BIOSCIENCES BIOTECHNOLOGY RESEARCH ASIA, September 2024. Vol. **21**(3), p. 1137-1143

State of Adenosine Deaminase in Patients with Dyslipidemia

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http://dx.doi.org/10.13005/bbra/3292

(Received: 25 April 2024; accepted: 23 July 2024)

Dyslipidemia is becoming more common across all age groups mainly in young individuals because of imbalanced diets, low physical activity, and sedentary work culture. Several studies reported that elevated serum adenosine deaminase activity was associated with dyslipidemia, but the results were not consistent. It is aimed to correlate adenosine deaminase and lipid profile parameters in patients with dyslipidemia. In this case-control study, a total of 60 subjects (30 diagnosed dyslipidemia patients and 30 age and gender-matched healthy individuals) were enrolled. Serum lipid profile parameters and adenosine deaminase levels were estimated in each subject. The mean levels of lipid profiles, mainly triacylglycerol (TG), low-density lipoprotein-cholesterol (LDL-C), and adenosine deaminase, were found to be significantly high, while high-density lipoprotein-cholesterol (HDL-C) was found significantly low in cases than controls ($p < 0.001$). adenosine deaminase has not shown any significant correlation with lipid profile parameters in patients with dyslipidemia and controls. The result showed that the serum adenosine deaminase and serum lipid profile levels were altered in patients with dyslipidemia.

Keywords: Adenosine, Adenosine deaminase, Case-control study, Dyslipidemia, Lipid profile.

Dyslipidemia is becoming more common across all age groups mainly in young individuals, because of imbalanced diets, low physical activity, and sedentary work culture[1,3]. Dyslipidemia was linked to an increased risk of developing atherosclerotic coronary and peripheral arterial disease as well as cardiovascular diseases (CVD) in later life[2]. About 30% of the urban and 20% of the rural population of India is living with dyslipidemia[4]. Joshi et al reported that the prevalence of hypercholesterolemia and hypertriglyceridemia was found 13.9% and 29.5%, respectively. In addition, low high-density lipoprotein-cholesterol (HDL-C) was 72.3%, high low-density lipoprotein-cholesterol (LDL-C) was found at 1.8%, and 79% had shown lipid abnormalities in any one parameter of lipid profile in the Indian population[5]. The National

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Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP-III) criteria were used to classify dyslipidemia; when total cholesterol (TC)>200 mg/dl or LDL-C >130 mg/dl indicated hypercholesterolemia, while HDL-C <40 mg/dl indicated hypercholesterolemia. A diagnosis of hypertriglyceridemia was made when the plasma triglyceride (TG) level was more than 150 mg/dl[6]. Elevated TC and reduced HDL-C levels have been found in Asian Indians as compared to other ethnic groups[7,8].

Adenosine deaminase (ADA) is an enzyme of the purine catabolism pathway that converts adenosine to inosine by deamination[9]. It is expressed in various cells and tissues and plays a significant role in the proliferation and maturation of lymphocytes, monocytes, and macrophages[10]. Adenosine suppresses glycogen synthesis and stimulates glycogenolysis in hepatic cells[11]. Adenosine regulates cholesterol synthesis by the liver and affects circulatory levels of TC and TG and fat tissue amounts[12]. ADA activity has been associated with obesity[13], obesity-associated complications[14], type 2 diabetes mellitus (T2DM)[15], and CVD[16,17], illustrated in Figure 1.

Asian Indians are more prone to dyslipidemia and its-associated complications that increase the risk factors for coronary artery disease (CAD) and CVD. Studies reported that elevated serum adenosine deaminase (ADA) activity was associated with dyslipidemia, but results were not consistent. We aimed to correlate ADA and lipid profile parameters in patients with dyslipidemia.

MATERIALS AND METHODS

Selection of subject

Thecase-control study included 60 subjects (30 diagnosed dyslipidemia patients and 30 age and gender-matched controls) were included aged 25-60 years from the University Medical Hospital OutPatient Department (OPD) of Medicine. A detailed demographical and medical history has been taken from each subject. Informed written consent was taken from each study subject.

Inclusion of subject

Cases were diagnosed as per the guidelines of NCEP ATP-III[6].

