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Internal Medicine Section

Correlation of Postprandial Hypertriglyceridemia with Carotid Intima Media Thickness in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Macro vascular disease is a major cause of death in diabetic individuals. Because many diabetic individuals have multiple risk factors for atherosclerosis, the relative risks of Ischemic Heart Disease (IHD) and Cerebro-Vascular Disease (CVD) are 2-4 fold and 2-3 fold higher respectively, than the risk in non-diabetic subjects. Several studies indicate that post-prandial metabolic derangements, most notably hyperglycemia and hypertriglyceridemia are important cardiovascular risk factors since they induce oxidative stress and endothelial dysfunction. Measurement of Carotid Intima Media Thickness (CIMT) by ultrasonography is a non-invasive and quantitative method of evaluating early atherosclerotic changes in the vasculature. It has been shown that an increase in CIMT is associated with an increased risk of IHD or CVD.

Aim: The present study was undertaken to find the correlation of postprandial hypertriglyceridemia with carotid intima media thickness in North Indian patients with type II Diabetes Mellitus.

Materials and Methods: The present study was done amongst 50 North Indian patients, between the age group of 35-75 years suffering from Type II Diabetes Mellitus for less than 1 year duration. All routine investigations and special investigations like Lipid Profile (Fasting)-total Cholesterol, HDL, LDL, Triglycerides, VLDL, Lipid profile {Postprandial (4 hours after a standard meal)} - Triglycerides, B- mode ultrasonography of common carotid artery were done in all the patients. An attempt was made to find the correlation between postprandial hypertriglyceridemia with carotid intima media thickness.

Results: Both PPTG and FTG showed a strong correlation with CIMT, the correlation coefficients being 0.879 and 0.764 respectively. If the subjects with normal FTG were taken to calculate correlation between PPTG and CIMT, correlation coefficient was 0.848 and if only the subjects with raised FTG were taken then the correlation coefficient was 0.735; suggesting a stronger correlation of PPTG with CIMT at normal fasting triglyceride levels.

Conclusion: Both, increased postprandial triglyceride levels and fasting triglyceride levels are risk factors for increasing carotid intima media thickness in patients with Type II Diabetes Mellitus.

Keywords: Atherosclerosis, Coronary heart disease, Ischemic heart disease

INTRODUCTION

Diabetes has been troubling mankind since time immemorial and, it perhaps is one of the oldest known diseases. First clinical description of diabetes dates back to 1500 BC in ancient Egyptian text Ebers papyrus, in which it was described as a condition of “too great emptying of urine”. Aretaues of Cappadocia, a Greek physician, gave a complete description of diabetes in first century AD and noted that in diabetes excessive amount of urine passes through kidneys. Since then clinicians have been trying to fight with diabetes. Ischemic Heart disease and stroke are leading causes of death in the world. Taken together with Diabetes mellitus these causes count to 15.6 million deaths around the world every year [1].

Around 80% mortality caused due to diabetes and most hospitalised cases with complications of diabetes are a consequence of atherosclerosis [2]. Diabetic patients are frequently hyperlipidemic (approximately 70% of diabetic patients are dyslipidemic) and, are at a high risk for coronary heart disease [3].

Type 2 Diabetes Mellitus is associated with development of premature atherosclerosis. Diabetic dyslipidemia is believed to play an important role in the pathogenesis of accelerated atherosclerosis. The most important components of this dyslipidemia are elevated Very low density lipoproteins (VLDL), total triglycerides (TGs) and a decreased High density lipoproteins (HDL) concentration in the serum. Several studies have proved that in Type II DM, elevated TG levels

may be a better predictor of IHD than elevated low density lipoproteins (LDL) cholesterol levels [4].

Recent studies have shown that postprandial triglyceride levels are an important factor determining endothelial dysfunction and atherosclerosis [5]. Human beings have a habit of having multiple meals in the form of snacks in between. The normal people with steady fasting triglycerides, also often show increased postprandial triglycerides. In normal healthy people, triglycerides are raised for about 3-4 hours after meals, while in diabetics and prediabetics, levels are raised for 6-10 hours [6,7]. Raised serum triglyceride levels are further stimulated by the next meal. The vascular endothelium is exposed to the effects of triglycerides more during postprandial state. This is the time when most endothelial damage takes place [8].

In addition to diabetics and prediabetics, other reasons for postprandial hypertriglyceridemia are first degree relatives of type 2 diabetes, obese persons and asymptomatic persons with higher fasting triglycerides in postprandial state. Previous case control studies have shown high post prandial triglyceride levels in patients with angiography proved coronary artery disease [9].

Usually, serum lipid concentration including triglycerides is measured after an overnight fast. But the fasting values are the lowest of a 24 hr triglyceride profile and thus can be misleading. However, several previous studies have lamented raised postprandial Triglyceride Rich Lipoprotein to be related coronary artery disease in diabetic and non-diabetic subjects [10].

