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Original Article

Lipid Profile, Renal Function Tests and Inflammatory Markers in Algerian Type 2 Diabetic Patients

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Abstract

Background: Several studies show the relationship between chronic hyperglycemia and the appearance of macroangiopathy, microangiopathy and neuropathy.The major objective of this study was to investigate the serum lipids, renal function tests and inflammatory markersin type 2 diabetes patients.

Methods: The study lasted eight years between Feb-2013 and Mar-2021 (Mascara, Algeria). Overall,197 patients and 197 controls were selected during general medicine examinations;enzymatic and immunoturbidimetric colorimetric methods were used to determine the serum levels offasting glycaemia, total cholesterol, highdensity lipoprotein cholesterol, triglycerides, low-density lipoprotein cholesterol, fibrinogen, urea, acid uric, albumin and creatinine, C protein reactive; the glomerular filtration rate is calculated according to the MDRD equation; the glycatedhaemoglobin levels were determined by an ion-exchange resin separation method.

Results: Patients had 2.44 times higher fasting glycaemia, 1.71 times higher HbA1c, 1.23 times higher body mass index, 1.30 times higher waist circumference and 1.25times higher systolic blood pressure than control subjects; the findings of the present study also indicate that a significant differences between patients and controls were observed regarding triglycerides (*P*=0.008), LDL-cholesterol*(P*=0.011), HDL-cholesterol (*P*=0.009), urea (*P*=0.013), uric acid (*P*=0.015), creatinine (*P*=0.007), glomerular filtration rate (*P*=0.006), albumin (*P*=0.018),fibrinogen (*P*=0.023) and C protein reactive (*P*=0.019).

Conclusion: All this metabolic disordercould facilitate the appearance of serious complications in future.

Keywords: C-reactive protein; Glomerular filtration rate; Serum lipids; Type 2 diabetes

Introduction

Diabetes mellitus is disorder of carbohydrate metabolism characterized by impaired ability of the body to produce or respond to insulin and thereby maintain proper levels of glucose in the blood (1).

Type 2 diabetes mellitus affects 392 million people worldwide (2), 17.7 million Americans (3), 31.7 million Indian (4) and 8.15 million Iranian (5), in Algeria, this disease affects 10.5% of the population (6). The emergence of the non-insulin-dependent diabetes mellitus is linked to a lifestyle like imbalance diet and physical inactivity (7), also smoking, drink, stress and anxiety (8).

Obesity is a major risk factor for non-insulin-dependent diabetes mellitus, regardless of gender, age or ethnicity (9). Clinical data points to a

stronger association of diabetes with android obesity like waist circumference (10) and general obesity as well as weight and body mass index (11, 12).

Type 2 diabetes mellitus is a major cause of microvascular disease, (including coronary heart disease and peripheral arterial disease) and microvascular disease (13), (including retinal and renal vascular disease), as well as nerve diseases (14).

Dyslipidemia is one of the main risk factors of cardiovascular disease in type 2 diabetes mellitus (15). The features of diabetic dyslipidemia are hypertriglyceridemia, low HDL cholesterol levels and increased level of small dense LDL-cholesterol particles (16). The lipid changes related with diabetes mellitus are associated to increased free fatty acid flux and insulin resistance (17).

Diabetic nephropathy is one of the leading causes of end-stage renal disease and mortality in type 2 diabetic patients (18). Diabetic nephropathy is characterized by four blood biomarkers that are albumin, urea, uric acid, and creatinine and estimated glomerular filtration rate (19).

Inflammatory Markers, including C protein reactive and fibrinogen, are increased in subjects with type 2 diabetes (20). Elevated levels of CRP and fibrinogen may be used for early diagnosis of non-insulin-dependent diabetes mellitus and can predict chronic diabetic complications (21).

We aimedto investigate the serum lipids, renal function tests and inflammatory markers in Algerian non-insulin-dependent diabetes mellitus patients compared to control subjects.

Materials and Methods

The study lasted eight years between Feb-2013 and Mar-2021 in the Department of General Medicine of Youcef Damardji hospital (Tiaret, Algeria), Meslem Tayeb hospital and Abdellah Ali Boukeroucha hospital (Mascara, Algeria).