Exclusion of subject

The subject has a medical history of type 1 or type 2 diabetes mellitus (type 1 or type 2), CVD, CAD, chronic kidney disease (CKD), liver cirrhosis, thyroid disorders, and infectious diseases such as tuberculosis, HIV, sexually transmitted diseases, hepatitis, and pregnant or lactating women were excluded from the study. The subject who was taking lipid-lowering medicine, such statin, was also excluded.

Collection of Sample

A total of 4 ml of peripheral venous blood was collected from each study subject in a plain vial after an overnight after 12 hours of fasting. It was centrifuged at 3000-4000 rpm for 5-10 min and the serum was separated and stored in a deep freezer (-20 °C) till further laboratory investigation.

Table 1. Clinical characteristics of cases and controls

Parameters	Cases (Mean ± SD) (n= 30)	Controls (Mean ± SD) (n= 30)	p-value
Age (years)	34.10±9.84	34.5±9.69	0.87
Gender (M/F)	22/8	20/10	0.78
TC (mg/dL)	256.12± 20.73	152.60 ± 26.42	<0.001*
TG (mg/dL)	159.63 ±40.91	100.93 ± 26.43	<0.001*
HDL-C (mg/dL)	40.20±6.27	51.23 ± 10.08	<0.001*
LDL-C (mg/dL)	103.03± 15.09	81.51± 21.22	<0.001*
VLDL-C (mg/dL)	32.04± 8.15	20.24± 5.28	<0.001*
ADA (IU/L)	35.22± 3.03	17.93 ± 5.32	<0.001*

Data represented as Mean ±SD.*p-value (< 0.05), considered statistically significant.
ADA: Adenosine Deaminase, HDL-C: High-Density Lipoprotein-Cholesterol, LDL-C: Low-Density Lipoprotein-Cholesterol, VLDL-C: Very Low-Density Lipoprotein-Cholesterol, TG: Total Triglyceride, TC: Total Cholesterol

Laboratory Investigation

ADA, TC, TG, and HDL-C were measured using the colorimetric method utilizing commercially available kits in Chemistry Semi-auto analyzer (Chem-7, Erba Diagnostics Pvt Ltd, Germany). LDL-C and VLDL-C were calculated by using Friedewald's formula[18-21].

Statistical Analysis

SPSS software (version 20.0) was used. Data were represented as Mean ± Standard deviation (SD). All quantitative clinical parameters were calculated in dyslipidemia patients and healthy control subjects. A p-value was calculated using a student unpaired *t-test*. A correlation analysis was performed on ADA and lipid profile parameters among cases and controls. A p-value (<0.05) was considered statistically significant.

RESULTS

Results showed that the mean levels of lipid profiles mainly TG and LDL-C and the ADA were found significantly elevated and HDL-C levels reduced in cases than controls ($p<0.001$), shown in Table 1. Mean of ADA levels in cases and controls is shown in Figure 2.

Results showed that ADA has not shown any significant association with lipid profile parameters in patients with dyslipidemia and controls as shown in Table 2.

DISCUSSION

Results showed that the mean levels of lipid profiles and ADA were found significantly elevated, while HDL-C was significantly reduced in cases than controls ($p<0.001$). Elevated lipid profiles mainly LDL-C and TG and decreased HDL-C in the blood are the primary diagnostic criteria of dyslipidemia[22]. Studies reported that mean levels of ADA were found to be significantly high in patients with dyslipidemia[23,24].

Results showed that ADA has not shown any significant association with lipid profiles in

