Asian Journal of Biochemistry, Genetics and Molecular Biology

5(3): 24-30, 2020; Article no.AJBGMB.61228
ISSN: 2582-3698

Evaluation of Lipid Profile and Atherogenic Index of Plasma in Patients with Type 2 Diabetes (AIP = log TG/HDL-c)

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Authors' contributions

This work was carried out in collaboration among all authors. Author MD designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors NKOB, PMK and RNS managed the analyses of the study. Author EHMN managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJBGMB/2020/v5i330132
Editor(s):
(1) Dr. Theocharis Koufakis, Aristotle University, Greece.
Reviewers:
(1) Uzuazokaro M. Agatemor, Novena University, Nigeria.
(2) Dere Kwadjo Anicet Luc, Alassane Ouattara University, Côte d'Ivoire.
(3) Venkatesan Natarajan, Aditya Bangalore Institute of Pharmacy Education and Research, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/61228

Original Research Article

Received 10 July 2020
Accepted 16 September 2020
Published 25 September 2020

ABSTRACT

Aims: The objective of our study was to evaluate the lipid profile and the plasma atherogenicity index obtained from the log (TG / HDL-c) in diabetics patients.
Study Design: This is a comparative and analytical study.

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Place and Duration of Study: Sample: MARC SANKALE Centre at the Abass Ndao Hospital in Dakar (Senegal), CHNU/Fann Biochemistry Laboratory, from June 2018 to November 2019.
Controls: For each patient, a witness of the same sex and the same age ± 2 years was recruited.
Methodology: The lipid balance parameters were assayed using enzymatic techniques with the Cobas c311 system (Roche Diagnostics, Switzerland). Plasma atherogenicity indices for each patient were calculated (CT / HDL-c, LDL / HDL-c and Log (TG / HDL-c)).
Data analysis was performed using XLSTAT software and a p value <0.05 was considered to be a statistically significant difference.
Results: Our study concerned 100 subjects with type 2 diabetes. The average age was 50.5 ± 10.80 years old and the sex ratio was 0.58. Evaluation of lipid parameters had shown an increase in diabetic subjects compared to controls for total cholesterol (2.30 g / l) and LDL-cholesterol (1.40 g / l) with significant differences ($p < 0.001$). We also found that 11% of patients had a CT / HDL-c ratio > 4.5, while 8% had an LDL-c / HDL-c ratio > 3.5 and 26% of patients had a log (Tg / HDL- c) > 0.21.
Conclusion: Lipid disturbances constitute significant abnormalities in type 2 diabetic subjects and would predispose them to cardiovascular complications. However, IAP = log (TG / HDL-c) could be considered the most sensitive predictor of cardiovascular risk.

Keywords: Lipids; atherogenic risk; diabetes; plasma atherogenicity index.

1. INTRODUCTION

The term diabetes mellitus refers to a group of metabolic diseases characterized by chronic hyperglycemia resulting from a defect in insulin secretion or insulin action or both. Chronic hyperglycemia is ultimately associated with specific organ complications, particularly affecting eyes, kidneys, nerves, heart and vessels [1,2,3].

In 2014, 8.5% of the world's adult population over the age of 18 was affected by diabetes, that being 415 million people [4]. If no action is taken, this figure could rise to 642 million by 2040. The International Diabetes Federation (IDF) which provided these figures assessed that 5 million people in the world died from diabetes in 2015, that being one death every six seconds [4]. By its frequency of occurrence and its long-term complications, diabetes is a public health problem of global concern, both in industrialized and emerging countries [5]. Today, cardiovascular prevention is the major preoccupation for diabetics, especially type 2 diabetes: three quarters of them will die from a cardiovascular cause, half of them from a myocardial infarction [6]. Diabetes is in fact accompanied by an acceleration in the development of atherosclerosis. Although the causes of diabetic macroangiopathy are not yet well established, it is increasingly evident that they involve several factors: metabolic disorders (hyperglycemia, advanced glycation products, lipid disorders, hyperinsulinism), hypertension, inflammation and impaired coagulation properties. Among the risk factors, dyslipidemia plays a very important role. For this reason, some researchers suggest that HDL-cholesterol, apolipoproteins A1 and B, triglycerides and atherogenic indices CT/HDL-C and Apo B/Apo A1 could be considered as the main markers of cardiovascular risk factors [7,8]. In addition, the log plasma atherogenicity index (TG/HDL-c) has recently been developed [9,10,11] and may provide a better understanding of the pathogenesis of atherosclerosis and its clinical complications. Indeed, the responsibility for excess circulating LDL-c, the induction and perpetuation of arterial wall inflammation in response to attack, and the process of atheromatous plaque formation and instability are well demonstrated [12].

