Original Article

Evaluation of Serum Adenosine Deaminase Levels in Patients with Thyroid Dysfunction: A Cross-Sectional Study from a Tertiary Health Care Centre in North Kerala

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Abstract

Background: Thyroid abnormalities are being diagnosed more frequently due to heightened knowledge of thyroid diseases. Autoimmune diseases of the thyroid gland are the predominant aetiology of thyroid dysfunction. Graves' disease (hyperthyroidism) and Hashimoto's thyroiditis are autoimmune disorders of the thyroid gland. Human tissues contain the enzyme adenosine deaminase (ADA), which is thought to be a reliable indicator of cell-mediated immunity. It is essential for lymphocyte proliferation and differentiation. Objective: To assess the serum Adenosine Deaminase (ADA) activity in hypothyroid patients and to link serum ADA levels with serum TSH levels. **Material and Methods:** A comparative cross-sectional study was conducted including 80 people, separated into two groups. Group 1 comprised 40 patients recently diagnosed with hypothyroidism. Group 2: Forty healthy adults. Serum adenosine deaminase and serum TSH levels were assessed in these patients. **Results:** The study indicates that serum ADA levels are considerably elevated in hypothyroidism. The average serum ADA value in hypothyroid individuals is 22.54 ± 6.77 U/L, which is elevated in comparison to controls. The serum ADA value in controls is 12.03 ± 1.67 U/L. A notable positive correlation exists between serum ADA and serum TSH (r = 0.395, P = 0.000). **Conclusion:** Serum adenosine deaminase levels were increased in persons with Hypothyroidism. The heightened ADA activity indicates an immunological dysregulation. It consequently confirms the concept that numerous thyroid illnesses are autoimmune. Immunological processes implicated in their pathogenesis. Adenosine deaminase may possibly serve as a significant indicator for forecasting modified immunity in individuals with thyroid problems.

Keywords: Adenosine Deaminase (ADA); TSH; Thyroid Dysfunction.

Received: 19 September 2025 Revised: 16 October 2025 Accepted: 28 November 2025 Published: 01 December 2025

Introduction

Thyroid disease is one of the chronic non-communicable diseases globally. The hormones released by the thyroid gland has important role in protein, fat, and carbohydrate metabolism. Thyroid disorders are medical illnesses marked by significant fluctuations in thyroid hormone levels. The two major hormones secreted by thyroid glands are thyroxine (T4) and triiodothyronine (T3). Thyroid stimulating hormone (TSH), synthesised by the pituitary gland, functions to promote hormone production in the thyroid gland. Hypothyroidism, characterised by insufficient thyroid hormone production, is prevalent in our nation. Thyroid diseases are far more prevalent in women than in men. Autoimmune diseases of the thyroid gland represent the predominant causes of thyroid dysfunction. These autoimmune illnesses result from aberrant proteins, known as antibodies, and white blood cells that collaboratively stimulate or harm the thyroid gland. Graves' illness (hyperthyroidism) and Hashimoto's thyroiditis are examples of such diseases. Hashimoto's thyroiditis is more prevalent, with its incidence rising with age.[1]

Adenosine Deaminase:

Adenosine deaminase is an enzyme (EC 3.5.4.4) which play main role in purine metabolism. It is essential for the catabolism of adenosine and for metabolism of nucleic acid in tissues. ADA has a role in the proliferation and differentiation of diverse lymphocytes, mainly T-lymphocytes.[2] It is present in both eukaryotes and prokaryotes.[3] ADA mediates the irreversible hydrolytic deamination of adenosine to inosine and 2'-deoxyadenosine to 2'-deoxyinosine. Inosine and 2'-deoxyinosine are metabolised to hypoxanthine, then to xanthine, and ultimately to uric acid.[4] ADA is considered as an effective indicator of cell-mediated immunity.[5] Elevated lymphocyte ADA activities were seen in conditions characterised by cell-mediated immune responses.[6] ADA is found in multiple locations within the human body corpus. It is considered as an effective indicator of

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DOI:
10.21276/amit.2025.v12.i3.210

How to cite this article: Rashid CP, Nasid PM, Maekha JN. Evaluation of Serum Adenosine Deaminase Levels in Patients with Thyroid Dysfunction: A Cross-Sectional Study from a Tertiary Health Care Centre in North Kerala. Acta Med Int. 2025:12(3):964-968.

cell-mediated immunity and functions as an essential function in proliferation and differentiation of lymphocytes. Although there are several reports accessible regarding levels of ADA in people with thyroid disorders are predominantly indeterminate. The current investigation was conducted to assess plasma Adenosine deaminase level and investigate its relation with hypothyroid diseases. Adenosine deaminase enzyme can exists in both monomeric form and dimeric form.[7] The active site of ADA comprises a zinc ion. This Zn ion is located in the deepest region the of the active site which is regulated by five atoms: His15, His17, and His214, Asp295 and the substrate. Zinc is the only cofactor requirement for this enzyme.

