https://doi.org/10.15218/zjms.2023.001

Atherogenic index of plasma as a biomarker of atherogenecity in type 2 diabetes mellitus in Erbil city

Received: 29/11/2021 Accepted: 19/04/2022

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Abstract

Background and objective: Atherogenic index of plasma (AIP) is a mathematical method logarithmically ratio between concentrations of triglycerides to HDL-cholesterol, AIP= Log (TG/HDL), so AIP increase with increase triglycerides and reversible with HDL level. The aim of this study is to evaluation the AIP as a stronger biomarker of atherosclerosis among type 2 diabetes mellitus (DM).

Methods: This was a cross sectional-study contacted. A total of 65 patients of type 2 diabetic patient group from Laila Qasim Center for Diabetes in Erbil City collection of blood samples from 65 patients of type 2 diabetic patient group from Laila Qasim Center for Diabetes in Erbil City, compared with 50 healthy volunteers (control group). Blood samples were collected into serum separation tube (gel tube) and (K_3EDTA) tube, allowed gel tube to clot at room temperature for 5 minutes then centrifuged at 4000 round per minute (rpm). The separated serum was used immediately for biochemical tests and all the laboratory investigation analysis were carried out from 2nd January to 2nd August 2021.

Results: The results of this study found that the level of serum glucose, HbA1C, albumin, CRP, and AIP in diabetics were significantly higher than healthy group, while decreasing S. HDL in diabetic patients compare with healthy individuals.

Conclusion: The study detected high level of AIP in type 2 DM patients. Accordingly, patients with type 2 DM should be followed up with regular dietary lipid intake, take lipid lowering drugs, with exercise in order to diminish AIP.

Keywords: Serum lipids; Atherogenesis index of plasma; Atherogenecity; T2 diabetes mellitus.

Introduction

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia caused by absolute or relative deficiency of insulin.[1] Diabetes more common worldwide according to this data in the year 2017, 463 million people had diabetes worldwide, the rate of 8.8% among adults, while type 2 diabetes make 90% of cases this data show that the type 2 was very rare than type1 diabetes. Another study shows that the number of patients with diabetes mellitus globally has four times as many in the past three decades.[2]

Type 2 diabetes mellitus (T2DM) and its complications regard as the major disease problem, uncontrolled diabetes mostly cause morbidity and mortality.[3]

Uncontrolled T2DM is causes both microvascular (nephropathy, neuropathy, and retinopathy) and macrovascular complications, including ischemic heart disease, myocardial infarction (MI), peripheral vascular disease, and stroke.[4] T2DM often remains undiagnosed, because mostly asymptomatic nature of this condition, vascular complications may be already present in the early phases of the disease and even in the prediabetes stage[5].

Lipoproteins are complex compounds that transport different lipids byspecific proteins

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https://doi.org/10.15218/zjms.2023.001

called apoproteins in plasma. Lipoproteins are classified according to density, size and lipid/ protein ratio. The lipids are mainly free and esterified cholesterol, triglycerides, phospholipids. The hydrophobic triglyceride and cholesteryl esters found in core of the lipoproteins and surrounded by apoproteins, phospholipids and free cholesterol. Apo B100 is required for the secretion of hepatic-derived VLDL and LDL. Apo B48 is synthesized in epithelial cell of small intestine that is required for absorption of chylomicrons from the small intestine.[6]

Recent studies revealed that abnormal elevation of any or all lipids and/or lipoproteins except HDL, known as hyperlipidemia is considered as a problem risk factors that play an important role in the pathogenesis of atherosclerosis.[6]

There is a strong correlation between atherogenic index of plasma (AIP) and atherosclerosis, myocardial infarction and coronary heart disease.[7] AIP reflect the true relationship between protective and atherogenic lipoprotein and is related to size of pre- and anti- atherogenic lipoprotein particle.[8] Triglycerides and HDL-cholesterol in AIP reflect the balance between the atherogenic and antitherogenic lipoprotein respectively.[9] Using the AIP, calculated as log (TG/HDL), with TG and HDL-C expressed in molar concentrations.[10]

The aim of present study was to assess serum lipid profile, atherogenic index of plasma (AIP) in type 2 diabetes mellitus and to compare it with normal individuals, lipid profile includes total cholesterol, triglycerides, VLDL-C, LDL-C, HDL, and LDL/HDL ratio.

