

Inflammatory Markers, Insulin Resistance and Carotid Intima-Media Thickness in North-Indian Type 2 Diabetic Subjects

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Abstract

Objective: To study the interrelationship of the inflammation, insulin resistance and atherosclerosis in recently diagnosed type 2 diabetes.

Methodology: Eighty-one newly diagnosed type 2 diabetic patients were compared with 81 healthy age, sex and BMI matched controls. Plasma glucose and insulin (fasting and after 2 hours of 75 gm of oral glucose), lipids and serum levels of C-reactive protein (CRP), fibrinogen and Tumour Necrosis Factor (TNF)- α were measured. Carotid (Intima-Medial Thickness) IMT was measured using high resolution B-Mode ultrasonography. Insulin resistance was calculated using HOMA – IR model. Electrocardiogram (ECG) and exercise ECG were recorded for the evidence of coronary heart disease (CHD).

Results: Carotid IMT was significantly thicker in diabetic patients than in control group across the whole age range ($p < 0.01$). In merged group of diabetes, composite IMT was significantly correlated with LDL-cholesterol, fasting insulin, serum cholesterol, BMI and HOMA-IR ($p < 0.01$). After controlling for age and sex, all glycaemic parameters were correlated with IMT in both diabetic and control group. HOMA – IR, waist hip ratio, serum triglycerides, serum cholesterol, fasting serum insulin and CRP were significant predictor of IMT. Concentrations of inflammatory markers were significantly higher in diabetic patients than in control group. Serum levels of CRP ($p < 0.05$) were found to be higher in diabetic patients with CHD than without CHD. CRP was significantly correlated with IMT ($r = 0.603$, $p < 0.01$) in diabetic subjects with and without CHD after controlling for age and sex.

Conclusion: Inflammatory markers are associated with type 2 diabetes but only CRP is associated with development of accelerated atherosclerosis and subsequent CHD. ©

INTRODUCTION

Type 2 diabetes is known to be associated with an excessively high rate of morbidity and mortality from macrovascular disease.¹ This increased risk has been attributed to high

prevalence of multiple atherosclerotic risk factors among diabetic patients. However, studies have also shown that the excess of CHD in Type 2 diabetes cannot be accounted for by the levels of four major risk factors identified for CHD viz. hypertension, smoking, total serum cholesterol and age, suggesting a role for other factors.²

Recently, "Inflammation" and "Inflammatory" cytokines have been postulated to be important pathogenetic factors in the development of insulin resistance and Type 2 diabetes.^{3,4} CRP, a non-specific marker of the inflammatory response, is most consistently associated with the development of Type 2 diabetes,^{5,6} however, a causal association remains unproven. CRP and interleukin-6 (IL-6) are associated with the risk of CHD and severity of atherosclerosis.^{7,8} Whether these molecules play a causative

role, or simply act as markers of the acute-phase reaction, is debatable. The molecular basis for the link between inflammation and diabetes likely relates to the action of cytokines such as IL-6 and TNF- α , which induces insulin resistance and stimulates the acute-phase inflammatory response.⁹ The macrovascular complications are essentially due to accelerated atherosclerosis because of endothelial dysfunction linked to hyperglycemia and other factors setting up pro-atherogenic pattern.¹⁰ A non-invasive and relatively inexpensive investigation for identifying atherosclerosis, even in an asymptomatic patient, is measurement of IMT of the extracranial carotid arteries by doppler ultrasound. Endothelial dysfunction is an early functional marker and IMT an early morphological parameter of atherosclerosis.¹¹

Ethnic differences in CHD morbidity and mortality,¹² in the prevalence and course of type 2 diabetes¹³ and in carotid IMT have been reported.¹⁴ Asian Indians have a high risk of diabetes and have an obesity phenotype characterised by lean BMI, central obesity and high body fat percentage. Also

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they have high degree of insulin resistance.¹⁵ The increased predisposition of certain population to type 2 diabetes raises important question and emphasize the need for studies on inflammatory markers, insulin resistance, IMT and its determinants in different populations. We studied the relation of inflammatory markers (CRP, TNF- α , fibrinogen), insulin resistance together with diabetic dyslipidemia and carotid IMT in North Indian Type 2 diabetic subjects.

METHODS

Study Design

The study was conducted as a prospective case-control study. All subjects gave written informed consent and the study was approved by the ethics committee.