Objective

1. To compare serum Adenosine deaminase level in patient with hypothyroidism and in euthyroid controls. Two groups of individuals were investigated.

Group 1: 40 cases of hypothyroidism.
Group 2: 40 euthyroid controls.

2. To find the correlation between serum ADA and TSH levels in the study groups.

Materials and Methods

A Comparative cross-sectional study was conducted among the patients attending the endocrinology clinic or admitted to the medicine ward at Government Medical College, Kozhikode. Ethical approval for this study was obtained from the Institutional Ethics Committee of Government Medical College, Kozhikode with approval Number Ref No. GMCKKD/ RP 2015-16/IEC/7/27-11 dated 27/11/15. Two study groups were selected.

Group 1 comprises of 40 patients who were newly-diagnosed with hypothyroidism in the Department of Medicine, GMC, Kozhikode in the age group 18-60 years.

Patients with acute illness, coronary artery disease, hepatic or renal dysfunction; patients who had used medicines containing corticosteroids; pregnant ladies and patients not giving written consent were excluded from the study.

Group 2 consists of 40 patients with no thyroid dysfunction in same age group from bystanders of other patients, medical and para-medical staff. Patients having thyroid dysfunction, pregnant ladies and persons not giving written consent were excluded from the study

The following parameters are compared in both study groups.

1. TSH: Measured by Chemiluminescence method

2. ADA: Fixed Kinetic Method by fully automated clinical chemistry analyser

Estimation of TSH By Chemiluminescence.[8]

The Elecsys TSH assay uses monoclonal antibodies that are specifically directed against human TSH. The antibodies labelled with a ruthenium complex consists of a chimeric construct made from human and murine-specific elements.

The estimation is conducted using the Sandwich principle.

First Incubation: A 50 µL of sample is incubated with biotinylated monoclonal antibody specific for TSH and another monoclonal antibody conjugated with ruthenium Complex .

A sandwich complex is formed between the antigen and the two antibodies.

Second Incubation: Following the addition of streptavidin-coated microparticles, the compound is tethered to the solid phase through the interaction of biotin and Streptavidin.

The reaction mixture is subsequently aspirated into the measurement cell, where the microparticles are magnetically captured on to the electrode's surface. Unbound substances are removed using ProCell/ProCell M. Upon application of voltage to the electrode a chemiluminescent reaction occurs and the emitted light is measured by a photomultiplier. Results are derived from a calibration curve which is instrument-specific, established through a two-point calibration and a provided master curve.

Anticipated values: 0.27-4.2 µIU/ml.

Estimation of Serum Adenosine Deaminase.[9]

The serum adenosine deaminase activity was measured using the Transasia EM 360 autoanalyzer with the adenosine deaminase assay kit from Erba Diagnostics.

Purine nucleoside phosphorylase converts inosine to hypoxanthine once adenosine is enzymatically deaminated to inosine. Hypoxanthine is further oxidized by xanthine oxidase to produce uric acid and hydrogen peroxide. The generated Hydrogen peroxide is now react with N-Ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline (EHSPT) and 4-aminoantipyrine in the presence of peroxidase to produce a quinone dye. The intensity of coloured complex is measured at 546 nm.

Anticipated Serum Value: 0-15 U/L.

Statistical Analysis

Information was displayed as mean ± SD, frequency, and percentage. Software called SPSS (SPSS Inc., Chicago, IL, USA) version 15.0 for Windows was used to perform statistical analysis. Data analysis was conducted utilising Microsoft Excel and the Statistical Package for the Social Sciences (SPSS Version 18) software for Windows. Results were statistically evaluated for significance using One-way ANOVA and the chi-square test. Results were considered significant at a p value of less than 0.05.

Results

A cross-sectional study was conducted selecting 2 groups of individuals. First group (Cases) included 40 patients who were newly diagnosed to have hypothyroidism with mean age of 40.7 years. Group 2(Controls) included 40, age and sex related apparently healthy individuals.

