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Original Research Article

Assessment of Lipid Profile and Inflammatory Markers in Stress Induced Diabetic Nephropathy Patients

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Abstract: Background: Several studies show the relationship between chronic hyperglycemia and the appearance of macroangiopathy, microangiopathy and nephropathy.The major objective of this study was to investigate the serum lipids, renal function tests and inflammatory markersin type 2 diabetes patients.
Methods: Haemoglobin A1c (HbA1c) and the lipid profile were assessed in plasma using an automated analyser called Integra 400 Plus (Roche Diagnostics, Germany). Additionally, turbidimetry, fluorescence polarimetry, and absorbance photometry were used. Electrochemiluminescence (ECL) was used to assess ApoA, ApoB, and hs-CRP for immunoassay analysis using a Cobas .
Results: In the DN group, inflammatory bio- markers (IL-6, TNF-α, and hs-CRP) had significant positive correlations with TC (P=0.003, P=0.001, P= 0.001).Further, TNF-αlevels showed a significant positive correlation with BMI (P=0.006) and SBP (P=0.039). In the control group, IL-6, TNF-α, and hs-CRP levels had significant positive correlations with WC (P=0.019, P<0.001, and P<0.001, respectively). Further, TNF-α had a significant positive correlation with BMI (r=0.535, P<0.001), DBP (P=0.010), TC (P=0.044), and ApoB(P=0.003); and a negative correla- tion with HDL (P=0.026).
Conclusion: Subclinical inflammation and ED were detected in young patients with T1DM compared to con- trols. This study revealed that lipid levels, liver enzymes, and inflammatory and ED biomarkers were significantly high- er in the DN group than the control group. Our work has confirmed a decline in kidney function

1. INTRODUCTION

Type 2 diabetic nephropathy (DN) can be classified into many phases based on renal haemodynamics, systemic blood pressure, urine results, and sensitivity to therapeutic therapies. Most type 2 DN patients had high glycosylated haemoglobin (HbA1c) values, which indicated uncontrolled diabetes (1).Immune-inflammatory abnormalities in type 2 diabetics are related with cell-mediated responses, abnormal T-lymphocyte function, and low-grade inflammatory state, all of which contribute to increased oxidative stress associated with type 2 DN. Inflammation and oxidative stress are inextricably linked and are known to play major roles in diabetic vascular problems (2).

India has the highest rate of type 2 diabetes, with an increasing frequency of diabetic neuropathic pain. Given the foregoing, the current study aims to investigate the relationship

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between blood glucose levels, HbA1c, lipid profiles, immune-inflammatory markers (ADA & CRP), oxidative stress markers (MDA, NO & COMET), and their susceptibility to patients with type 2 diabetes and the development of end-stage renal disease (ESRD).In T1DM, endothelial dysfunction (ED) and inflammation have been found to be early indicators of vascular illness (3). Furthermore, by hastening the development of atherosclerotic plaques, the emergence of a pro-inflammatory state throughout childhood may have a significant role in the later development of CVD.(4,5)

In young patients with type 1 diabetes, the study sought to ascertain the relationship between several indicators of lipid profile, inflammation, and ED. The purpose of this study was to ascertain the relationship between: (1) serum lipid levels (high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), total cholesterol (TC), lipoprotein-(Aa) (ApoA), and lipoprotein-B (ApoB)); (2) markers of inflammation (interleukin-6 (IL-6), adiponectin, tumour necrosis factor-α (TNF-α), and C-reactive protein (hs-CRP)); and (3) ED biomarkers (intracellular adhesion molecule-1 (ICAM), vascular cell adhesion molecule-1 in cases with stress-induced diabetic nephropathic patients).

2. MATERIALS AND METHODS

Study subjects
The study population comprised 120 participants in total, comprising patients enrolled from the Department of Nephrology and an index medical college number of healthy persons from the local community who were free of systemic illnesses (medical history & physical examination)

The study's inclusion criteria were met by all type 2 DN patients who had been diagnosed with the disease for at least five years, with fasting blood sugar levels greater than 110 mg/dl and postprandial blood sugar levels greater than 140 mg/dl, respectively, and serum creatinine levels between 40 and 60 years old in both genders.
Exclusion criteria: Participants in the trial were not allowed to have AIDS, cancer, congestive heart failure, liver illness, or systemic inflammatory disease. The study excluded patients receiving therapy with ACE inhibitors, lipid-lowering medications, anti-inflammatory pharmaceuticals, antioxidant supplements, and multivitamins.