Subjects

A total of 81 recently diagnosed (duration of diabetes 3-12 months) type 2 diabetic subjects (34 males and 47 females) according to the revised American Diabetes Association criteria (ADA-2004) i.e., fasting plasma glucose ≥ 126 mg/dl (≥ 6.1 mmol/L) and 2 hours postprandial plasma glucose ≥ 200 mg/dl (≥ 11.1 mmol/L). None of the subjects were below 30 years of age at the time of diagnosis (Table 1). Those having acute metabolic complications like hypoglycemia, diabetic ketoacidosis, hyperosmolar hyperglycaemic state, acute myocardial infarction, cerebrovascular accidents, acute infections, inherited disorders of lipid and lipoprotein metabolism and/or family history of such disorders and deranged liver functions were excluded. All subjects were in good general health and taking no medications (other than a sulfonylurea compound) known to affect carbohydrate or lipoprotein metabolism. None of the subjects had ever been treated with insulin. The subjects were recruited from the endocrine clinic of the department of medicine, J.N. Medical College, Hospital, Aligarh Muslim University, Aligarh in the year January 2003 to June 2004.

Eighty one (39 male and 42 female) age, sex and BMI matched non-diabetic subjects with no evidence of cardiovascular, cerebrovascular or peripheral vascular disease were also recruited as controls.

Clinical and Biochemical Parameters

Patients went through a clinical examination including measurements of body weight in light clothes to the nearest 0.5 kg, body height to the nearest 0.5 cm and blood pressure in the sitting position after 5-10 minutes rest. The circumference around the waist (umbilical level) and hips (greater trochanter level) were measured, and waist-hip ratio was calculated. CHD, cerebrovascular disease and peripheral vascular disease were diagnosed on the basis of a thorough clinical examination and medical history. Angina pectoris was defined on the basis of a medical history of exercise-induced central chest pain relieved by stopping the activity or by sublingual nitroglycerine. Resting electrocardiogram (ECG) confirmed CHD when pathological Q-waves (i.e., Q-wave duration of >0.045 s or $Q>1/4$ of the QRS complex in more than one lead) were present. Exercise

ECG was performed in all subjects and was defined as confirming CHD with horizontal ST-segment depression of at least 1 mm in at least two contiguous leads combined with typical chest pain appearing during or immediately after exercise.

The subjects were asked to report to the endocrinology laboratory after an overnight fast of 10-12 hours. A blood sample was drawn and analysed for plasma glucose (by glucose oxidase peroxidase method), serum cholesterol, HDL-cholesterol and triglycerides (by enzymatic methods; Pointe Scientific Michigan, USA). LDL-cholesterol was calculated using the Friedwald formula. HbA_{1c} was measured by cation exchange resin method (Pointe Scientific Inc Michigan, USA). Plasma for insulin was also collected and separated within 3 hours of sample collection (both fasting and postprandial) and stored at -20°C and assayed within one week of collection. Serum levels of insulin were measured by radioimmunoassay (Immunotech, Czech Republic, RIA kit) with an intra-assay coefficient of variation $<8\%$. Insulin resistance was calculated using the homeostasis model assessment (HOMA-IR):

$$\text{HOMA-IR} = \frac{\text{Fasting plasma insulin } (\mu\text{U/ml}) \times \text{fasting plasma glucose}}{22.5}$$

High sensitive CRP (hs-CRP) levels in plasma were measured by enzyme immunoassay technique (UBI Magiwell™ CRP quantitative AD-401). Quantitative measurement of fibrinogen levels in plasma was done by clotting method of Gauss (FIBRI-PREST®2). TNF- α was also estimated by immunoenzymometric assay (BIOSOURCE TNF- α EASIA kit).

Measurement of Carotid IMT

The IMT of the carotid arteries was determined using a high resolution B-mode ultrasonography system (Logic 500 Proseries, Wipro GE) having an electrical linear transducer (multifrequency probe of 5 to 9 MHz). The images were recorded as well as photographed. The scanning for each patient was done for an average of 20 min. Extracranial carotid arteries (common carotid and internal carotid arteries; carotid bulbs) were examined on both sides and the distance between two echogenic lines (the inner line representing the lumen intima interface and the outer line representing the media-adventitia interface) was taken as the intima-media thickness (IMT) in millimetres (mm). A mean of six measurements on either side was taken. An IMT of more than 1.0 mm was considered to represent early changes of atherosclerosis. Composite IMT was calculated as a mean of IMT in the common carotid artery on the right and left sides, and the mean of IMT in the carotid artery bulb on the right and left sides. The mean IMT of the common carotid artery and carotid artery bulb was calculated as composite IMT.

