Volume 17 • Number 2 • June 2026 • em00859 ISSN: 1309-6621 (Online)

JOURNAL OF CLINICAL AND EXPERIMENTAL INVESTIGATIONS

RESEARCH ARTICLE

Investigation of serum prolidase enzyme levels in patients with adenotonsillar hypertrophy

Adnan Ekinci [1*], *Hakan Dagistan* [2]

[1] Hitit University, Faculty of Medicine, Department of Otorhinolaryngology, Çorum, TÜRKİYE

[2] Bozok University, Faculty of Medicine, Department of Otorhinolaryngology, Yozgat, TÜRKİYE

ABSTRACT

Objective: We investigated serum prolidase enzyme activity (SPEA) in patients with adenotonsillar hypertrophy (ATH) and compared the results with those of healthy children. We determined the enzyme levels again after adenotonsillectomy in the patient group to determine any differences.

Methods: The study consisted of a total of 60 patients. The control group and the study group each included 30 patients. SPEA levels were compared between the groups. Pre- and post-operative SPEA levels were also compared in the patient group.

Results: The mean SPEA value was 213.51 U/L pre-operative group and 177.73 U/L post-operative group. The decrease in SPEA levels after the adenotonsillectomy was statistically significant ($p < 0.05$). When the patient and control groups were compared, SPEA levels in the patient group were statistically significantly higher than in the control group ($p < 0.05$). The mean SPEA value was 188.87 U/L in the control group, whereas it was 213.51 U/L in the patient group.

Conclusions: SPEA levels were significantly higher in ATH patients than in healthy children. SPEA levels were found to decrease significantly after adenotonsillectomy. This finding suggests that SPEA may play a role in the etiopathogenesis of ATH.

Keywords: tonsillar hypertrophy, adenoid hypertrophy, prolidase

Correspondence:

Adnan Ekinci, Dr.

Address: Department of Otorhinolaryngology, Faculty of Medicine, Hitit University, 19200 Çorum, TÜRKİYE

Email: draekinci@hotmail.com

Received: 12.09.2025,
Accepted: 14.03.2026
https://doi.org/10.29333/jcei/18285

INTRODUCTION

The tonsils (palatine tonsils) and pharyngeal tonsils (pharyngeal tonsils) are lymphoid tissues and are elements of the tissue system called "Waldeyer's ring." These tissues protect the body against various infections. Enlargement of the adenoids and tonsils is defined as adenotonsillar hypertrophy (ATH) and leads to upper respiratory tract obstruction in childhood. Secondary hypertrophy occurs as a result of recurrent tonsil and nasal infections [1, 2].

Both tonsillectomy and adenoidectomy are among the most commonly performed surgeries in childhood. General surgical indications for adenotonsillectomy include recurrent episodes of infection, upper respiratory tract obstruction, eustachian tube dysfunction, bad breath, sore throat, and suspected malignancy [3, 4]. Currently, the pathophysiology of ATH is still unclear.

Prolidase is a metalloenzyme and has been detected in many tissues throughout the body [5]. Studies have reported that an increase or decrease in serum prolidase enzyme activity (SPEA) plays a role in the development of many diseases [6]. The aim of this study was to compare SPEA levels in ATH patients and healthy children and to examine the effect of adenotonsillectomy on SPEA levels.

Our literature review revealed that the relationship between tonsil and adenoid disease and SPEA has not been previously investigated. Therefore, our study is the first to explore this topic in the literature.

MATERIALS AND METHODS

We conducted our study between January 1, 2018 and March 1, 2019 at the otorhinolarygology clinic at Hitit University. The study protocol was approved by the

Hitit University Clinical Studies Ethics Committee (project number: 2018/24). Thirty patients aged between 2 and 12 years old and diagnosed with ATH were included in the study. To diagnose ATH, patient medical history was taken, and detailed physical, radiological, and endoscopic examinations were performed. The control group also included 30 healthy children. The ages of the children in both groups were similar. They also had no active infection or respiratory problems.