The research protocol was validated by the public health officer of cities of Tiaret and Mascara, Algeria according to article 25 of the decree No. 387 of July 31, 2006 on ethical trials. In addition, the purpose of the study was explained to all participants and investigation was carried out with their written consent.

The investigated cohort was selected during general medicine examinations; study subjects were 197 controls who were not suffering from type 2 diabetes mellitus of median age 51± 5.35 yr and 197 volunteers of median age 54 ± 4.08 yr with a confirmed type 2 diabetes mellitus diagnosis for at least since two years and taking antidiuretic medications. The inclusion criteria were subjects aged between 40 and 60 yr of both gender; the type 2 diabetes mellitus was defined according to the WHO(22): A Fasting glycemia: ≥7.00 mmol/L and HbA1c level is ≥6.5%. Patients under lipid-lowering drugs during the investigation, as well as those with hypothyroidism, hepatic dysfunction and gestating woman were excluded from this research.

Anthropometry

Anthropometric indicators were taken in the morning while subjects minimally clothed without shoes. Weight was measured using a digital scale (SECA 869, Germany, Capacity: 250 kg, Graduations: 100 g) and height was measured using a portable stadiometer (SECA 214, Germany; measuring range: 220 cm, graduation: 1 mm). The body mass index (BMI) was then calculated as follows: BMI (kg/m^2) = weight (kg)/height^2 (m^2). Waist circumference (WC) was measured at the midway between iliac crest and lower rib margin, without depressing the skin, using unstretchable tape (SECA 203, measuring range: 200 cm, Graduation: 1 mm), without any pressure to body surface. Blood pressure was measured for all subjects in the study using a standardized mercury sphygmomanometer in the right arm in sitting posture(PIC, Italia).

Lipid and glycemicprofile

Venous blood samples were collected 12 h after a nocturnal fast. Enzymatic colorimetric methods (GOD-PAP, Allemagne) were used to determine the serum concentrations of glucose. Theglycatedhaemoglobin(HbA1c) levels were deter-

mined by an ion-exchange resin separation method (Spinreact Reagents, Spain).The serum lipidssuch as total cholesterol level, LDL-cholesterol and HDL-cholesterol were determined by the colorimetric enzymatic method with cholesterol esterase, cholesterol oxidase and peroxidase (Biocon, Allmagne). Triglyceride level was quantified by colorimetric enzymatic method with lipase, glycerokinase and glycerophosphate oxidase (Biocon, Allmagne).

Renal function tests and inflammatory markers

Fibrinogen level was determined by the enzymatic method with thrombin (Cypress, Belgique). C protein reactive level (CRP) was quantified by the immunoturbidimetric method (Biolabo, France). Urea level was determined by the kinetic enzymatic technique with urease-GLDH (Biocon, Allmagne). The uric acid level was determined by the enzymatic technique with uricase-peroxidase (Biocon, Allmagne). Albumin was determined by a colorimetric method with bromocresol green (Biolabo, France). The creatinine level was quantified by the reaction of Jaffé with alkaline picrate (Biocon, Allmagne). Glomerular filtration rate (GFR) was obtained by the abbreviated MDRD (Modification of Diet in Renal Disease study) equation: GFR (ml/min/1.73 m2) = 186.3 × (serum Cr)$^{-1.154}$ × (age)$^{-0.203}$ (×0.742 in female) (23).

Statistical analysis

Data were analyzed by SPSS software version 15.0 (IBM Corporation; Chicago, IL). Results are expressed as average ± standard deviations. Independent Student's t-test was used for comparing mean values between the two groups (patient's *vs* controls). A *P*-value lower than 0.05 was considered statistically significant with a 95% confidence interval (95% CI).

Results

Anamnesis

The Table 1 below illustrates some of the main characteristics of the studied population. A significant differences between patients and controls were observed regarding fasting glycaemia (*P*=0.002), HbA1c (*P*=0.003), body weight (*P*=0.005), Body mass index (*P*=0.019), Waist circumference (*P*=0.004) and Systolic blood pressure (*P*=0.036). Whereas, no significant differences were found between type 2 diabetic patients and control subjects regarding Height and Diastolic blood pressure (Table 1).