Methods

Design of the Study: This is a cross-sectional study.

The subjects of our study were classified into two groups:

Type 2 diabetic patients (group 1): sixty-five (65) patients with type 2 diabetics from Laila Qasim Center for diabetes in Erbil city, Healthy individuals (group 2): Control (50) subjects served as control; all were healthy volunteers and had no evidence for any blood diseases, were eligible for the study, all the laboratory investigation analysis was carried out from 2 January to 2 August 2021.

Fasting blood samples were collected from both groups using disposable syringes, 5 ml of venous blood samples from each subject collected in a gel tube for 15 minutes at room temperature. Serum was separated by centrifugation at 4000 rpm for five minutes, stored and frozen at -20 C. The clear serum samples were used for evaluation of serum total cholesterol, Triglycerides, LDL-cholesterol, HDL-cholesterol, glucose, HbA1C, CRP and albumin.

Determination of Serum Lipid Profiles and other biochemical compounds

Serum lipid profile (TC, TGs, LDL-C, HDL-C) and glucose, HbA1C, CRP, and albumin were estimated by using Cobas diagnostic kit (Roche/COBAS 311 INTEGRA), with fully automated chemical analyzer.[11] VLDL calculated by TG/5, AIP calculated by log (TG/HDL)[7].

Statistical Analysis

Data were analyzed using the statistical package for social sciences (SPSS, version 20). All descriptive data are expressed as mean± standard error of the mean (SEM) and standard deviation (SD) for selected variable. Differences between type 2 diabetes mellitus and controls were assessed using independent sample t-tests; Statistical significance was inferred at a two-tailed *P* value <0.001.

Results

Demographics of the type 2 Diabetes Patients and Healthy Controls

Demonstrated that the Mean ± SD, of each of age and body mass index (BMI), (Kg/M^2) indicated that BMI in T2DM was significantly higher than that of controls ($P = 0.004$).

The Mean ± SD, of each of lipid profile, indicated that each of S. triglycerides and

https://doi.org/10.15218/zjms.2023.001

S. cholesterol and S. LDL in type 2 diabetes were significantly higher than that of controls (P = 0.001), while S.HDL in type 2 diabetics was significantly lower than that of control group (P = 0.03), also AIP in type 2 diabetics was significantly lower than that of control group (P = 0.047).

The Mean ± SD, of each of S. glucose, HbA1C, CRP, and Albumin indicated that each of them in type 2 diabetic patients were significantly higher than that of control group. P <0.001, so all the parameters in T2 diabetic patients were highly significant compare with control group.

Table 1 Demographics (age and BMI) of the type 2 diabetes and healthy individuals

Groups	No.	Age (year) Mean ± SD	*P*-Value	Body mass index BMI (Kg/M^2) Mean ± SD	*P*-Value
T2DM	65	51.82± 11.924	<0.001	28.54± 3.7	0.004
Control	50	44.44± 15.71		24.36± 2.4	

Table 2 Mean ± SD of lipid profile levels (mg/dl) of control and diabetic patient groups

Parameters	Type 2 diabetic group NO. (65)	Control group NO. (50)	*P* value
S. Triglycerides(mg/dl)	220.27 ± 20.15	138.8± 6.55	0.001
S. Total cholesterol(mg/dl)	181.72± 5.74	161.72± 4.22	0.009
S.LDL(mg/dl)	121.95± 5.38	89.06± 2.74	0.001
S.HDL(mg/dl)	42.04± 1.02	44.38± 0.81	0.03
S. VLDL(mg/dl)	45.58± 6.24	27.76±1.5	0.001
LDL/HDL Ratio	2.9 ± 4.1	2.007 ± 5.65	0.078
AIP log(TG/HDL)	0.73± 0.103	0.50 ± 0.091	0.047

Table 3 Mean ± SD of serum glucose, HbA1c, albumin, and C-Reactive protein

Parameters	Type 2 diabetic (65)	Control group (5)	*P*-Value
Glucose (mg/dl)	253.38±15.97	99.48±1.6	< 0.001
HbA1C (%)	9.26± 0.26	5.49 ± 0.05	< 0.001
CRP (mg/L)	10.77 ± 2.24	1.01 ± 0.5	< 0.001
Albumin (g/dl)	4.17 ± 0.05	4.56 ± 0.09	< 0.001

