THE INFLUENCE OF SERUM LDL-CHOLESTEROL AND HDL-CHOLESTEROL ON SYSTOLIC BLOOD PRESSURE OF TYPE II DIABETIC PATIENTS WITH VARIOUS KIDNEYS FUNCTION NOT YET ON DIALYSIS

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Background: This study was undertaken to elucidate whether and how in patients with type II diabetes the serum lipid concentrations affect the blood pressure of the patients. **Methods:** Blood pressure (BP) of the patients were measured. For patients glycosylated hemoglobin (HbA1c) and serum lipids consisting of Triglycerides, cholesterol, High density lipoproteinwere measured using standard methods. Serum LDL-was calculated. **Results:** The present study included 122 patients (f=82, m=40). The mean patient's age was 63 (±10) years. The mean length of the time they were diabetic was 7.4 (±5.8) years (median: 6 years). The duration of hypertension was 3.2 (±4.6) years (median: 96 months). The mean serum LDL-chol was 112(±37) mg/dl (median: 112 mg/dl) .The mean serum HDL-c was 47(±18) mg/dl (median: 44 mg/dl) .In this study a significant inverse correlation of serum HDL with mean systolic BP.In this study also a significant positive correlation of serum LDL-c with mean systolic BP was found too. **Conclusion:** This study has important implications for the increased susceptibility to vascular disease associated with LDL-c in diabetic patients. Hence, higher plasma concentrations of LDL-c though with in the normal range, could be an independent risk factor for developing hypertension or its aggravation. This study addressed the hypothesis the new therapeutic methods like statin groups may be identified to reduce LDL-C levels, which may prove to be useful in diabetic patients even in earlier onset of type II diabetes .

Key words: Hypertension, ,lipids, Diabetes Mellitus, glycosilated hemoglobine(HbA1c)

INTRODUCTION

Over the last decade there has been increasing interest in the clinical association between hypertension and diabetes.[1,2] The prevalence of hypertension (HTN) is two times higher in diabetics than in non-diabetics. In type 1 diabetes mellitus (T1DM), the incidence of hypertension is similar to the incidence of nephropathy.[3] In type 2 diabetes, hypertension is often present as part of the metabolic syndrome of insulin resistance also including central obesity and dyslipidemia, while in type 1 diabetes, hypertension may reflect the onset of diabetic nephropathy.[4] Hypertension substantially increases the risk of both macrovascular and microvascular complications, including stroke, coronary artery disease, and peripheral vascular disease, retinopathy, nephropathy, and possibly neuropathy.[4,5] Observational and clinical trial data have demonstrated that elevated systolic blood pressure (SBP) confers significantly higher risk of total and coronary heart disease mortality than elevated diastolic blood pressure (DBP) or combined systolic/diastolic hypertension, especially in those with diabetis mellitus.[6,7] It was shown that atherogenic dyslipidemias were associated with the subsequent development of hypertension among healthy women[6],even young, slender normotensive subjects with a positive history of hypertension may show various alterations in lipid metabolism, suggesting a positive correlation between lipid metabolism and hypertension heredity as well.[9] In essential HTN the disturbances of glucose and lipid metabolism may be related to both insulin resistance and compensatory hyperinsulinemia, and that insulin-resistant patients with essential hypertension may have more risk factors for arteriosclerotic complications than essential HTN.[10] Indeed NIDDM and hypertension commonly co-exist and may be part of the insulin resistance or metabolic syndrome.[11] This syndrome describes a group of clinical and biochemical features which are strongly associated with accelerated atherosclerosis. These features include obesity, mixed dys- lipidaemia (high triglycerides and low HDL [high density lipoprotein] cholesterol levels) and hyperinsulinaemia, as well as hypertension. The underlying association between hypertension and diabetes in this syndrome remains unknown, but it is possible that endothelial dysfunction as a result of both hypertension and diabetes could be an important factor in the high incidence of vascular disease in individuals with both conditions.[12] In this study we aimed to elucidate whether and how in patients with type II diabetes with various kidney function not yet on dialysis the serum lipid concentrations affect the blood pressure of the patients.