Table 1: Sex distribution among the study group

Category		Sex		Total
		Female	Male	
Hypothyroidism	Count	30	10	40
	% within category	75.0%	25.0%	100.0%
Normal	Count	23	17	40
	% within category	58%	42%	100.0%

Total	Count	53	27	80
	% within category	66%	34%	100%

Groups were compared according to gender. There is no statistically significant difference between the groups.

Table 2: Mean age distribution among the study groups

	Number	Mean	Std. Deviation
Hypothyroidism	40	40.70	10.690
Normal	40	35.48	8.140
	p=0.016		

Mean age groups in hypothyroidism and normal individuals are 40.70 ± 10.69 and 35.48 ± 8.140 respectively.

Table 3: Mean serum TSH value among the study group

TSH LEVEL	Number	Mean (IU/ml)	Std. Deviation
Hypothyroidism	40	7.0913	1.72516
Normal	40	1.8962	1.02998
p = 0.000			

Our study shows significant difference in serum TSH between groups. Hypothyroid groups shows significantly higher value (mean 7.09 ±1.725 IU/ml).

Table 4: Mean serum ADA level among the study group

ADA	Number	Mean (U/L)	Std. Deviation
Hypothyroidism	40	22.545	6.7721
Normal	40	11.170	3.9553
p = 0.00			

Hypothyroid groups shows significantly higher value (mean 22.545 ±8.46.77 U/L).

Table 5. Comparison of Age, TSH & ADA among study group

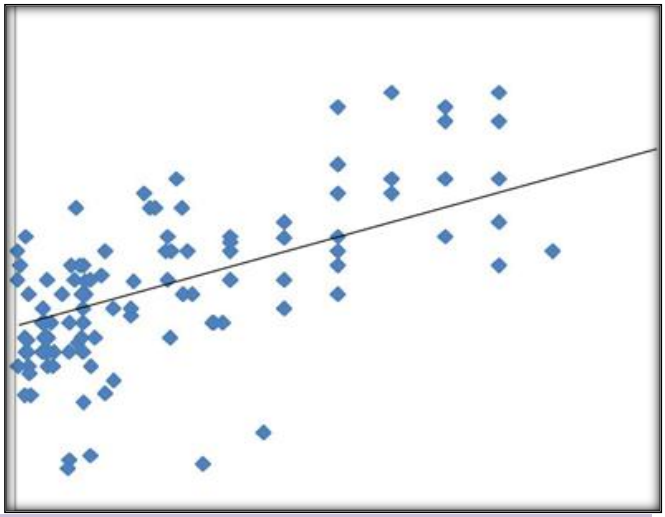
	HYPOTHYROIDISM		NORMAL	
	Mean	SD	Mean	SD
Age in Years	40.70	10.69	35.48	8.14
TSH (IU/ml)	7.09	1.72	1.896	1.029
ADA (U/L)	22.545	6.77	11.17	3.95

The mean age, TSH and ADA in hypothyroidism group is 40.70± 10.69, 7.09± 1.72 and 22.545±6.77 respectively. The mean age, TSH and ADA in normal group is 35.48± 8.14, 1.89± 1.29 and 11.17±3.95 respectively.

Table 6: Correlation of Serum TSH with other parameters

Correlation of Serum TSH with other	Pearson correlation	
Parameters	R	P
Age	0.003	0.972
ADA	0.395	0.000

A statistically significant positive correlation was observed between serum TSH and ADA levels(r=0.395;p=0.000).However, the correlation between TSH and age was not statistically significant (r=0.003;p=0.972).



Scatter plot 1: Serum TSH with Serum ADA

A positive correlation was observed between serum TSH and serum ADA levels.

Discussion

The following observations were noticed in the study

1. Serum ADA Level:

(a) The mean serum ADA level in hypothyroid patients was 22.545± 6.77 U/L which is significantly higher than that of euthyroid controls which is 11.17 ± 3.95U/L.

(b) Among the 40 hypothyroid patients 68% having high serum ADA level.

2. Serum TSH Level:

The mean value of serum TSH in hypothyroid patients is 7.09 ± 1.72 IU/ml and in euthyroid controls it is 1.896 ± 1.02 IU/ml

3. Serum TSH level showed a positive and statistically significant correlation with serum ADA level(p =0.000).
4. The Pearson correlation coefficient indicated a significant

positive correlation between serum TSH and Serum ADA levels among the study participants (r = +0.395).