Statistical Analysis

All statistics were analyzed by using SPSS for Windows 11 software (Chicago Inc.). The results were presented in number, percentage, mean and standard deviation. Serum

triglycerides and serum fasting insulin levels were skewed. For these variables geometric mean was calculated and log transformation was performed before any statistical analysis. Intergroup comparison was done by using Student 't' test, ANOVA with Scheffe's post-hoc analysis. The Pearson correlation was used for correlation analysis. Simple linear regression and stepwise multiple regression was performed to study the determinants of composite IMT and inflammatory markers (CRP, Fibrinogen and TNF- α). Two sided $p < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows subject characteristics in diabetic patients and healthy controls. As expected control subjects had significantly lower systolic and diastolic blood pressure and waist to hip ratio. Thirty patients (37%) in the diabetic group had evidence of coronary artery disease. 15 patients (18%) had diabetic retinopathy.

As anticipated, diabetic patients had significantly higher total serum cholesterol, triglyceride and LDL-cholesterol levels as compared to control subjects.

Twenty eight diabetic patients were current smokers, 42 were ex-smokers and 11 patients never smoked. Among control group there were 30 subjects who were current smokers, 38 were ex-smokers and 13 never smoked.

IMT in diabetic patients and control group

In general IMT was significantly higher in diabetic patients than in healthy controls and also in diabetic subjects with CHD than those without clinical CHD. Although age, gender and smoking attenuated the difference between diabetic and healthy control groups, for most IMT variables differences remained significant. On the other hand, in diabetic patients with and without CHD, the difference in

IMT measures were not seen after adjusting for age, gender and smoking.

The mean carotid IMT in diabetic subjects was 1.3 ± 0.29 mm versus 0.77 ± 0.22 mm in controls ($p < 0.01$). The range of carotid IMT and diabetic and control group was 0.98-1.60 mm and 0.55-0.99 mm, respectively. None (0%) of healthy control had evidence of carotid artery atherosclerosis while 23% of diabetic subjects (19/81) showed features of carotid artery atherosclerosis in the form of diffuse thickening, atheroma formation, stenosis and calcified plaque formation ($p < 0.01$).

The mean carotid IMT was higher among the diabetic subjects in all age groups compared with control group. At age 30-40 years, mean IMT in diabetic group was 0.90 ± 0.22 mm while in the control group it was 0.70 ± 0.22 mm, in the 41-50 year group 0.93 ± 0.24 mm, in the diabetic group and 0.73 ± 0.04 mm in the control group, at 51-60 years 0.96 ± 0.30 mm in diabetic group and 0.77 ± 0.24 mm in control group. In subjects more than 60 years of age it was 1.02 ± 0.33 mm in the diabetic group and 0.89 mm in control subject. The difference in carotid IMT levels was significant in all age groups ($p < 0.01$).

In merged group of diabetes composite IMT was significantly correlated with LDL cholesterol ($r = 0.238$, $p < 0.05$), fasting insulin ($r = 0.227$, $p < 0.05$), serum cholesterol ($r = 0.162$, $p < 0.05$), BMI ($r = 0.103$, $p < 0.05$) and HOMA-IR ($r = 0.385$, $p < 0.01$). After adjusting with age and sex, significant correlation was seen with BMI ($r = 0.221$, $p < 0.05$), LDL-C ($r = 0.393$, $p < 0.01$) and HOMA-IR ($r = 0.681$, $p < 0.01$). Composite IMT shows significant correlation with fasting plasma glucose ($r = 0.271$, $p < 0.05$) in control group but not with postprandial plasma glucose and HbA_{1c}. However, after controlling with age and sex using partial correlation