Table 1: Anamnesis of the studied population

Characteristics	*T2DP (n = 197)*		*Controls (n = 197)*		**P-value*
	X ± SD	95% CI	X ± SD	95% CI	
Age (yr)	54 ± 4.08	48 – 57	51 ± 5.35	42 – 55	0.958
Gender ratio (Mens/Women)	99 / 98		99 / 98		
Fasting glycaemia (mmol/L)	13.8 ± 1.83	11.05 – 14.03	5.65 ± 0.53	5.02 – 6.11	0.002
HbA1c (%)	10.51 ± 1.35	8.91 – 12.13	6.12 ± 1.02	5.44 – 7.21	0.003
Anthropometry					
Body weight (Kg)	80.03 ± 5.64	73.89 – 91.63	67.18 ± 3.71	61.74 – 71.35	0.005
Height (m)	1.61 ± 0.09	1.52 – 1.69	1.64 ± 0.07	1.59 – 1.77	0.827
BMI (Kg/m²)	30.87 ± 3.97	25.89 – 34.54	24.98 ± 1.76	20.06 – 26.19	0.019
WC (cm)	104.16 ± 9.58	82.27 – 109.71	79.61 ± 2.74	78.91 – 96.05	0.004
Blood pressure					
SBP (mm Hg)	13.93 ± 0.85	12.97 – 15.43	11.09 ± 1.01	10.32 – 12.21	0.036
DBP (mm Hg)	7.53 ± 0.92	7.46 – 8.78	6,87 ± 1.11	6.82 – 8.05	0.625

**P*-value: Significant difference between type 2 diabetic patients and controls using independent sample Student's *t*-test; T2DP: Type 2 diabetic patients; X: Average; SD: Standard deviation; CI: Confidence interval, HbA1c: glycatedhaemoglobin; BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Lipid profile

Table 2presents serum lipids levels. We noted a significant increase in triglycerides and LDL-Cho with 132% and 32%, respectively. However, the results indicate a significant decrease in HDL-Cho with 55% in patients compared to control subjects.

Renal function tests and inflammatory markers

Renal function tests and inflammatory markers are reported in Table 2. The logistic regression analysis shows that type 2 diabetic patients had 1.65 times higher urea, 1.12 times higher uric acid, 1.87 times higher creatinine, 1.35 times higher fibrinogen, 1.63 times higher C reactive protein levels, 1.85 times lower glomerular filtration rate (GFR) and 1.91 times lower albumin than control subjects, which was statistically significant (P<0.05).

Table 2: Serum lipids, renal function tests and inflammatory markers of the studied population

Characteristics	*T2DP (n = 197)*		*Controls (n = 197)*		**P-value*
	X ± SD	95% CI	X ± SD	95% CI	
Serum lipids					
Triglycerides (mmol/L)	1.81 ± 0.58	1.52 - 2.03	0.78 ± 0.31	0.69-0.82	0.008
Total cholesterol (mmol/L)	3.36 ± 0.27	3.07 - 3.62	3.34 ± 0.19	3.27 - 3.46	0.972
LDL-Cholesterol (mmol/L)	2.02 ± 0.41	1.74 - 2.36	1.53 ± 0.32	1.41 - 1.66	0.011
HDL-Cholesterol (mmol/L)	0.29 ± 0.08	0.22 - 0.35	0.65 ± 0.12	0.59 - 0.73	0.009
Renal function tests					
Urea (mmol/L)	8.11 ± 2.42	7.05 - 8.89	4.91 ± 0.37	4.70 - 5.05	0.013
Uric acid (µmol/L)	351.6 ± 62.07	312.57 - 390.84	219.8 ± 34.63	204.09- 237.02	0.015
Creatinine (µmol/L)	139.01 ± 27.53	113.28 - 173.92	74.11 ± 13.17	70.21 - 77.5	0.007
GFR (ml/min)	58.00 ± 12.57	41.55 - 76.01	107.39 ± 37.61	94.67 - 115.58	0.006
Albumin (g/L)	30.94 ± 5.13	23.62 - 41.05	59.17 ± 4.83	58.03 - 66.01	0.018
Inflammatory markers					
Fibrinogen (g/L)	1.67 ± 0.34	1.60 - 1.87	1.23 ± 0.19	1.12 - 1.4	0.023
CRP (g/L)	1.42 ± 0.27	1.29 - 1.94	0.87 ± 0.12	0.8 - 0.97	0.019