MATERIAL AND METHODS

This cross-sectional study was conducted on diabetic mellitus patients under treatment of either oral hypoglycemic agent and /+ biguanids or Insulin NPH and/+ regular injections with various dosages who admitted in the hospital for controlling the diabetes . Among study patients ones who had hypertension , took antihypertensive consisting of amlodine or diltiazem,beta blockers and/or thiazide diuretics at various doses. Exclusion criteria included the presence of any chronic or acute infections and use of lipid-lowering medications.

The study carried out from July to August of 2005in Hajar Medical Educational and Therapeutic Center of Shahrekord University of Iran. All patients signed the consent forms for participation in this study .

After admission all patients underwent history taking consisting the length of the time they were diabetic and/or hypertensive, their medicament for DM and HTN using a questionnaire. Patients also examined for blood pressure (BP) , body mass index measurement as well as heart , lower extrimities pulses and feet were examined too.

Blood Pressure Measurement

A trained physician measured all baseline BP using a random-zero manometer .Two BP and heart rate measurements were averaged to create the baseline BP and heart rate variables. Follow-up BP represents two measures on a single day after at least 30 minutes of rest. Hypertension was diagnosed according to WHO guidelines (13) and the seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure (14).

Laboratory methods

Blood samples were collected after an overnight fast(12 hour overnight fasting) . Each blood samples were centrifuged within 15 min of venopuncture. For patients glycosilated hemoglobine(HbA1c) was meseared by chromatography method using Hb-Gold of UK, the normal value in our laboratory is[less than or equal to]6.1%.Levels of serum creatinine(creat) , blood urea nitrogen(BUN) total protein were measured using standard methods.Serum lipids consisting of Triglycerids (Tg) , cholestrol (Chol) , High density lipoprotein(HDL-c) were measured using standard methods. Body mass index (BMI) calculated using the standard formula (weight in kilograms/height in square meters ;kg/m^2) . Serum LDL-cwas calculated by friedewald's formula (15). Creatinine clearance(CrCL) was evaluated from serum creatinine, age and body weigh (16).

Statistical analysis

Results are expressed as the mean ± SD and median values. Statistical correlations were assessed using a partial correlation test.Comparison between female and male genders data was assessed using students't test .

All analyses were performed with the SPSS statistical package (version 11.00 for Windows; SPSS, Chicago).

Statistical significance was determined at a p-value <0.05.

RESULTS

The present study included 122 patients (f=82 ,m=40). Base line characteristics of patients are described in table one .The mean patient's age was 63 (±10) years. The mean length of the time they were diabetic was 7.4 (±5.8) years (median: 6 years). The duration of hypertension was 3.2 (±4.6) years (median: 96 months). The mean systolic and diastolic BP were 138(±23) mmHg and 83(±12) mmHg respectively. The mean serum cholestrol was 198 (±52) mg/dl (median: 192 mg/dl). The mean serum LDL-chol was 112(±37) mg/dl (median: 112 mg/dl) .The mean serum HDL-chol was 47(±18) mg/dl (median: 44 mg/dl) .In this study a significant inverse correlation of serum HDL with mean systolic BP (r= - 0.177p=0.050;figure 1) (data adjusted for age and HgbA1c).In this study also a significant positive correlation of serum LDL-c with mean systolic BP (r= 0.196 p=0.031;figure 2) (data adjusted for age and HgbA1c) was found too.No significant correlation of serum triglyceride and cholesterol with duration of HTN or mean systolic BP were seen (P.N.S).More over no significant association of serum lipids with mean diastolic BP were seen too (P.N.S).

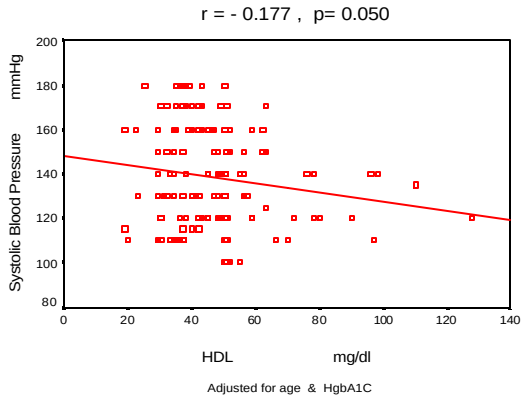

Figure 1: Significant inverse correlation of serum HDL-c with mean systolic blood pressure

Table 1: Minimum, Maximum, Mean ±SD and Median values of patients' data also laboratory tests of the patients.