Table 1 : Demographic profile of diabetic and control group

Variables	Diabetic Subjects (n=81)	Control Subjects (n=81)	t	p
Sex (Male/Female)	34/47	39/42	—	
Age (years)	46.98 \pm 9.54	47.77 \pm 9.32	0.539	NS
Systolic B.P. (mm Hg)	135.42 \pm 18.28	125.58 \pm 10.30	4.246**	<0.01
Diastolic B.P. (mm Hg)	85.20 \pm 10.30	77.80 \pm 6.38	5.533**	<0.01
BMI (kg/m ²)	28.29 \pm 3.52	27.67 \pm 2.81	0.405	NS
Waist-to-hip ratio	1.08 \pm 0.11	0.96 \pm 0.06	2.788*	<0.05
Coronary artery disease (n)	30	—		
Retinopathy (n)	15	—		
Smoking (n)	28	30		
Duration of diabetes (months)	3.37 \pm 2.19	—		
Family history of diabetes	39	—		
Fasting plasma glucose (mmol/L)	7.70 \pm 2.54 (6.12-9.29)*	5.72 \pm 0.18 (5.52-5.94)*	5.857**	<0.01
Postprandial plasma glucose (mmol/L)	10.83 \pm 3.27	8.08 \pm 0.67	7.392**	<0.01
HbA _{1c} (%)	8.63 \pm 0.55	6.10 \pm 0.31	35.796**	<0.01
Nat log of fasting serum insulin (μ U/ml)	3.66 \pm 0.87	1.26 \pm 0.14	24.22**	<0.01
Postprandial serum insulin (μ U/ml)	81.35 \pm 45.67	31.8 \pm 9.53	5.899**	<0.01
HOMA-IR	11.80 \pm 7.65	2.31 \pm 0.42	5.984**	<0.01
Total serum cholesterol (mmol/L)	4.53 \pm 0.72	3.95 \pm 0.49	5.978**	<0.01
Nat log triglyceride (mmol/L)	0.41 \pm 0.39	0.18 \pm 0.07	5.120**	<0.01
Serum LDL cholesterol (LDL-C) (mmol/L)	2.90 \pm 0.70	2.26 \pm 0.61	6.224**	<0.01
Serum HDL cholesterol (HDL-C) (mmol/L)	1.15 \pm 0.11	1.18 \pm 0.24	1.024	NS

Data are mean \pm S.D. t is value of student 't' test, p value indicate significant, NS is non significant.

all glycaemic parameters were not significantly correlated with composite IMT in both diabetic and control group.

Inflammatory Markers and Composite IMT

Table 2 displays the concentration of inflammatory markers and the parameters of carotid IMT in diabetic subjects without CHD, diabetic subjects with CHD and control group. There was significant difference in all three inflammatory markers i.e. CRP ($p<0.01$), TNF- α ($p<0.05$) and fibrinogen ($p<0.05$) among merged group of diabetes (without and with CHD) and control group. A significant increase in CRP levels ($p<0.01$) was found in diabetic subjects with CHD as compared to those without CHD. There was significant difference in the mean IMT, bulb mean IMT and composite IMT when merged group of diabetic patients were compared with controls. However, there was no significant difference seen in diabetic patients with and without CHD.

Pearson correlation shows significant correlation of composite IMT with CRP ($r=0.603$, $p<0.01$) in merged group of diabetes after controlling for age and sex. However, there was no correlation with TNF- α and fibrinogen with composite IMT in both diabetic and control groups.

Simple linear regression was performed in merged group of diabetes (with and without CHD) with composite IMT as dependent variable and plasma glucose fasting, postprandial plasma glucose, serum cholesterol, Nat log of fasting serum insulin, HOMA-IR, HbA_{1c}, BMI, WHR, Nat log of triglycerides, LDL cholesterol, HDL cholesterol, age, gender, composite IMT, CRP, TNF- α and fibrinogen as covariates. HOMA-IR, waist-to-hip ratio, serum triglycerides, serum cholesterol, Nat log of fasting serum insulin, CRP and age significantly predicted the variance of the composite IMT, collectively explaining 17.6% variability in the composite IMT.

Inflammatory Markers and Insulin Resistance

Partial correlation of inflammatory markers with glycaemic parameters in merged group of diabetes (after age and sex control) shows significant correlation of CRP with plasma glucose fasting ($r=0.303$, $p<0.01$), postprandial ($r=0.353$, $p<0.01$), HbA_{1c} ($r=0.644$, $p<0.01$). TNF- α was also significantly correlated with plasma glucose fasting ($r=0.439$, $p<0.01$) and postprandial ($r=0.433$, $p<0.01$). Fibrinogen was significantly correlated with plasma glucose postprandial

($r=0.200$, $p<0.01$) and HbA_{1c} ($r=0.230$, $p<0.01$) but not with fasting plasma glucose.