The control group underwent all necessary examinations and was found not to have ATH. Patients experiencing acute or chronic tonsillitis attacks and those with active infection were excluded from the study. A control group was formed by selecting 30 healthy children who had no complaints in the head and neck region and no infection or other systemic disease. Patients with malignancy, severe systemic disease, allergies, nasal polyps, asthma, allergic rhinitis, immunodeficiency, and obesity were excluded from the study and control groups. The adenoid-to-nasopharyngeal (AN) ratio was determined radiologically, and the ratio of adenoid depth to nasopharyngeal diameter was measured on a lateral radiograph. Children with this ratio greater than 0.67 were included in the patient group [7].

Tonsil size was also graded using the Brodsky classification. Accordingly, grade 1 = small tonsils confined to the tonsillar columns; grade 2 = tonsils slightly extending beyond the columns; grade 3 = tonsils extending beyond the columns but not reaching the midline; and grade 4 = large tonsils nearly obscuring the midline [8]. The study group included children with an AN ratio greater than 0.67 and tonsil hypertrophy of grade 3 or greater.

The protocol requirements of the Declaration of Helsinki were observed at all stages of the study. Explanatory informed consent forms were obtained from all individuals participating in the study. Pre-operative biochemical, hematological, and ELISA tests were performed on the patients and controls participating in the study. Those with normal laboratory test results were allowed to continue the study.

The same clinician used a standard cold knife surgical technique under general anesthesia for all patients. Blood samples were collected half an hour before the operation and two months after the operation. Blood tests were performed on all patients included in the study between 8:00 and 10:00 a.m. 30-45 minutes after placing a 10 ml venous blood sample in a vacuum biochemistry tube,

Blood samples were centrifuged at 4,000 rpm. The separated serum was then stored in a -80 °C refrigerator. An automated ELISA device called Radim ALIS-I was used to measure SPEA levels. The coefficient of variation criterion within the group was determined to be less than 8% and between the groups was determined to be less than 10%. The assay range was between 93.75 and 6,000 mU/ml. The assay sensitivity was 93.75 mU/ml.

Table 1. Comparison of SPEA levels between pre- and post-operative

	N	M ± SD	Median (min-max)	p
Pre-operative	30	213.51 ± 32.44	209 (169-280)	< 0.05*
Post-operative	30	177.62 ± 30.98	176 (149-206)	

Note. *Statistically significant p < 0.05

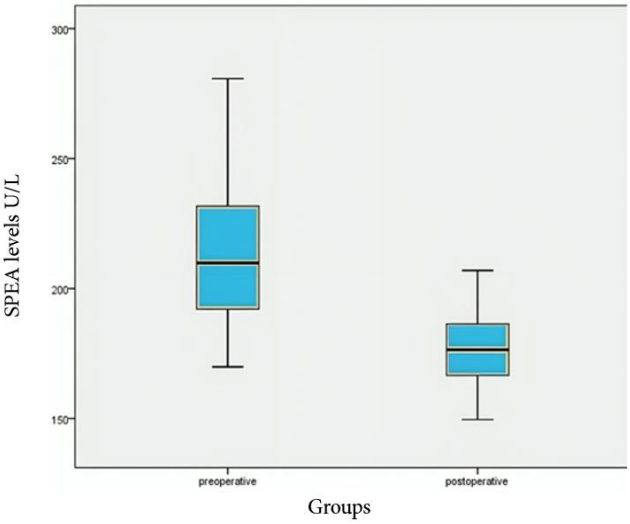

Figure 1. Box blots of mean changes of SPEA levels between pre- and post-operative groups (Source: Authors' own elaboration)

Statistical Analysis

The SPSS package program was used for statistical analysis. The Shapiro-Wilk test was used to examine the normal distribution of the data. When presenting continuous variables, mean (M) ± standard deviation (SD) and median (min-max) values were given, while numbers and percentages were used in presenting categorical variables.

The Mann-Whitney U test was used to compare prolidase levels in the case-control groups because the data obtained did not show a normal distribution between the groups.