In this regard, the objective of our study was to evaluate the lipid profile and the plasma atherogenicity index (log (TG/HDL-c)) in subjects with type 2 diabetes.

2. MATERIALS AND METHODS

2.1 Place and Design of Study

This is an analytical study conducted at the Marc Sankale Centre at the Abass Ndao Hospital in Dakar (Senegal) and CHNU/Fann Biochemistry Laboratory.

2.2 Study Population

The recruitment of patient in this study was done in collaboration with the Marck Sankalé Centre of

the Abass Ndao Hospital in Dakar (Senegal). All consenting type 2 diabetic patients with microangiopathic complications were included. For each patient, a witness of the same sex and the same age ± 2 years was recruited. Pregnant women and non-consenting patients were not included.

2.3 Sampling

Blood samples were taken from fasting subjects, at rest and by venipuncture at the elbow groove with tourniquet. Blood was collected in a tube with Li heparinate for the quantitative analysis of lipid profile parameters.

2.4 Methods

Lipid profile parameters (total cholesterol, HDL-cholesterol, triglycerides) were tested using enzymatic techniques with the Cobas c311 system (Roche Diagnostics, Switzerland) and the LDL-cholesterol fraction was calculated using the Friedwald formula (LDL-c (g/l)) = Total Cholesterol - HDL-c - TG/5). The plasma atherogenicity indices for each patient were also calculated (CT/HDL-c, LDL-c/HDL-c and Log (TG/HDL-c)) [9].

2.5 Statistical Analysis

Data recording was performed in Excel and explored with XLSTAT 2019. The Student T-test was used to compare the average values and a p-value lower than 0.05 was considered as a statistically significant difference.

3. RESULTS

Our study included 100 patients monitored at the Marc Sankale Centre. The average age of our population was 50.5 years old with extremes of 32 and 87 years old. The distribution by sex had shown a sex ratio of 0.59 (see Table 1).

The average total cholesterol in diabetic subjects was 2.30 ±0.049 g/l compared to 1.72 g/l in control subjects. Comparison of average values showed a statistically significant difference ($p < 0.001$) (See Table). Similarly, for LDL-cholesterol, higher levels were found in diabetic subjects (1.39 g/l) compared to control subjects (0.97 g/l) and the comparison also showed a significant difference ($p<0.001$) (see Table 2). Furthermore, we also got a significant difference for HDL-cholesterol ($p<0.001$) and no significant difference was noticed for triglycerides ($p=0.12$) (See Table 2).

The Evaluation of plasma atherogenicity indices by our study enabled to find that 11% of patients had a CT/HDL-c ratio > 4.5 while 8% had an LDL-c/HDL-c ratio > 3.5. However, 6% of the subjects had an increase in both indices simultaneously. And for the Log (TG/HDL-c) > 0.21 a frequency of at least twice as high as the two previously mentioned indexes was found rating 26% (See Fig. 1).

Table 1. General characteristics of the study population

	Diabetics				Subjects			
	Minimum	**Mean**	**Maximum**	**SD**	**Minimum**	**Mean**	**Maximum**	**SD**
included	100				100			
Average age (years)	32	50.5	87	11.32	33	51.5	86	11.40
Sex ratio	0.59				0.59			
BMI	18.72	26.06	39.19	4.55	-			
Diabetes duration (years)	1	8.1	33	5.98	-			

BMI: Body Mass Index

Table 2. Comparison of the mean concentrations of the parameters of the lipid balance

	Diabetics	**Control Subjects**	**p**
Cholesterol total (g/l)	2.30	1.72	<0.001*
HDL-cholesterol (g/l)	0.75	0.54	0.006*
LDL-cholesterol (g/l)	1.40	0.97	<0.001*
Triglycerides (g/l)	0.76	1.09	0.12