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Discussion

The serum lipids and lipoproteins were including S. TCh, TGs, LDL, and HDL. In this study the mean of serum for each of the triglycerides, and LDL in type 2 DM were significantly higher than that of controls (*P* <0.001), total serum cholesterol in type 2 DM were significantly higher than control group (*P* <0.009). While S.HDL in type 2 DM group was significantly lower than control group (*P* <0.03). These results are in agreement with results obtained by other researchers.[12] Recent studies revealed that abnormal elevation of any or all lipids and/ or lipoproteins except S. HDL which known as hyperlipidemia is considered as modifiable risk factors that play an important role in the pathogenesis of atherosclerosis in type 2 DM, MI, and biological etiology of the ischemic stroke.[13] The atherogenic index of plasma (AIP),[14] which can reflect the characteristics of abnormal lipid metabolism in diabetic patients and can quantify the degree of abnormal lipid metabolism. In addition, the AIP is correlated with the degree of insulin resistance,[15] which can also correlate with the degree of abnormal glucose metabolism.

It has been reported that AIP plays as predictive risk for atherosclerosis,[7,16] and can be used as an available index of highest sensitivity for assessing cardiovascular risk factors, and acute coronary events.[17] Moreover, in situations where all atherogenic parameter are normal, AIP may be the alternative screening tool.[18] In this study most of participants didn't have any risk factor. This study was a national and provincial large scale survey that was a marked strength of it.[19]

Strengths and limitations

In this study, all subjects were representative of a limited geographical country region (Iran) and may not reflect the AIP patterns from the other countries. So, future large population based multi-center studies are recommended. Furthermore, our cross sectional study cannot conclude on causality or temporal trends. As a result, it is unclear if longitudinal changes in BMI, abdominal obesity or physical activity can result in corresponding changes in AIP.

Atherosclerosis occurs by a complex mechanism, and epidemiological studies suggest that the internationally recognized risk factors for coronary heart disease include; hyperlipidemia, hypertension, diabetes and smoking.[20] In type 2 diabetes, atherosclerosis by the same mechanism, lipids and inflammation can also cause damage to cardiovascular system.[20] There is a direct association between inflammatory cytokines, interleukins and matrix-metalloproteinase 12 (MMP-12), as well as an inverse association between MMP-12 and HDL.

Conclusion

Our study illustrated that AIP was significantly higher in type 2 diabetic patients. AIP may be useful as a biomarker of plasma atherogenecity. So, patients with type 2 DM should be followed up with diminishing AIP to normal level. In addition, we can advise to change in lifestyle, such as regular aerobic exercise, reducing weight, drug reducing lipid and also proper diet management.

Funding

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Sultana M, Akhter Y, Parvin M, Alam M, Naznin L, Wahab M. Lipid Profile Pattern in Type 2 Diabetes Mellitus Patients. JAFMC Bangladesh. 2018; 14(2):177–9. https://doi.org/10.3329/jafmc.v14i2.45903
2. Florian K, Barbara K, Stefan K, Claudia L, Lyudmyla K, Christa M. Plasma Concentrations of Afamin Are Associated with the Prevalence and Development of Metabolic Syndrome. Circulation: Cardiovascular Genetics. 2014; 7(6):822–9. DOI: 10.1161/CIRCGENETICS.113.000654.