Wilcoxon Signed Rank test was used to examine pre- and post-operative prolidase levels. The criterion for statistical significance was $p < 0.05$.

RESULTS

The control group included a total of 30 healthy children (14 females and 16 males), while the patient group also consisted of 30 individuals. Half of the patient group were male and half were female. The study groups were similar in terms of gender ($p = 0.873$). The mean age of the control group was 7.26 ± 2.47 years, while the patient group was 7.67 ± 2.85 years. The mean pre- and post-operative SPEA values were 213.51 U/L and 177.73 U/L, respectively. The decrease in SPEA levels after adenotonsillectomy was statistically significant ($p < 0.05$) (**Table 1** and **Figure 1**).

Table 2. Comparison of SPEA levels between patient and control groups

	N	M ± SD	Median (min-max)	p
Patient group	30	213.51 ± 32.44	209 (169-280)	0.001
Control group	30	188.87 ± 21.30	186 (154-231)	

Note. *Statistically significant p < 0.05

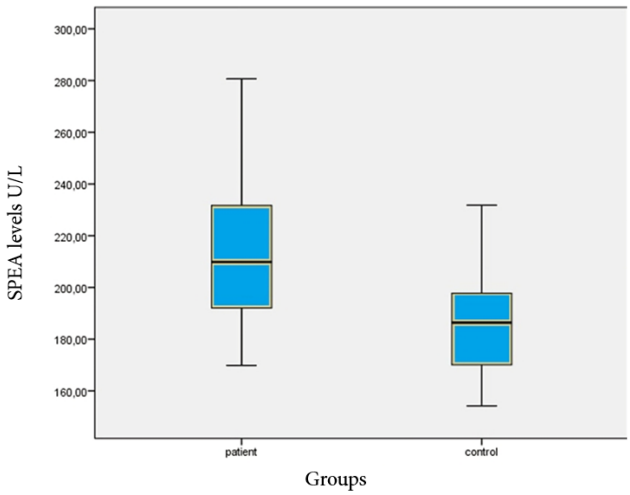

Figure 2. Box blots of mean changes of SPEA levels between patient and control groups (Source: Authors' own elaboration)

SPEA levels were higher in the patient group than in the other group and this difference was statistically significant ($p < 0.05$) (**Table 2** and **Figure 2**). The mean SPEA value in the control group was 188.87 U/L, while it was 213.51 U/L in the patient group.

DISCUSSION

Despite all studies, the etiology of ATH has not yet been clearly explained. Viral and bacterial diseases, genetic causes, immunological diseases, and humoral changes have been implicated in the etiology [9]. Collagen contains abundant amino acids, making it the most important substrate for the prolidase enzyme. Prolidase enzyme activity increases with increasing chronic inflammation in tissues.

In cases where collagen production and destruction are increased, prolidase enzyme activity was also found to be high [10]. Normally, there is a balance between the production and degradation of the extracellular matrix, but if this balance is disrupted, fibrosis occurs [11]. According to our literature search, we have not yet found any published studies on prolidase in children with ATH. Our study is the first to investigate SPEA as a biochemical marker in children with ATH [12]. Apart from a few studies examining the relationship between nasal polyps and prolidase, there are very limited research articles in the literature linking prolidase enzyme to ear, nose, and throat diseases.

Prolidase is a metalloenzyme belonging to the hydrolases class. Prolidase plays a primary role in collagen biosynthesis and also plays a role in collagen degradation. Proline and hydroxyproline are formed as a result of collagen catabolism. Prolidase plays a role in the intracellular degradation of proline and hydroxyproline.

Therefore, collagen metabolism can be determined by measuring SPEA and tissue prolidase enzyme activity (TPEA) levels [13]. The tissues in which prolidase enzyme has been detected are primarily the liver, kidney, stomach, pancreas, brain, heart, and amniotic fluid [14]. Because collagen is present as a structural component of the extracellular matrix of many organs and tissues, it can be affected by many pathological events [15]. An increase or decrease in prolidase activity may occur in many diseases. Studies have reported decreased SPEA in asthma and chronic obstructive pulmonary disease (COPD) [15, 16]. Value-added scientific studies have reported increased SPEA in alcoholic liver disease, pancreatitis, chronic hepatitis C, and some cancers [17, 18]. Another study reported that SPEA levels in patients with nonalcoholic steatohepatitis were significantly higher than in patients with simple steatosis. Furthermore, a significant relationship between the progression of liver fibrosis and serum SPEA levels has been noted [19].