** statistically significant difference*

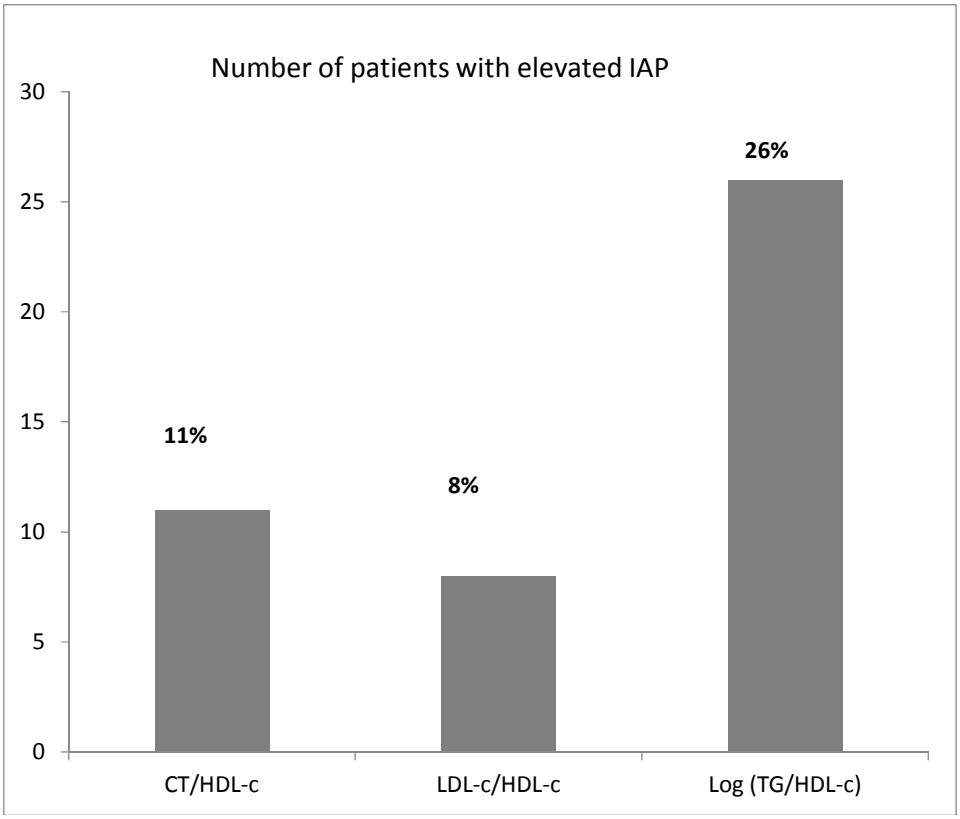

Fig. 1. Assessment of plasma atherogenicity indexes in our population

In patients with a CT/HDL-c ratio greater than 0.45, the study has found hypercholesterolemia at 2.58 g/l associated with an increase in LDL cholesterol with a level of 2.30 g/l (p= 0.005). Similarly, for patients with an LDL-c/LDL-c ratio greater than 0.35 the study found the same lipid disturbances with a significant difference for total cholesterol (p=0.048). However, in patients with a Log (TG/HDL-c) > 0.21, the evaluation of lipid parameters had found a hypercholesterolemia with an average value of 1.66 g /l. Moreover, higher values of lipid parameters were obtained in diabetic subjects with an index >0.21. The comparison of average values had shown significant differences for all lipid balance parameters (See Table 3).

4. DISCUSSION

Diabetes is a condition of chronic hyperglycemia that can lead to long-term complications. The latter can be of several types, but the highest prevalence is diabetic macroangiopathy, pathophysiology of which is partly based on lipid disturbances. This study therefore aims to evaluate lipid disorders in diabetic subjects and also to compare the value of the plasma atherogenicity index log (TG / HDL-c) compared to two other indexes previously used.

After data mining, we found that lipid disturbances were not uncommon in diabetic subjects. Thus, study's results showed that 71% of our study population presented at least one abnormality in one of the lipid profile parameters, Thus, the results of the study showed that 71% of the population in our study had at least one abnormality in one of the parameters of the lipid profile. Hypercholesterolemia predominated with 51%. In the literature, we have noted similar findings including the study by Rochdi H et al. carried out in 2017 on the prevalence of dyslipidemia in diabetics. They found that hypercholesterolemia was the most frequent dyslipidemia with 56% [13]. Moreover, Sow D and al. in their study (in 2016) in Dakar on 410 diabetic subjects had found hypercholesterolemia with a frequency of 55.62% thus corroborating our results [14]. Similarly, Sidibe AT and al. had found this increase in 54.6% of his study population in Mali [15]; in Morocco Azgaou I and al. had obtained an