3. Narayan KMV. Type 2 diabetes: why we are winning the battle but losing the war? Diabetes Care. 2016; 39(5):653–63. DOI: 10.2337/dc16-0205.
4. Ferdinando G, Michael B. "Oxidative stress and diabetic complications," Circulation Research. 2010;107(9):1058–70. DOI: 10.1161/CIRCRESAHA.110.223545
5. International diabetes foundation (IDF) Diabetes Atlas, 9th Edition. IDF. 2019. P. 13–9.
6. Young SG, Davies BSJ, Voss CV, Gin P, Weinstein MM, Tontonoz P, et al. GPIHBP1, an endothelial cell transporter for lipoprotein lipase. 2011; 52(11):1869–84. DOI: 10.1194/jlr.R018689
7. Asaad D A, Sultan A S, Hassan Z N. Atherogenic Index of Plasma among Type2 Diabetic Patients Cross-Sectional Study In Iraq. Medico Legal Update. 2020; 20(1):260–4 DOI: 10.37506/v20/i1/2020/mlu/194382
8. Dobiášová M, Frohlich J, Šedová M, Cheung MC, Brown BG. Cholesterol esterification and atherogenic index of plasma correlate with lipoprotein size and findings on coronary angiography. J Lipid Res. 2011; 52(3):566–71. DOI: 10.1194/jlr.P011668. PubMed: PMC3035693/
9. Okpa H, Enang O, Effa E. Comparative analysis of atherogenic index of plasma and is relationship with cardiovascular risk among patients with diabetes mellitus and concurrent diabetes mellitus with hypertension attending endocrinology clinic in a tertiary hospital in south Nigeria. IOSR-JDMS. 2015; 14(4):102–7. DOI: 10.9790/0853-1488102107
10. Tan M, Johns D, Glazer N. Pioglitazone reduces atherogenic index of plasma in patients with type 2 diabetes. Clin Chem. 2014; 50:1184-8. DOI: 10.1373/clinchem.2004.031757.
11. Carl A, David E. Tietz fundamentals of clinical chemistry and molecualar diagnosis.7th edition. 2015; 407–10.
12. Zheng Q, Kuo Z, Yueping L, Wanjun C, Zhijian W, Jianlong W, et al. The atherogenic index of plasma plays an important role in predicting the prognosis of type 2 diabetic subjects undergoing percutaneous coronary intervention: results from an observational cohort study in China. Cardiovascular Dialectology. 2020; 19(23):1–11. DOI: 10.1186/s12933-020-0989-8
13. Koskinas KC , Siontis GCM , Piccolo R, Franzone A , Haynes A, Rat-Wirtzler J, et al. Impact of diabetic status on outcomes after revascularization with drug-eluting stents in relation to coronary artery disease complexity: patient-level pooled analysis of 6081 patients. Circ Cardiovascular Interv. 2016; 9:e003255. DOI: 10.1161/CIRCINTERVENTIONS.115.003255.
14. Ting-Ting W, Ying G, Ying-Ying Z, Yi-Tong M, Xiang X. Atherogenic index of plasma (AIP): A novel predictive indicator for the coronary artery disease in postmenopausal women. Lipids in Health and Disease. 2018; 17:197. https://doi.org/10.1186/s12944-018-0828-z
15. Anping C, Guang L, Jiyan C, Xida L, Liwen L, Yingling Z. Increased serum level of Lp-PLA2 is independently associated with the severity of coronary artery diseases: a cross-sectional study of Chinese population. Cardiovascular Disorders 2015; 15:14. DOI: 10.1186/s12872-015-0001-9
16. Junmeng L, Ruiyue Y, Min Z, Wen M, Hongxia L, Haijian Z, et al. Fractional esterification rate of cholesterol in high-density lipoprotein associates with risk of coronary heart disease. Lipids in Health and Disease. 2017; 16:162. DOI: 10.1186/s12944-017-0545-z
17. Dadgarmoghaddam M, Khajedaluee M, Khaodem- Rezaiyan M, NiroumandSH,Abrishami M, Joya M, et al. Risk Factors for Non-Communicable Disease: a population based study in Mashhad (Iran). BJMMR. 2015; 7(6):503–11. DOI: 123456789/180358
18. Khazaal MS. Atherogenic Index of Plasma (AIP) As a Parameter in Predicting Cardiovascular Risk in Males Compared to the Conventional Dyslipidemia Indices (Cholesterol Ratios). Karbala J Med. 2013; 6(1):1506–13.
19. Liao J, Farmer J. Arterial stiffness as a risk factor for coronary artery disease. Curr Atheroscler Rep. 2014; 16:387. DOI: 10.1007/s11883-013-0387-8.
20. Kozakova M, Morizzo C, Goncalves I, Natali A, Nilsson J, Palombo C. Cardiovascular organ damage in type 2 diabetes mellitus: the role of lipids and inflammation. Cardiovasc Diabetol. 2019; 18:61. DOI: 10.1186/s12933-019-0865-6