In merged group diabetes (after age and sex controlled) using partial correlation, CRP was significantly correlated with systolic blood pressure ($r=0.3231$, $p<0.01$), diastolic BP ($r=0.258$, $p<0.05$), triglycerides ($r=0.321$, $p<0.01$), LDL-cholesterol ($r=0.59$, $p<0.01$), serum cholesterol ($r=0.330$, $p<0.01$), fasting serum insulin ($r=0.626$, $p<0.01$), postprandial serum insulin ($r=0.325$, $p<0.01$) and HOMA-IR ($r=0.506$, $p<0.01$). There was no correlation with HDL-cholesterol. TNF- α correlated significantly with triglycerides ($r=0.243$, $p<0.05$), serum cholesterol ($r=0.276$, $p<0.01$), fasting ($r=0.492$, $p<0.01$) and postprandial ($r=0.278$, $p<0.01$) serum insulin. There was no significant correlation with systolic and diastolic B.P., LDL-C, HDL-C and HOMA-IR with TNF- α .

Fibrinogen was significantly correlated with serum cholesterol ($r=0.299$, $p<0.05$), fasting serum insulin ($r=0.272$, $p<0.05$) and HOMA-IR ($r=0.284$, $p<0.01$). There was no significant correlation with systolic and diastolic B.P., triglycerides, LDL-C, HDL-C and postprandial serum insulin.

In merged diabetic group after age and sex control using partial correlation, CRP was significantly correlated with BMI ($r=0.396$, $p<0.01$). There was no correlation with waist hip ratio. TNF- α and fibrinogen however, have no correlation with BMI and waist hip ratio.

Multiple stepwise regression was performed in merged group of subjects with diabetes (with and without CHD) with inflammatory markers (TNF- α , CRP and fibrinogen) as dependent variable and plasma glucose fasting and postprandial, Nat log of fasting insulin, HOMA-IR, HbA_{1c}, BMI, WHR, Nat log of triglycerides, LDL-cholesterol, HDL-cholesterol, age, gender, composite IMT as covariates (Table 3). Plasma glucose fasting (fasting) ($p<0.01$), Nat log of fasting insulin ($p<0.01$), HOMA-IR ($p<0.05$) and HbA_{1c} ($p<0.05$) were independent predictors of the variance of TNF- α . Fasting serum insulin Nat log ($p<0.01$), LDL-C ($p<0.01$), Nat log of triglycerides ($p<0.01$), age ($p<0.05$), and HbA_{1c} ($p<0.05$) were significant predictors of variance of the CRP. HOMA-IR ($p<0.01$), fasting serum insulin Nat log ($p<0.05$) were significant predictors of variance of the fibrinogen.

Table 2 : Inflammatory marker (CRP, TNF- α , Fibrinogen) in diabetic and control subjects

Variables	Diabetic Subjects (n=81) (n=51)	Diabetic Subjects without CHD (n=30)	Diabetic Subjects with CHD	Controls Subjects (n=81)	Difference (p)	
					Controls vs patients with CHD	Patients without vs
CRP (ng/ml)	3.58±0.79	2.08±1.15	5.08±0.76	0.90±0.41	<0.01	<0.01
TNF- α (pg/ml)	4.54±2.71	4.39±2.61	4.69±2.27	3.24±1.41	<0.05	NS
Fibrinogen (gm/l)	4.04±1.6	4.15±1.8	3.91±1.28	3.33±1.62	<0.05	NS
Mean IMT CCA (mm)	—	0.93±0.34	1.8±0.34	0.77±0.22	NS	<0.01
Bulb mean (mm)	—	1.8±0.83	2.21±1.2	0.93±0.31	NS	<0.01
Composite IMT	—	1.52±1.03	2.0±1.3	0.83±0.26	NS	<0.01

Values are mean±S.D., ANOVA Scheffe's post-hoc analysis p-value indicate difference. NS, not significant.

DISCUSSION

To our knowledge this is the first study to demonstrate the relationship of these three markers of inflammation in patients with Type 2 diabetes with and without cardiovascular disease and carotid IMT and insulin resistance, that too in North Indian counterparts, although individual marker have been studied extensively.¹⁶ We have studied the association of inflammatory marker (CRP, TNF- α and fibrinogen) in Type 2 diabetic subjects with and without coronary heart disease and non-diabetic control. Concentration of CRP, TNF- α and fibrinogen were significantly increased in diabetic patients when compared with non-diabetic controls. However, CRP but not TNF- α or fibrinogen were significantly elevated in diabetics patients with CHD when compared with diabetic patients without CHD.