Advancements in diagnostic methodologies and molecular biology have yielded significant insights into the epidemiology and aetiology of the widely prevalent thyroid diseases globally.[10] There is a notable increase in the incidence of thyroid diseases, particularly subclinical hypothyroidism.[11] The majority of persons with hypothyroidism in this study were aged 30-49 years, with females comprising 75% of the population. ADA in humans is mainly implicated in the formation and functioning of the immune system. ADA has important role in the epithelial cell differentiation, neurotransmission, and the maintenance of gestation.[12]

A comparable study by Rajendra Duwal indicated that females are significantly more susceptible to thyroid diseases in comparison to males, due to more susceptibility to exacerbated autoimmunity.[13] In comparison to normal euthyroid people, the ADA level was shown to be significantly higher in overt hyperthyroid and overt hypothyroid situations. The ADA level was dramatically elevated in cases of overt hyperthyroidism and Hypothyroid individuals in contrast to typical euthyroid persons. Our discovery aligns to the research conducted by Abbas et al,[14] in comparison to the study performed by Vishnu et al,[15] indicates that ADA levels in hyperthyroid individuals were within the normal range, which contradicts our study. We also observed a substantial variation in ADA intermediate tier between Group 2 and Groups 3, 4, and 5. Numerous research have been conducted on disorders like as Diabetes Mellitus exhibiting a notable elevation in ADA levels.[16-20] A study by Lu CF et al. revealed that serum ADA levels in Gestational diabetes patients were considerably elevated compared to those in healthy controls, and that these levels were closely associated with thyroid function.[21] Similar results were shown by Abed AH.[22] The current investigation revealed a notable increase in ADA levels in hypothyroid individuals compared to the control group. The elevated plasma ADA activity may result from atypical T-lymphocyte responses or proliferation and could indicate a pathogenic process involving its release into circulation. Many data indicates that the suppression of ADA is advantageous for alleviating certain disorders. Pentostatin is a powerful inhibitor of ADA that demonstrated anti-atherosclerotic effects in atherosclerotic mice by diminishing macrophage interaction and improving endothelial function.[23] In hyperthyroid pigs, the injection of pentostatin markedly increases adenosine levels and augmented the A1 adenosinergic system, which subsequently produced negative inotropic effects and may ultimately ameliorate myocardial ischemia.[24] Furthermore, a 2020 review indicated that some frequently used medications, including simvastatin, metoprolol, and aspirin, could markedly suppress ADA function at standard dosages.[25] Consequently, the inhibition of ADA in patients with Gestational diabetes is both promising and straightforward to execute. A major weakness of this study is its limited sample size and cross-sectional case control design. The relationship between serum ADA and Hs CRP and TSH was not examined due to small sample size and time constraints. Cause of thyroid disorders has not been taken into account in our study. Further research are necessary to ascertain the pathogenic role, if any, of increased ADA in thyroid dysfunctions.