Methods:
Haemoglobin A1c (HbA1c) and the lipid profile were assessed in plasma using an automated analyser called Integra 400 Plus (Roche Diagnostics, Germany). Additionally, turbidimetry, fluorescence polarimetry, and absorbance photometry were used. Electrochemiluminescence (ECL) was used to assess ApoA, ApoB, and hs-CRP for immunoassay analysis using a Cobas e411 (Roche Diagnostic, Mannheim, Germany). To quantify TNF-α (KHC3011) and IL-6 (EH2IL6), enzyme-linked immunosorbent assays (Invitrogen, Thermo Fischer Scientific Systems) were employed

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3. RESULTS

Table 1. Anthropometric and clinical variables for the study participants				
All study subjects (n=120)		Cases (DN) (n=60)	Control (n=60)	*p-value*
Age (y)	40.3 ± 6.6	41 ± 6.4	40.2 ± 6.8	
Gender, n (%)				
Female	80 (60.3)	80 (59.5)	75 (61.2)	0.764
Male	40 (39.7)	40 (40.5)	45 (38.9)	
Diabetes duration (y)	-	9.3 ± 5.7	-	
BMI (kg/m^2)	24.2 ± 5.5	24.8 ± 5.3	23.7 ± 5.7	0.007
WC (cm)	79.2 ± 15.6	80.6 ± 13.7	77.9 ± 17.2	0.033
SBP (mm Hg)	126.0 ± 10.9	128.0 ± 10.8	114.0 ± 10.6	<0.001
DBP (mm Hg)	72.3 ± 8.8	73.0 ± 10.1	71.5 ± 7.3	0.005
Data are presented as mean ± SD unless otherwise indicated.				

Table 2. Lipid profile values, and inflammatory and endothelial dysfunction biomarkerlevels in the T1DM and control groups				
	All study subjects (n=120)	Cases (DN) (n=60)	Control (n=60)	*P-Value*
Lipid Profiles				
HDL (mmol/L)	1.6 ± 0.9	1.7 ± 0.6	1.5 ± 0.4	<0.001
LDL (mmol/L)	2.6 ± 0.8	2.6 ± 0.8	2.6 ± 0.8	0.558
TG (mmol/L)	1.4 ± 1.7	1.8 ± 2.3	0.9 ± 0.5	0.003
TC (mmol/L)	4.9 ± 1.5	5.7 ± 1.9	4.3 ± 0.9	<0.001
ApoA (g/L)	1.9 ± 0.7	2.3 ± 0.8	1.6 ± 0.4	<0.001
ApoB (g/L)	1.1 ± 0.5	1.6 ± 0.5	0.9 ± 0.2	<0.001
Glycemic Profile				
HbA1c (%)	6.1± 2.5	8.9 ± 2.1	4.9 ± 0.4	<0.001
Inflammatory Biomarkers				
IL-6 (pg/mL)	2.9 ± 2.3	4.1 ± 2.8	1.9 ± 1.3	0.003
Adiponectin (ng/mL)	9.5 ± 6.0	10.7 ± 6.9	8.4 ± 5.4	<0.001
TNF-α (pg/mL)	7.7 ± 5.4	8.7 ± 5.8	6.1 ± 4.8	0.012
hs-CRP (mg/dL)	4.5 ± 5.3	5.3 ± 5.3	2.8 ± 5.2	<0.001

In the DN group, inflammatory bio- markers (IL-6, TNF-α, and hs-CRP) had significant positive correlations with TC (P=0.003, P=0.001, P= 0.001).Further, TNF-αlevels showed a significant positive correlation with BMI (P=0.006) and SBP (P=0.039). In the control group, IL-6, TNF-α, and hs-CRP levels had significant positive correlations with WC (P=0.019, P<0.001, and P<0.001, respectively). Further, TNF-α had a significant positive correlation with BMI (r=0.535, P<0.001), DBP (P=0.010), TC (P=0.044), and ApoB(P=0.003); and a negative correla- tion with HDL (P=0.026). hs-CRP was positively correlated with BMI (P<0.001) and WC (P<0.001), and negatively correlated with HDL (P<0.001). TNF-α was the only inflammatory biomarker that positively correlated with DBP (P=0.010) and ApoB (P=0.003) levels.

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4. DISCUSSION:

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 (7). 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 (8-11).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 (12). 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 remodelling. 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 (13-16), 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 (17-22).

Similar to our findings, the SEARCH case-control study with and without diabetes reported an association between inflammation and obesity, hyperglycemia, and dyslipidemia in youths. Increased systemic inflammation was found in youths with diabetes compared with youths without diabetes, with similarities in age and Tanner stage, independent of race/ethnicity, sex, hyperglycemia, and obesity. Increased hs-CRP, fibrinogen, and leptin levels were reported to be associated with being overweight or obese, and this relationship did not differ between youths with and without DN. In the present study, all values known to pro- mote inflammation and ED were higher in patients with DN than the controls. The over-all lower levels of ED biomarkers among the controls may explain the lack of association between cardiovascular risk factors and the probability of having higher levels of ED bio- markers

5. CONCLUSION:

Subclinical inflammation and lipid profile levels were detected in young patients with T1DM compared to controls. This study revealed that lipid levels, liver enzymes, and inflammatory biomarkers were significantly higher in the DN group than the control group. 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.

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