Number of patients=122	Minimum	Maximum	Mean ±SD	Median
Age(years)	25	84	63±11	64
Duration of DM(years)	0.1	25	7.4±6.8	6
Duration of HTN(years)	0.00	25	3.2±4.5	0.80
BMI(kg/m^2)	30	53	25.5±4.5	25.3
Cretinine Clearance (ClCr) (cc/min)	10	110	64±24	64
HgbA1C %	3.9	13.3	7.6±1.9	7.6
Chol(mg/dl)	90	388	198±52	192
Tg(mg/dl)	37	580	183±102	155
LDL(mg/dl)	44	210	112±37	112
HDL(mg/dl)	19	128	47±18	44
Creatinine(mg/dl)	0.6	10	1.32±1.34	1

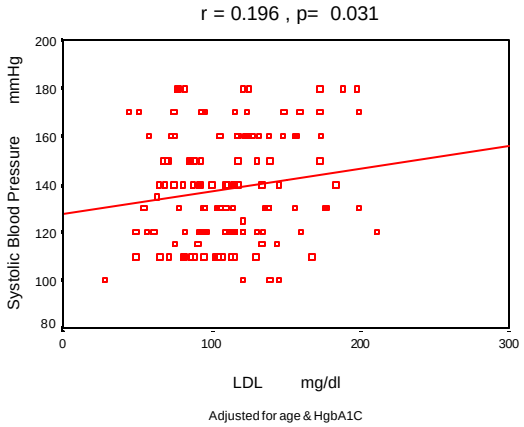

Figure 2: Significant positive correlation of serum LDL-c with mean systolic blood pressure.

DISCUSSION

In this study while there were not any significant association between serum lipids with mean diastolic blood pressure ,a significant positive correlation of serum LDL-c with mean systolic blood pressure and a significant inverse correlation of serum HDL-c with mean systolic blood pressure were found. Patients with type 2 diabetes can have many lipid abnormalities, including hyperchylomicronemia; elevated levels of very low-density lipoprotein cholesterol (VLDL-c), low-density lipoprotein cholesterol (LDL-c), and triglycerides; and low levels of high-density lipoprotein cholesterol (HDL-c) These patients have a preponderance of abnormalities in the composition of LDL-c (smaller, denser particles), which increase atherogenicity even if the absolute concentration of LDL-C is not significantly increased.[17] Both diabetes mellitus and hypertension alter lipid and lipoprotein metabolism and increase the risk of coronary artery disease.[18] It is well documented that loss of endothelial function not only is characteristic of diseases such as genetic or secondary hypertension, hypercholesterolemia, and atherosclerosis.[19] Raised low-density lipoprotein cholesterol (LDL-c) may increase angiotensin II (Ang II)sensitivity, The present study in healthy, young subjects with isolated hypercholesterolemia shows an increased sensitivity to angiotensin II that partly can be restored by LDL-c-lowering therapy. These findings indicate that LDL-c levels directly influence Ang II sensitivity.[20] In young male subjects, responsiveness to Ang II is determined by the LDL-cholesterol serum level even in the normal range of LDL-cholesterol, thereby potentially contributing to the cardiovascular risk of LDL-cholesterol even within the so-called normal range.[21] Our study has important implications for the increased susceptibility to vascular disease associated with LDL-c in diabetic patients. hence, higher plasma concentrations of LDL-c though with in the normal range, could be an independent risk factor for developing hypertension or its aggravation. This study addressed the hypothesis the new therapeutic methods like statin groups may be identified to reduce LDL-C levels, which may prove to be useful in diabetic patients even in earlier onset of type II diabetes .

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