*P-value: significant difference between type 2 diabetic patients and controls using independent sample Student's t-test; T2DP: type 2 diabetic patients; X: average; SD: standard deviation; CI: confidence interval, GFR: Glomerular filtration rate; CRP: C protein reactive

Discussion

As mentioned in the literature review, HbA1c level is an indicator of the average blood glucose concentrations over the preceding 2 to 3 months that is recommended by IDF for the diagnosis of diabetes (24). The results of this study showed that patients had 1.71 times higher HbA1c and 2.44 times higher fasting glycaemia than control subjects; these results are consistent with those of other studies and suggest that an increased mortality risk and cardiovascular events are associated with elevated HbA1c levels in non-insulin-dependent diabetes mellitus patients (25-28).Patients had an increase in body weight, body mass index and waist circumference; this finding corroborates the ideas that suggested waist circumference and body mass index are predictive of future type 2 diabetes mellitus (29). On the other hand, the systolic blood pressure was significantly greater among the diabetics than the controls; that is 13.93 mm Hg, compared to 11.09 mm Hg. These findings seem to support several studies describing that patients with diabetes mellitus experience increased peripheral artery resistance caused by vascular remodeling

and increased body fluid volume associated with insulin resistance-induced hyperinsulinemia and hyperglycemia,both of these mechanisms elevate systolic blood pressure (30-33).

We noted a significant increase in triglycerides levels in patients compared to controls. Insulin resistance is the primary mechanism leading to lipid derangements in individuals with diabetes (34-36), resistance to insulin increases the release of free fatty acids from adipose tissue, taken up by the liver; increased hepatic uptake of free fatty acids leads to more synthesis of triglycerides (37-40).Dyslipidemia observed in patients is related to the increase in LDL-Cholesterol levels (41, 42), however, the HDL-Cholesterol levels is decreased (43, 44), the pattern of dyslipidemia usually presents with elevated triglycerides and small dense LDL and reduced levels of high density lipoprotein cholesterol (45-47), small dense LDL particles are more atherogenic and are associated with a higher rate of nephropathy and an elevated risk for cardiovascular disease (48-51), individuals with diabetes have also been noted to have lower HDL-Cholesterol levels (52-54).

Our results indicated an increase in urea, creatinine and uric acid levels. Moreover, there was a decrease in glomerular filtration rate (GFR) and albumin levels, the patients are at risk of kidney failure (nephropathy) (55-59), in fact, hyperglycemia play a role in the development of diabetic nephropathy include advanced glycosylation end products (AGEs) (60-63).Statistical tests revealed a significant increase in fibrinogen and C reactive protein (CRP) levels in patients compared with controls. In addition, high levels of fibrinogen are associated with obesity, type 2 diabetes mellitus, hypertriglyceridemia, and a risk of coronary ischemia (64-67). On the other hand, the increase of the CRP levels is correlated with atherosclerosis (68-70), in fact, CRP can bind to LDL and the complex CRP/LDL activates the phagocytic function of macrophages, the origin of the foam cells during the development of atheroma (71-74).

Conclusion

Our work has confirmed a decline in kidney function. While urea, creatinine and uric acid levels were significantly increased, glomerular filtration rate were reduced. Moreover, this study indicated a significant increase in fibrinogen, CRP, triglycerides and LDL-Cholesterol levels but HDL-Cholesterol level was decreased.

We propose to evaluate oxidatif stress in type 2 diabetes mellitus (Oxidant status and Antioxidant status) which represent indicators of appearance of serious complications, in future. For this, the adaptation of a healthy lifestyle by increasing physical activity, weight loss and maintaining a diet rich in plant foods, antioxidants and fiber as Mediterranean diet could provide for the installation of non-insulin-dependent diabetes mellitus.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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