The present study shows that the mean carotid IMT is increased in diabetic patients compared with non-diabetic subjects both in men and women, the increase being greater in men. Moreover, at every age point, diabetic patients had increased IMT compared with their non-diabetic counterparts. Twenty three percent of diabetic subjects showed features of carotid artery atherosclerosis in the form of diffuse thickening, compared to none (0%) in healthy controls ($p < 0.01$). Carotid IMT (mean IMT, bulb mean IMT and composite IMT) were significantly higher in diabetic group (with and without CHD) when compared with the control group ($p < 0.01$). However, there was no significance in the parameters of IMT when the two groups of diabetes (with and without CHD) were compared. Thus diabetes per se augments the process promoting IMT. Our data are complementary to previous studies showing that carotid IMT is thicker in diabetic patients than healthy

Table 3 : Stepwise multiple regression model showing contribution to the variance of the inflammatory markers

	Variable	β -Coefficient	p-value	R ²
TNF- α	Plasma glucose fasting (mmol/L)	.493	<.01	.243
	Fasting serum insulin (Nat log) (μ U/ml)	.340	<.01	.336
	HOMA-IR	.167	<.05	.357
	HbA _{1c} (%)	.318	<.05	.384
	Fasting serum insulin (Nat log) (μ U/ml)	.626	<.01	.392
CRP	LDL-cholesterol (mmol/L)	.418	<.01	.543
	HOMA-IR	.158	<.01	.561
	Nat Log	.168	<.01	.585
	Triglycerides (mmol/L)			
Fibrinogen	Age (years)	.129	<.05	.601
	HbA _{1c} (%)	.212	<.05	.612
	HOMA-IR	0.284	<0.01	0.081
	Fasting serum insulin (Nat log) (μ U/ml)	0.175	<0.05	0.104

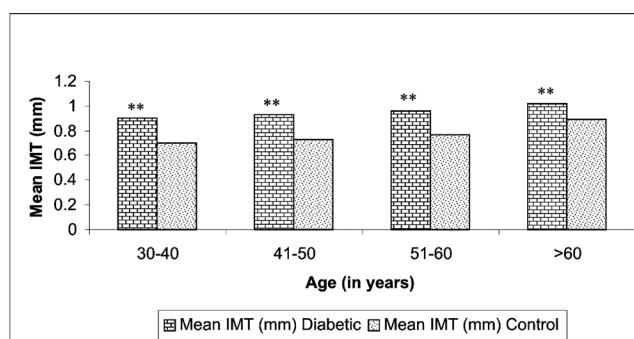


Fig. 1 : Distribution of IMT Levels according to age group. ** $p < 0.01$

controls.¹⁷

Composite IMT was significantly correlated with plasma glucose fasting ($p < 0.05$), but not with postprandial plasma glucose and HbA_{1c}. However, this significance was not seen after age and sex adjustment. Further, composite IMT was significantly correlated with BMI ($p < 0.05$) in both diabetic and control group after adjustment with age and sex. Composite IMT was also significantly correlated with LDL-C ($p < 0.05$), HOMA-IR ($p < 0.01$) and BMI ($p < 0.05$) in diabetics after adjustment with age and sex. However, no correlation of composite IMT with systolic BP, diastolic BP, waist hip ratio, triglycerides, HDL-C, serum cholesterol, fasting and postprandial insulin levels was noted. Composite IMT was also correlated with CRP in diabetic population ($r = 0.303$, $p < 0.01$) but even after adjustment with age and sex no such association found with TNF- α and fibrinogen. In simple linear regression, HOMA-IR, waist hip ratio, triglycerides, serum cholesterol, LDL-C, fasting insulin, CRP and age were significant predictors of variance of composite IMT in our study group of diabetes. In the present study, Type 2 diabetic patients have significantly higher insulin resistance as measured by fasting insulin, postprandial insulin and HOMA-IR. Furthermore, fasting insulin levels were correlated with CRP ($p < 0.01$), TNF- α (< 0.01) and fibrinogen ($p < 0.05$) and the postprandial insulin was correlated with CRP (< 0.01) and TNF- α (< 0.01) but not with fibrinogen. HOMA-IR was correlated with CRP ($p < 0.01$) and fibrinogen ($p < 0.01$) but not with TNF- α .

