Fibrinogen, Lp(a), Microalbuminuria and Left Ventricular Mass Index: Cardiovascular Disease Risk factors in Diabetes

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Abstract The present work was undertaken to study interrelation of Fibrinogen, Lp(a) and LVMI in Type II diabetes patients with or without nephropathy. 100 Type II Diabetic patients attending OPD/IPD of DMC&H, Ludhiana were included. They were divided in two groups. Group I: 50 patients without microalbuminuria (MAU). Group II: 50 patients with MAU. Fibrinogen (Clauss method), Lp(a) and MAU were estimated on Multichannel Autoanalyzer Hitachi-911 (Roche). LVMI was estimated by echocardiography using formula of Devereux and Reichek. Type II diabetes patients with MAU had significantly raised levels of Fibrinogen, Lp(a), and LVMI as compared to normoalbuminuric diabetics ($P < 0.01$). Group II patients had positive correlation between Lp(a) and LVMI but no relation between Fibrinogen and LVMI. MAU, marker of microangiopathy, is associated with higher Fibrinogen and Lp(a) levels. This becomes basis of increase cardiovascular risk as demonstrated by higher mean LVMI in Group II patients.

Keywords LVMI · Microalbuminuria · Cardiovascular disease

Introduction

Prevalence of diabetes have been increasing in developing countries. Incidence of diabetes, as reported on World Diabetes Day (2010) is 40 million in India alone. Poor glycemic control in these patients results in development of micro and macrovascular complications which are the cause of death in 75–80% adult diabetics [1].

Microalbuminuria (MAU), a marker of microangiopathy, is an early renal manifestation of diabetes. Persistent hyperglycemia causes hyperfiltration, advanced glycation products and activation of cytokines. All this causes glomerular damage and endothelial dysfunction leading to increased systemic vascular permeability [2]. It modulate the metabolism of cardiovascular risk factors like fibrinogen, Lp(a) and left ventricular mass (LVM) [3–5].

LVM hypertrophy predisposes individuals to ischemic heart disease, ventricular arrhythmias, sudden death and cardiac failure. It is associated with MAU in diabetes [6]. Fibrinogen, hemorheologically active plasma protein plays an important role in arterial pathogenesis. It is clinically important as it influences RBC aggregation and blood viscosity after vascular injury. High levels have been associated with diabetes, hypertension, stroke, smoking and CVD [7]. Lp(a) is significantly raised in type 2 diabetes patients and even higher levels are reported with vascular complications and MAU. It is synthesised in liver in response to aging vascular system and microfissures in endothelial vascular wall. It is sticky in nature, so highly potent in patching ability. It has tendency to attract other Lp(a) particles, trap LDL, VLDL, blood infiltrates and calcium forming atheromatous plaque in response to vessel injury. Antifibrinolytic activity and adhesiveness makes it much more atherogenic than LDL [8].

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Aim of the study was to evaluate the relationship of LVMI with Lp(a) and fibrinogen in diabetics with microangiopathy.

Materials and Methods

100 patients of Type II diabetes (age 45–65 years) visiting Endocrinology OPD of DMC&H were included in the study. Patients with previous history of CVD, hypertension, smokers were excluded from the study. Patients were divided into two groups of 50 each. Group I: without MAU and Group II: with MAU (30 Male and 20 females in each group).

Overnight fasting blood and urine sample was collected for biochemical investigations. FBS, HbA1c, Lp(a) and MAU were analysed on autoanalyzer Hitachi 911(Roche). Fibrinogen was estimated by Clauss Method using Sigma diagnostic kits. LVM was calculated by echocardiography using formula from Devereux and Riechek.

$$\text{LVM} = 1.04 \left[(\text{STD} + \text{LVDD} + \text{PWTD})^3 \right] - 13.6 \text{ g}$$

$$\text{LVMI} = \text{LVM} / \text{Body surface area}$$

STD: Ventricular septum thickness; LVDD: Left ventricular end diastolic diameter; PWTD: Posterior wall thickness in diastole.

Results

There was no significant difference in age of both the group patients. FBS of all the patients was >140 mg/dl and HbA1c was >7.0 g% showing poor glycemic control.

Diabetic patients with MAU (group II) had significantly higher levels of LVMI, Fibrinogen and Lp(a) as compared to diabetic patients without MAU ($P < 0.01$). Table 1.

Group II patients had positive correlation between Lp(a) and LVMI

Discussion

Cardiovascular risk factors were studied in uncontrolled Type II diabetic patients in presence of MAU and the

results were compared with patients without MAU. MAU is outcome of microangiopathy due to persistent hyperglycemia and poor metabolic control. Diabetic patients with MAU (Group II) showed significantly raised LVMI as compared to patients without MAU (Group I). Association of LVMI and MAU have been reported by other workers as well [9]. Metabolic abnormality in these patients contribute to development of left ventricular hypertrophy (LVMI >150). LVM hypertrophy is an ominous prognostic sign. It represents remodeling of heart architecture to normalise wall stress. Initially it is an adaptive process but once a critical mass is reached it becomes pathological [10].

Fibrinogen plays an important role in pathogenesis of atherosclerosis and vascular events. It binds LDL and stimulates proliferation of vascular smooth muscle. It also promote platelet aggregation in vessels initiating occlusive arterial blood clot [11]. Raised fibrinogen levels in diabetes contribute significantly to thrombus formation due to increased blood viscosity and sluggish blood flow. Higher fibrinogen levels in presence of MAU (group II) as compared to normoalbuminuric patients (group I) is in agreement with earlier studies [4, 12]. High fibrinogen is result of increased synthesis not compensated by proportional increase in its clearance. It is expression of poor glycemic control [13].

High Lp(a) levels pose greater risk of clot formation and blockage in diabetes [14]. Lp(a) is antigenic variant of LDL having apo-a linked to apo B by disulfide bridge. Apo(a) is structural analogue of plasminogen so competes with it to bind fibrin and endothelial cell surface receptors thus inhibiting fibrinolysis [15]. Diabetic patients (group I) had high Lp (a) levels (>20 mg/dl) and presence of MAU in diabetics (group II) resulted in further significant increase in levels ($P < 0.01$). This is in agreement with earlier reports [16]. Elimination of Lp(a) is altered in presence of proteinuria, may be some protein factor needed for its elimination are lost in proteinuria. Kidneys are known to regulate metabolism of Lp(a) [17].

Persistent hyperglycemia is associated with metabolic derangement making diabetes a progressive disease. So prevention of microvascular complications by optimal glycemic control and monitoring each of these hidden risk factor can reduce cardiovascular events associated with diabetes.

Table 1 Mean LVMI, fibrinogen and Lp(a) in diabetic patients with and without MAU

Investigations	Group I	Group II
LVMI g/m ²	111.56 ± 22.1	154.95 ± 24.46*
Mean fibrinogen (mg/dl)	282.9 ± 59.8	340.7 ± 40.36*
Mean Lp(a) (mg/dl)	22.17 ± 3.8	25.9 ± 3.2*

* $P < 0.01$

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