It was reported that increased inflammation in the liver is associated with collagen destruction and increased SPEA levels [20]. They attributed this to prolidase being an extracellular matrix element and responsible for the degradation of intracellular collagen [20]. In a study conducted in children, it was reported that SPEA levels were significantly higher in chronic hepatitis patients than in normal healthy children [10].

It was found that elevated SPEA levels in acute pancreatitis patients are due to inflammation and collagen destruction. In this study, they reported that elevated SPEA levels increased in direct proportion to the severity of pancreatitis [21].

It was found higher SPEA levels in patients with viral hepatitis, chronic hepatitis, and cirrhosis compared to healthy individuals [22]. Therefore, they concluded that SPEA monitoring could be a good and independent marker for the diagnosis and follow-up of liver disease [22]. The study in [12] compared SPEA and TPEA levels in patients with nasal polyps with those in patients with turbinate hypertrophy and deviated septum. They concluded that both SPEA and TPEA levels were higher in patients with nasal polyposis than in other groups. They reported that elevated SPEA and TPEA levels were due to chronic inflammation, and that elevated enzymes may be indicative of fibrotic processes in nasal polyp development [12].

The study in [23] examined serum and tissue prolidase levels in the nasal polyp group. They found that SPEA levels were higher in the control group, but TPEA levels were significantly higher in the nasal polyp group [23]. It was found that serum prolidase levels were higher in patients

with nasal polyps compared to healthy individuals. They reported a significant decrease in prolidase levels after oral steroid treatment. Therefore, they argued that high prolidase levels may be an effective factor in nasal polyp development [24].

The study in [15] found that asthmatic patients were more exposed to oxidative stress. However, they found that serum prolidase levels were significantly lower in asthmatic patients compared to healthy individuals. They reported that this may be due to a defect in collagen metabolism, particularly due to correlation accumulation in the basement membrane [15]. The study in [25] found a direct correlation between increased oxidative stress and increased prolidase enzyme levels in a study of patients with Parkinson's disease. In another study, it was concluded that serum prolidase activity was higher in individuals with COPD than in healthy individuals [26].

Cellular damage can occur due to oxidative stress in any situation caused by respiratory hypoxia. Prolidase may repair this damage through collagen synthesis, or conversely, elevated prolidase may play a role in protein degradation and exacerbate the damage.

In our study, we believe that the reason for the high prolidase enzyme levels in the ATH group is the patients' exposure to hypoxia. This suggests that prolidase is used in damage mechanisms in ATH patients and may not contribute to repair mechanisms. The increased inflammatory events in many studies, while decreased in others, may be related to this dual function of the prolidase enzyme. In conclusion, we believe that prolidase enzyme levels may be a warning sign for other systemic diseases that this ATH disease may cause in the future.

In our study, we found significantly higher SPEA levels in ATH patients compared to healthy children. We also noted a significant decrease in SPEA levels in children who underwent tonsillectomy after the operation. These findings suggest that high prolidase levels may cause hypertrophy in the tonsillar and adenoid tissues of children and lead to frequent infections.

A disadvantage of our study is the small number of patients participating in the study. However, since this is the first study on this subject, we believe it can provide a sufficient preliminary idea. Another limitation is that prolidase enzyme levels in tonsillar and adenoid tissues were not investigated. There is no research on ATH and prolidase enzymes in the otolaryngology field in the literature. Therefore, we were unable to make a comparison with a similar study on this topic in the discussion section. While the sample sizes are small, they are acceptable for a preliminary study.