Hypothetically an association between diabetes duration and atherosclerosis might be explained with the inflammation. Diabetes has been linked to several inflammatory markers such as CRP and interleukin-6.^{4,5} Furthermore, inflammation is also seen in patients with accelerated atherosclerosis.^{8,9}

While many mechanisms are undoubtedly involved in the development of vascular disease in diabetes, insulin resistance is thought to play a major role in acceleration of atherosclerosis. The biological mechanisms underlying the association between insulin resistance and haemostatic variables are not yet completely clear. It is now recognized that impaired fibrinolytic potential is major feature of insulin resistance.¹⁸ The association with HOMA-IR, fasting and postprandial insulin with fibrinogen and CRP is consistent

with suggestion that insulin resistance is associated with inflammatory cytokines.

The correlation between CRP and traditional risk factors may be a reflection of its dependence on these factors. The significant correlation between CRP with triglycerides, LDL cholesterol, blood pressure, fasting and postprandial insulin levels, which are also known risk factors for cardiovascular disease in Type 2 diabetics, suggests that CRP concentration might be related to these risk factors. Although further studies are required to confirm these observations, the findings raise questions on the mechanisms of increased inflammatory markers in diabetic patients with and without CHD.

The study has some limitations. Although the patients were carefully selected to exclude those who may have disease associated with acute phase response we cannot absolutely exclude the presence of occult subclinical state that could increase serum markers of inflammation. This is a case control study that has evaluated an association of inflammatory markers, insulin resistance and carotid IMT in diabetic and the results should be interpreted with the limitations of such an observational study. Although we did not use direct measures of insulin resistance,¹⁹ HOMA-IR has been shown to be significantly correlated with insulin sensitivity and to predict to CVD in subjects with diabetes.²⁰

In conclusion, patients with newly diagnosed diabetes had increased atherosclerosis, increased inflammation and insulin resistance than in the normal subjects of the same age, sex and similar anthropometrical features. Inflammatory markers (particularly CRP) are associated with Type 2 diabetes and several risk factors for the development of cardiovascular disease in Type 2 diabetic patients. Moreover, inflammation is also associated with atherosclerosis in Type 2 diabetes and has severe consequences at the level of carotid wall. However, it is not yet clear that whether insulin resistance and inflammation is a primary phenomenon in patients of Type 2 diabetes leading to accelerated atherosclerosis. More detailed studies in Asian Indians are warranted to understand the complex relation of insulin resistance, inflammation and type 2 diabetes. Our results have strongly supported the inclusion of inflammatory markers particularly CRP in the risk assessment of diabetic patients. Those with elevated levels of CRP should be managed aggressively to prevent the development or progression of cardiovascular disease.

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Announcement



Election Results of API/ICP

The election results of the Office Bearers, Members of the Governing Body of Association of Physicians of India and Office Bearers and Faculty Council Members of Indian College of Physicians for 2008-2009.

Governing Body of API

President Elect

Dr. AK Agarwal, New Delhi

Vice President

Dr. Alaka Deshpande, Mumbai

Members of Governing Body

Dr. Narinder Pal Singh, New Delhi,
Dr. Madhukar Rai, Varanasi
Dr. Surendra Daga, Kolkata
Dr. S Arulraj, Tuticorin

Zonal Members

Central Zone

Dr. Sanjiv Maheshwari, Ajmer

East Zone

Dr. Samar Kumar Banerjee, Kolkata

Mid East Zone

Dr. Kamlesh Tewary, Muzaffarpur

Mid South Zone

Dr. G Narasimulu, Hyderabad

North Zone

Dr. Rajesh Upadhyay, New Delhi

North West zone

Dr. Gurpreet Singh Wander, Ludhiana

South Zone

Dr. A Muruganathan, Tirupur

West Zone

Dr. Ashit M Bhagwati, Mumbai

Faculty Council of ICP

Dean Elect

Dr. BB Thakur, Muzaffarpur

Vice Deans

Dr. SK Goyal, Kota

Dr. OP Kalra, New Delhi

Dr. Anil Chaturvedi, New Delhi

Members Faculty Council

Dr. S Chandrasekaran, Chennai

Dr. Vinay Goel, New Delhi

Dr. RK Goyal, Ajmer

Dr. Rajat Kumar, New Delhi

Dr. MP Singh, Ranchi

Dr. Sandhya Kamath
Hon. Gen. Secretary