increase in LDL cholesterol in 57.1% of the subjects included in the study [16]. It should also be noted that hypercholesterolemia found in our study is more related to an increase in LDL-cholesterol. The average LDL-cholesterol in our patients was 1.40 g/l against 0.97 g/l (<0.001) in controls. Similar results were also found by Ouhdouch F and al. in Marrakech with an average of 1.41 g/l. Indeed, type 2 diabetic patients with LDL cholesterol levels identical to those of a normal population, showed in vivo 28% decrease in LDL catabolism balanced by a decrease in their production [17]. Thus, despite a normal plasma level, LDL in diabetic patients show a slowdown of their catabolism, i.e. an increase in their plasma residence time, which may make them more atherogenic. This slowing of LDL catabolism is found to be partly linked to a decrease in the number of LDL receptors, as proven in vivo [18]. This decrease in the number of LDL receptors is found to be secondary to « relative » insulin deficiency. Indeed, the insulin is a factor inducing the expression of LDL receptors [19] while the insulin treatment in type 2 diabetics restores normal LDL receptor numbers [20].

Furthermore, hypertriglyceridemia was barely seen in our study (0.49%), but it is described during diabetes in the literature and is raised in several studies [21,22,23]. Hypertriglyceridemia in metabolic syndrome and type 2 diabetes is mainly due to an increase in VLDL and in IDL [21,24] but to a lower scale for the latter. Seventy percent of the increase in triglycerides is related to an increase in triglyceride-rich lipoproteins [25]. Also, there is an increase in the VLDL size with predominance of triglyceride-rich VLDL1 subfractions [21,26]. One of the mechanisms questioned in this hypertriglyceridemia is an increase in hepatic production of VLDL, more specifically the VLDL1 [27,28]. This is found to be related to several factors including an increase in substrates for triglyceride biosynthesis (free fatty acids), to a resistance to inhibitory effect of insulin on VLDL production and secretion, and, possibly to an increase in de novo lipogenesis in the hepatocyte [20].

We evaluated three plasma atherogenicity indexes in our population and the log (TG/HDL-c) proved to be the best index to detect atherogenic risk against the obtained frequency. In 2000, Dobiasova and Frohlich [29] suggested this parameter which is about the logarithm of the ratio of the molar concentration of triglycerides and the HDL-c. AIP is inversely correlated with LDL particle size. Thus, AIP in addition to quantitatively estimating the relationship between TG and HDL-c, is inversely correlated with LDL particle size. Therefore, it can be an effective surrogate for small LDL particle size to reflect diabetic dyslipidemia and assess the risk of type 2 diabetes. AIP reaches high positive values (>0.21) in 26% of patients in our study. Authors have stated that IAP reflects a balance between actual plasma TG and HDL-C concentrations, which may predetermine the direction of intravascular cholesterol transport [30].

Furthermore, the study noted that the use of this index has obvious limits: for example, on one hand in a group of very high-risk individuals with familial hypercholesterolemia, either homo or heterozygous, AIP may be low despite accelerated atherogenesis in these patients; on the other hand, in patients with familial hypertriglyceridemia (with low Apo B without a family history of vascular disease) or in patients with chylomicronemia, our index exaggerated the risks.

However, despite these exceptions, we believe that AIP remains important in the evaluation of lipid disorders in cardiovascular disease. Indeed, it is derived from more precise measurements of atherogenic lipoprotein profiles such as fractional cholesterol esterification rate and LDL particle size. Also, given the wide availability of TG and HDL-C values, this index can be used in common practice as an alternative marker of plasma atherogenicity [31].

Table 3. Comparison of lipid parameters between patients with normal or elevated IAP

	Log (TG/HDL-C) > 0.21	Log (TG/HDL-C) normal	p
Cholestérol Total (g/l)	2.32	2.27	0.006 *
HDL-cholestérol (g/l)	0.48	0.79	0.001 *
LDL-cholestérol (g/l)	1.66	1.31	< 0.001*
Triglycérides (g/l)	1.13	0.81	< 0.001*

statistically significant difference

5. CONCLUSION

Diabetes and dyslipidemia pair expose patients to a high risk of cardiovascular disease and more specifically to diabetic macroangiopathy. In this study, AIP (log TG/HDL-c) is found to be a predictive, relevant and delicate marker for the diagnosis of patients at risk and thus enables their rapid care.

CONSENT

Written and informed consent was obtained from each participant.

ETHICAL APPROVAL

The conduct of this study was approved by the Research Ethics Committee (CER) of Cheikh Anta Diop University (UCAD) according to the rules issued by the National Ethics Committee for Health Research (CNERS) of Senegal under number: 0227/2017 / CER / UCAD.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/61228