CONCLUSION

In conclusion, we found that SPEA levels were statistically significantly higher in patients with ATH compared to the normal population. We found that prolidase levels were statistically significantly higher in patients with adenoid and tonsil hypertrophy compared to normal children. Furthermore, a significant decrease in SPEA levels was observed in the patient group after adenotonsillectomy. Based on these findings, we believe that prolidase may be a potent enzyme in the etiopathogenesis of ATH and a marker of clinical improvement. Further advanced and detailed studies on this topic would be beneficial.

Author contributions: Both authors have sufficiently contributed to the study and agreed with the results and conclusions.

Funding: No funding source is reported for this study.

Ethical statement: The authors stated that the study was approved by the Clinical Research Ethics Committee at Hitit University on 5 June 2017 with approval number 2017-43. Written informed consents were obtained from the participants.

AI statement: The authors stated that the study did not use generative artificial intelligence or AI-based tools.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Kenna MA. Tonsils and adenoids. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics. 16th edition. Philadelphia, PA: WB Saunders; 2000. p. 1267-8.
2. Lee P-C, Hwang B, Soong W-J, Meng CCL. The specific characteristics in children with obstructive sleep apnea and cor pulmonale. ScientificWorldJournal. 2012;2012:757283. doi:10.1100/2012/757283 PMid:22645449 PMCid:PMC3356724
3. Verma SP, Stoddard T, Gonzalez-Gomez I, Koempel JA. Histologic analysis of pediatric tonsil and adenoid specimens: Is it really necessary? Int J Pediatr Otorhinolaryngol. 2009;73(4):547-50. doi:10.1016/j.ijporl.2008.11.001 PMid:19193449
4. Kiroglu AF, Noyan T, Oger M, Kara T. Oxidants and antioxidants in tonsillar and adenoidal tissue in chronic adenotonsillitis and adenotonsillar hypertrophy in children. Int J Pediatr Otorhinolaryngol. 2006;70(1):35-8. doi:10.1016/j.ijporl.2005.05.006 PMid:15961164
5. Dolenga M, Hechtman P. Prolidase deficiency in cultured human fibroblasts: Biochemical pathology and iminodipeptide-enhanced growth. Pediatr Res. 1992;32(4):479-82. doi:10.1203/00006450-199210000-00020 PMid:1437403