Conclusion

1. Based on this study, it was shown that serum ADA level was quite high in hypothyroidism and the increase is significant compared to euthyroid controls
2. There is significant correlation between serum ADA with TSH in the study groups.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Owen CA., Jr. A review of auto-immunization in Hashimoto‘s disease. The Journal of Clinical Endocrinology & Metabolism. 1958;18(9):1015–1023
2. Wilson D K, Rudolph F B, Quiocho FA. "Atomic structure of adenosine deaminase complexed with a transition-state analog: understanding catalysis and immunodefi- ciency mutations". Science.May 1991 ;252 (5010): 1278– 1284.
3. Pospisilova H , Frebort I. Aminohydrolases acting on adenine, adenosine and their Derivative. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.2007 Jun; 151(1):3-10.
4. Hoshino T, Yamada K, Masuoka K, et al. Elevated adenosine deaminase activity in the serum of patients with DM. Diabetes Res Clin Pract .Sep 1994; 25: 97-102.
5. Sullivan J L, Osborne W R, Wedgewood R J. Adenosine deaminase activity in lymphocytes. Br J Haematol .1977 Sep; 37(1): 157-58.
6. Prakash MS, Chennaiah S,Murthy YSR, et al. Altered adenosine deaminase activity in Type 2 diabetes mellitus. JIACM .2006; 7(2): 114-7.
7. Cristalli G, Costanzi S, Lambertucci C, Lupidi G, Vittori S, Volpini R, Camaioni E. "Adenosine deaminase : functional implications and different classes of inhibitors". Medicinal Research Reviews .Mar 2001; 21 (2): 105–128.
8. Keffer JH: Preanalytical Considerations in testing thyroid function. Clin Chem 1996; 42:1, 1125-35.
9. Kobayashi F , Ikeda T , Marumo F , Sato C : Adenosine deaminase enzyme 88: 266 -271
10. Yazdaan HE, Jaya F, Sanjna F, Junaid M, Rasool S, Baig A, Natt MZ, Maurya N, Iqbal S, Yeldo BA, Khan AS, Varrassi G, Kumar S, Khatri M, Awan SK. Advances in Thyroid Function Tests: Precision Diagnostics and Clinical Implications. Cureus. 2023 Nov 17;15(11):e48961.
11. Yoo WS, Chung HK. Subclinical Hypothyroidism: Prevalence, Health Impact, and Treatment Landscape. Endocrinol Metab. 2021;36(3):500-513.
12. Kaljas Y, Liu C, Skaldin M, Wu C, Zhou Q, Lu Y, Aksentijevich I, Zavialov AV. Human adenosine deaminases ADA1 and ADA2 bind to different subsets of immune cells. Cell Mol Life Sci. 2017 Feb;74(3):555-570.
13. Duwal R, Khan SA, Das BK, Gelal B. Serum adenosine deaminase activity in thyroid disorders. Thyroid Res Pract 0;0:0.
14. Abbas AK, Kadhim FH, Waheeb ZT. A study on the relationship between thyroid hormones and adenosine deaminase enzyme activity in patients with auto- immune hyperthyroid disease. Iraqi

Post Med J 2008;7:164-7.
15. Vishnu M, Sampath KV, Mohanty S. Role of ADA in immunological disorders - Diabetes mellitus and thyroid dysfunction. J Health Sci 2013
16. Lee JG, Kang DG, Yu JR, Kim Y, Kim J, Koh G, et al. Changes in adenosine deaminase activity in patients with type 2 diabetes mellitus and effect of dpp-4 inhibitor treatment on ADA activity. Diabetes Metab J 2011;35:149-58.
17. Khemka VK, Bagchi D, Ghosh A, Sen O, Bir A, Chakrabarti S, et al. Raised serum adenosine deaminase level in nonobese type 2 diabetes mellitus. ScientificWorldJournal 2013;2013:404320.
18. Kurtul N, Pence S, Akarsu E, Kocoglu H, Aksoy Y, Aksoy H. Adenosine deaminase activity in the serum of type 2 diabetic patients. Acta Medica (Hradec Kralove) 2004;47:33-5.
19. Hoshino T, Yamada K, Masuoka K, Tsuboi I, Itoh K, Nonaka K, et al. Elevated adenosine deaminase activity in the serum of patients with diabetes mellitus. Diabetes Res Clin Pract 1994;25:97-102.
20. Prakash MS, Chennaiah S, Murthy YS, Anjaiah E, Rao SA, Suresh C. Altered adenosine deaminase activity in type 2 diabetes mellitus. J Indian Acad Clin Med 2006;7:114-7.
21. Lu CF, Liu WS, Ge XQ, Xu F, Su JB, Wang XQ, Wang Y. The association between serum adenosine deaminase levels and Graves' disease. Endocr Connect. 2021 Sep 28;10(10):1227-1233.
22. Abed AH, Altaee MF. Immunological Assessment of Human Adenosine Deaminase Activity in Iraqi Female With Thyroid Autoimmune Disease. The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90 (2), Page 2303-2307.
23. Kutryb B, Mierzejewska P, Slominska E , Smolenski RT. Therapeutic Perspectives of Adenosine Deaminase Inhibition in Cardiovascular Diseases. Molecules. 2020; 25. 4652.
24. Pak K, Zsuga J, Kepes Z, Erdei T, Varga B, Juhasz B, Szentmiklosi AJ, Gesztelyi R. The effect of adenosine deaminase inhibition on the A1 adenosinergic and M2 muscarinergic control of contractility in eu- and hyperthyroid guinea pig atria. Naunyn Schmiedebergs Arch Pharmacol. 2015 Aug;388(8):853-68.
25. Bagheri S, Saboury AA, Haertlé T. Adenosine deaminase inhibition. Int J Biol Macromol. 2019 Dec 1;141:1246-1257.