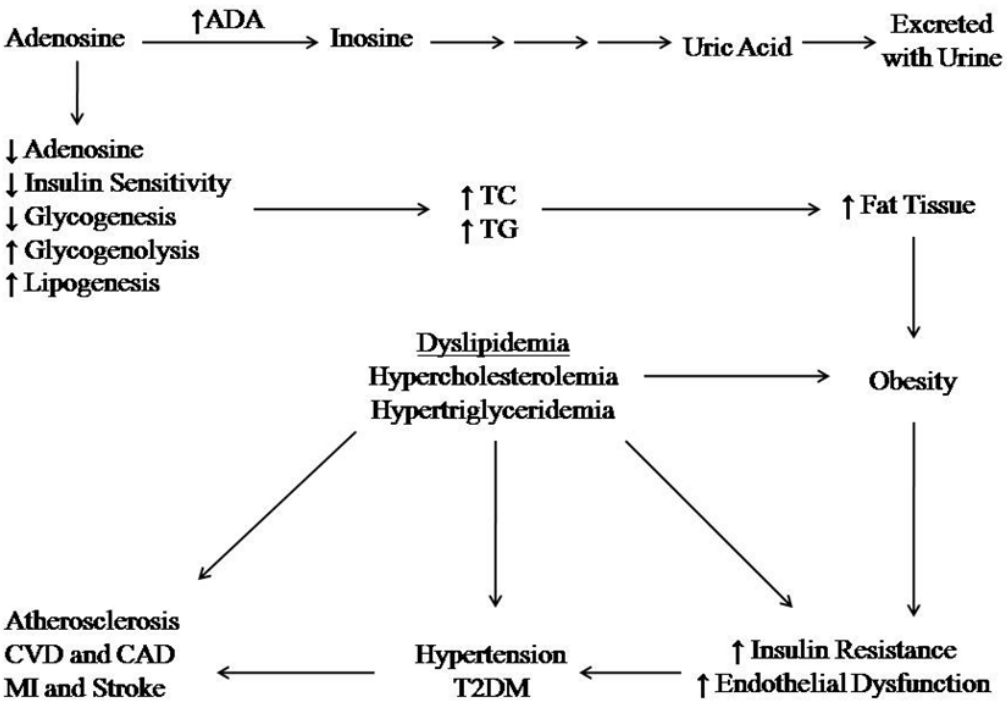

Fig. 1. Association of elevated ADA and dyslipidemia.
ADA: Adenosine deamianse, CAD: Coronary artery disease, CVD: Cardiovascular disease, MI: Myocardial infarction, TC: Total cholesterol, TG: Triglyceride, T2DM: Type 2 diabetes mellitus

patients with dyslipidemia and controls. Similarly, ADA has not shown any significant association with lipid profiles in patients with dyslipidemia[23]. However, it was reported that ADA has a significant association with hypercholesterolemia and LDL-C[25]. In addition, it was reported that serum ADA has shown a significant relationship with coronary artery calcification in patients with T2DM[26]. It was further suggested that ADA should be considered as a biomarker for atherosclerosis severity in patients with T2DM.

Table 2. Correlation of ADA (IU/L) and lipid profile among cases and controls

Parameters	Case (*r)*	Control (*r)*
Age (years)	-0.014	0.034
TC(mg/ dL)	-0.249	-0.051
TG(mg/dL)	0.217	-0.160
HDL-C(mg/dL)	-0.226	0.037
LDL-C(mg/dL)	-0.302	-0.042
VLDL-C(mg/dL)	0.221	-0.159

** 0.01 or *0.05 level (2-tailed) was considered significant correlation.ADA: Adenosine Deaminase. HDL-C: High-Density Lipoprotein-Cholesterol, LDL-C: Low Density Low-Density Lipoprotein-Cholesterol, TG: Total Triglyceride, TC: Total Cholesterol, VLDL-C: VLDL-C: Very Low Density Lipoprotein-Cholesterol

Abnormal TG and HDL-C levels are the main parameters for the diagnosis of metabolic syndrome along with fasting blood sugar, blood pressure, and waist circumference[6,27]. Dyslipidemia is a predictor of CVD and CAD. It is a leading cause of atherosclerosis and the pathophysiology of CVD[2]. Age shifting pattern was observed in the incidence of CVD and its associated mortality in the Indian population. The incidence of heart attack (10%) was observed in young individuals (< 40 years) and more than 50% of CVD-associated deaths were observed in old individuals (>70 years). CVD and CAD-associated deaths were three-fold higher in the Indian population than in other developed countries[28,29].