6. Arata J, Umemura S, Yamamoto Y, Hagiyama M, Nohara N. Prolidase deficiency: Its dermatological manifestations and some additional biochemical studies. Arch Dermatol. 1979;115(1):62-7. doi:10.1001/archderm.115.1.62 PMid:760660
7. Hsu W-C, Kang K-T, Weng W-C, Lee P-L. Impacts of body weight after surgery for obstructive sleep apnea in children. Int J Obes (Lond). 2013;37(4):527-31. doi:10.1038/ijo.2012.194 PMid:23183325
8. Brodsky L, Moore L, Stanievich JF. A comparison of tonsillar size and oropharyngeal dimensions in children with obstructive adenotonsillar hypertrophy. Int J Pediatr Otorhinolaryngol. 1987;13(2):149-56. doi:10.1016/0165-5876(87)90091-7 PMid:3667094
9. Bicknell PG. Role of adenotonsillectomy in the management of pediatric ear, nose and throat infections. Pediatr Infect Dis J. 1994;13(1 Suppl 1):S75-8; discussion S78-9. doi:10.1097/00006454-199401001-00016 PMid:8159521
10. Şen V, Uluca Ü, Ece A, et al. Serum prolidase activity and oxidant-antioxidant status in children with chronic hepatitis B virus infection. Ital J Pediatr. 2014;40:95. doi:10.1186/s13052-014-0095-1 PMid:25425101 PMCid:PMC4247636
11. Friedman SL. Mechanisms of disease: Mechanisms of hepatic fibrosis and therapeutic implications. Nat Clin Pract Gastroenterol Hepatol. 2004;1(2):98-105. doi:10.1038/ncpgasthep0055
12. San I, Ulas T, Bozkus F, et al. Prolidase activity and oxidative stress parameters in patients with nasal polyps. Clin Ter. 2013;164(3):209-13.
13. Myara I. Effect of long preincubation on the two forms of human erythrocyte prolidase. Clin Chim Acta. 1987;170(2-3):263-70. doi:10.1016/0009-8981(87)90136-7 PMid:3436060
14. Gürdöl F, Genç S, Yalçin Ö, Gültepe M. The presence of prolidase activity in amniotic fluid and its evaluation as a maturity test. Biol Neonate. 1995;67(1):34-8. doi:10.1159/000244140 PMid:7748973
15. Cakmak A, Zeyrek D, Atas A, Celik H, Aksoy N, Ozcan Erel E. Serum prolidase activity and oxidative status in patients with bronchial asthma. J Clin Lab Anal. 2009;23(2):132-8. doi:10.1002/jcla.20303 PMid:19288447 PMCid:PMC6649124
16. Gencer M, Aksoy N, Dagli EC, et al. Prolidase activity dysregulation and its correlation with oxidative-antioxidative status in chronic obstructive pulmonary disease. J Clin Lab Anal. 2011;25(1):8-13. doi:10.1002/jcla.20347 PMid:21254236 PMCid:PMC6647584
17. Brosset B, Myara I, Fabre M, Lemonnier A. Plasma prolidase and prolinase activity in alcoholic liver disease. Clin Chim Acta. 1998;175(3):291-5. doi:10.1016/0009-8981(88)90105-2 PMid:3416488
18. Duygu F, Koruk ST, Karsen H, Aksoy N, Taskin A, Hamidanoglu M. Prolidase and oxidative stress in chronic hepatitis C. J Clin Lab Anal. 2012;26(4):232-7. doi:10.1002/jcla.21510 PMid:22811354 PMCid:PMC6807348
19. Kayadibi H, Gültepe M, Yasar B, et al. Diagnostic value of serum prolidase enzyme activity to predict the liver histological lesions in non-alcoholic fatty liver disease: A surrogate marker to distinguish steatohepatitis from simple steatosis. Dig Dis Sci. 2009;54(8):1764-71. doi:10.1007/s10620-008-0535-0 PMid:18989777
20. Kurien BT, Patel NC, Porter AC, D'Souza A, Miller D, Matsumoto H, Wang H, Scofield RH. Prolidase deficiency and the biochemical assays used in its diagnosis. Anal Biochem. 2006;349(2):165-75. doi:10.1016/j.ab.2005.10.018 PMid:16298326
21. Mayer J, Rau B, Schoenberg M, Beger HG. Mechanism and role of trypsinogen activation in acute pancreatitis. Hepatogastroenterology. 1999;46(29):2757-63.
22. Alparslan S, Gultepe M. Serum prolidase activity: Its value as an indicator of collagen accumulation in chronic liver diseases. Turk J Biochem. 1993;18:1-9.
23. Salihoğlu M, Güngör A, Özcan Ö, Çeşmeci E, Müftüoğlu T, İpçioğlu OM. Tissue and serum prolidase activity in patients with nasal polyposis. Gulhane Tıp Derg. 2014;56:209-12. doi:10.5455/gulhane.168323
24. Ekinci A, Kayadibi H, Demir E, Ozcan M. The effects of oral steroid therapy on prolidase enzyme activity in patients with nasal polyps. Turk J Biochem. 2021;46(4):473-7. doi:10.1515/tjb-2019-0204
25. Verma AK, Raj J, Sharma V, Singh TB, Srivastava S, Srivastava R. Plasma prolidase activity and oxidative stress in patients with Parkinson's disease. Parkinsons Dis. 2015;2015:598028. doi:10.1155/2015/598028 PMid:26347150 PMCid:PMC4546767
26. Ekin S, Arısoy A, Gunbatar H, et al. The relationships among the levels of oxidative and antioxidative parameters, FEV1 andprolidase activity in COPD. Redox Rep. 2017;22(2):74-7. doi:10.1080/13510002.2016.1139293 PMid:26870880 PMCid:PMC6837489