10.2007, the protocol number: 2007/146) and only the patients who wanted to give samples were evaluated. Considering that it might alter the serum ADA levels in the parasitic diseases, the intestinal parasites were examined by the native iodine, the material of perianal region with cellophane and sedimentation methods in the patient and control groups. In the study, the forty *E. vermicularis* positive patients formed the experimental group. In addition, of the *E. vermicularis* positive patients, those who had different parasites in their feces, those who took any hormone drugs, smokers and alcohol users were excluded from the study considering that it would cause differences in the levels of ADA. In the control group, of those who volunteered to work, those who weren't encountered a parasitic infection, non-smokers, those who took any hormone drugs and alcohol were evaluated. In the research, after the necessary explanations to the patients with *E. vermicularis* for the study, 5 ml blood was drawn from the volunteers; their serums were separated and were stored at -20 °C until being studied.

The ADA levels of the sample were measured by using the Ellis and Goldberg methods. The Blood ammonium ion released by the action of the adenosine deaminase enzyme from the adenosine created green and blue colored indophenol complex as a result of Boertholet reaction. The intensity of the resulting color increased in proportion to the concentration of enzyme in the environment. This complex was read at a wavelength of 632 nm in a spectrophotometer [13].

### Statistical Analysis

Power analysis suggested at least 40 individuals (in each group) with a significance level (alpha) of 0.05 and an 80.0% power and the considered difference using a two-sided Mann Whitney U test. The data were expressed by median (min-max). The Shapiro-Wilk test was used for the normality distribution. In the statistical analysis, Mann Whitney U test was used. The  $p < 0.05$  was considered statistically significant.

## Results

In the study, the descriptive statistics for the ADA levels were given in table 1. The average age of patients are  $35.2 \pm 5.4$ , 20 of them are male and 10 of them are female. The average age of 40 healthy people with negative *E. vermicularis* are  $40.23 \pm 7.01$ , 31 of them are male, and 9 of them are female.

**Table 1:** Patient and the ADA levels of the control groups

Variable	Group	n	Median (Min-Max)	P
<i>Enterobius vermicularis</i>	Patient	40	6 (1-93)	0.0001
	Control	40	19.25 (1.25-55.75)	

A significant reduction was observed at the ADA levels between the control group and *E. vermicularis* positive patients ( $p < 0.0001$ ).

## Discussion

It has been reported that the helminths antigens can cause T helper (Th) 2 responses [6]. It has been reported that the *E. vermicularis* can stimulate the formation of regulatory cytokines as IL-10 which provides both host and parasite viability [7].

Also Villarreal et al. reported that the levels of eosinophils and IgE increased in the *E. vermicularis* infection [14]. Ustun et al. could not find a significant difference between the eosinophil levels of the normal control patients and intestinal parasitic patients. But they found the levels of IL-5 in the patients with intestinal helminthiasis statistically fewer than the patients with the intestinal protozoan [15].

At the increased serum ADA level both cellular and humoral immunity are out of order [4,17,18]. It has been identified that the ADA activity is important for the normal lymphocyte function [4,18]. The adenosine deaminase enzyme accepted as the T cell marker increases in the body fluid or plasma in the diseases where the stimulation of immunity occurs through the cells [19]. The ADA activity increases in autoimmune diseases such as typhoid which the cellular immunity is stimulated, infectious mononucleosis, brucellosis, acute pneumonia, tuberculosis, sarcoidosis, liver diseases, acute leukemia, a variety of malignancies and rheumatoid arthritis, systemic lupus erythematosus (SLE) and Behcet Disease [17,20-22]. Furthermore, it has been suggested that the ADA levels increase also in the patients with primary immune deficiency

(Leukocyte adhesion deficiency, hyper IgM and Wiscott-Aldrich Syndrome, Chronic granulomatous disease) [23]. In addition, it has been reported that the ADA activity is routinely used in the differential of other etiologies of tuberculous pleurisy, it has been determined that the ADA height also reflects the severity of the disease. Similarly, Balasaniants et al. [24] have determined that the serum ADA height reflects the destructive and infiltrative changes in the lungs of the patients with tuberculosis and they have reported that it can be used in monitoring the effectiveness of treatment due to the decrease of its level after treatment. Again, Kiran et al. [25] have identified significant differences between the *Entamoeba coli* and control groups and compared to the controls, they have observed significant increase in the ADA level. The researchers have reported that the highly detected ADA activity in the serums of the patients with *Entamoeba coli* can be an indicator of the induced cellular immune response.

It has been indicated that while the ADA activity is increasing in cases when the immune system is activated, it abates when suppressed [2]. In the study, a significant decrease has been detected in the ADA levels of the *E. vermicularis*-positive patients compared to the control group. It has been reported that a drop is detected in the ADA activity in the visceral leishmaniasis [26]. Again, Karaman et al. [18] has found a significant decrease in the ADA activity in patients with seropositive *Toxoplasma gondii* and *Giardia intestinalis* compared to the healthy controls. They have reported that the low level of ADA does not cause an increase in T lymphocytes because of the old toxoplasmosis infection or it also can be caused by the increased oxidative stress in parasitic infections.

It can be thought that the ADA levels of the *E. vermicularis* positive patients in this study may be decreased due to increased oxidative stress because of the parasitic infection. However, in the obtained source information, it has been reported that the parasite can cause limited, moderate ulcerative and hemorrhagic lesions in the small and large intestines, it hasn't led to remarkable immunopathological findings such as the helminths which can spread to the tissues for its continued life in the intestinal lumen [24]. This condition seems to support the low ADA level obtained in the research. However, in the study, there are no data about lymphocyte levels, because the lymphocytes of *E. vermicularis* positive patients and the control group have not been examined. It is thought that the research will shed light on the studies about the controlled experimental animals in the future.

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