It is necessary to find new markers that can be used for early screening of dyslipidemia and its associated pathophysiology such as atherosclerosis, CVD, and CAD in the Indian population. ADA may play a significant role in this regard. However, ADA is a predictor of hyperglycemia and regulates insulin sensitivity. ADA activity increases with increasing glycated hemoglobin

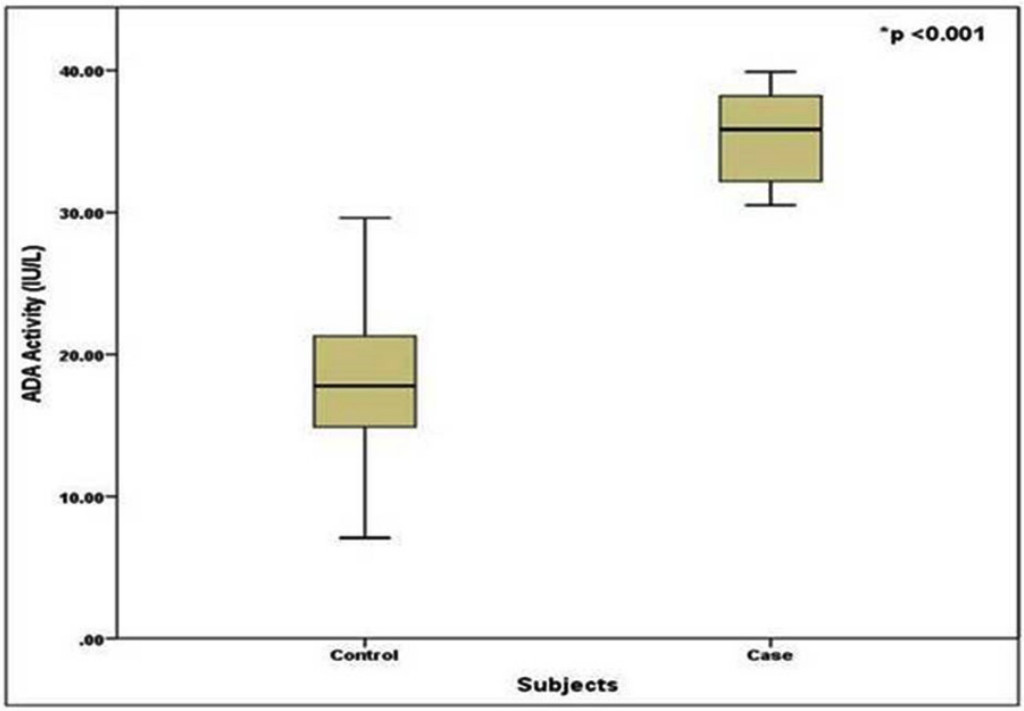

Fig. 2. Comparison of mean of Adenosine deaminase (ADA) levels between cases and controls

(HbA1c) in patients with T2DM[15]. Hyperglycemia causes an abnormal lipid profile, which resulting hypercholesterolemia and dyslipidemia[30]. In addition, oxidative stress triggers lipid peroxidation in patients with dyslipidemia which is a form of the oxidative marker malondialdehyde (MDA). Elevated MDA levels were reported in patients with hypertension and T2DM[31,32]. Hypertension and T2DM increase 2-4 times the risk of CVD, atherogenic dyslipidemia, and their associated morbidity and mortality[33].

CONCLUSION

The result showed that the serum ADA and serum lipid profile levels were altered in patients with dyslipidemia. This suggested that serum ADA levels to be assessed in dyslipidemia patients to redcue the further complications.

Limitations and future prospects of the study

The present study used a small sample size. Further study with a large sample size is required to verify the association between ADA and dyslipidemia. Because elevated ADA activity reduces the levels of adenosine by deamination. However, Adenosine regulates glucose and lipid metabolism. Elevated ADA activity and diminished adenosine levels altered the glucose and lipid metabolism resulting in dyslipidemia, T2DM, and CVD[12].

ACKNOWLEDGEMENT

We are grateful to the Prof. (Dr.) Abha Chandra, Dean, Integral Institute of Medical Sciences & Research (IIMSR) for the invaluable help and encouragement to carry out research work without any hindrance.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (IEC Approval No. IEC/IIMS&R/2022/16) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Written informed consent was obtained from all individual participants included in the study.

Funding

This study was not funded by any funding agency or company.

Conflicts Of Interest

Authors declared that they have no conflict of interest.

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