AIM

- Estimation of Fasting and postprandial triglyceride levels in patients with Type 2 Diabetes mellitus.
- Estimation of Carotid intima media thickness by Doppler ultrasonography.
- To correlate postprandial triglyceride levels (4 hours after standard meal) and Carotid intima media thickness.

MATERIALS AND METHODS

A comparative study was conducted in Government Medical College and Hospital Amritsar, in the year 2014-15 (over a period of one year). After taking due approval of institutional ethical committee, the study was done on 50 patients, aged 35-75 years, belonging to North Indian population, all of which were known cases of diabetes mellitus without any evidence of Ischemic heart disease, cerebrovascular disease and peripheral vascular disease. The inclusion criterion for the study was: known cases of diabetes mellitus, age between 35-75 years, and history of diabetes mellitus for more than one year. The exclusion criterions were: Age<35, >75 years, evidence of ischemic heart disease, cerebro vascular disease, peripheral vascular disease and chronic kidney disease, history of diabetes for < 1 year.

After obtaining an informed consent, a thorough history was taken and relevant clinical examination was done. All the subjects were subjected to following routine investigations: Haemoglobin, total leukocyte count, differential leukocyte count, erythrocyte sedimentation rate, random blood sugar, Blood urea, Serum creatinine, Fasting blood sugar, postprandial blood sugar, urine albumin, urine sugar, ECG, and special investigations like Lipid profile (Fasting)-total Cholesterol, HDL, LDL, triglycerides, VLDL, Lipid profile {Postprandial (4 hours after a standard meal)}- Triglycerides, B- mode ultrasonography of common carotid artery.

Blood samples were taken after an overnight fast to obtain fasting lipid profile. For postprandial triglyceride estimation a blood sample was taken after four hours of a standard meal that had a total energy of 9 Kcal/Kg with 60-65% of this energy being supplied by carbohydrate, 15-20% by protein and 20% by fat, after taking insulin or oral hypoglycaemic agent. Patients are sensitised prior to the test, they are given a chart of what all can constitute a standard meal and are instructed to come in 4 hours interval after consumption of standard meal in breakfast. Total cholesterol, triglycerides and HDL levels were estimated according to standard laboratory technique. LDL was calculated using Friedewald's formula:

LDL Cholesterol= Total Cholesterol- (HDL+Triglycerides)

Carotid artery examination was done by using linear mid frequency range probe (5-8 Megahertz) and B-mode images were obtained to estimate the intima media thickness (IMT) on both the sides. A plaque free area of common carotid artery 1cm proximal to bifurcation was chosen for estimation of the IMT and mean average values were obtained.

The data was systematically collected, compiled and statistically analysed using IBM SPSS 22.0 Software to draw cross-tabs and make relevant conclusions. Data was expressed as means, standard deviation, number and percentages, Chi-square test was applied to calculate p-values, The p-value of <0.05 was considered as significant, p-value of <0.001 as highly significant and p-value >0.05 was considered as non-significant. To find out correlation amongst the various parameters studied Pearson's correlation coefficient was used.

RESULTS [TABLE/FIG-1]

For the purpose of making comparisons, the study population was divided into three groups on the basis of fasting and postprandial triglyceride levels:

1. Normo-normo (NN) Group

This group consists of individuals with normal fasting triglyceride level (<150mg/dL) and normal postprandial triglyceride level (< 200mg/dL).

2. Normo-hyper (NH) Group

This group consists of Individuals with normal fasting triglyceride level (<150mg/dL) and elevated postprandial triglyceride level (>200mg/dL).

3. Hyper-hyper (HH) Group

This group consists of Individuals with elevated fasting triglyceride level (>150mg/dL) and elevated postprandial triglyceride level (>200mg/dL).

On statistical analysis the p-value was found to be 0.001

Parameters	NN	NH	HH
PPTG (mg/dl)	180.40 + 15.84	285.55 + 37.73	378.50 + 102.49
FTG (mg/dl)	130+ 13.55	133.91+ 11.37	252.17+ 79.52
CIMT (mm)	0.68 + 0.12	1.17 + 0.17	1.52 + 0.33

[Table/Fig-1]: Showing the values of PPTG: Post prandial triglyceride; FTG: Fasting Triglyceride CIMT: Carotid Intima Media thickness in Normo-normo (NN) Group, Normo-hyper (NH) Group and Hyper-hyper (HH) Group.

and the difference was statistically highly significant. Also the Pearson correlation coefficient was calculated as 0.879, depicting a strong correlation between PPTG and CIMT values.

Both PPTG and FTG showed a strong correlation with CIMT, the correlation coefficients being 0.879 and 0.764 respectively. If only the subjects with raised FTG levels were taken to calculate the correlation coefficient between FTG and CIMT, correlation coefficient was 0.656, if only subjects with normal FTG levels were taken then correlation coefficient was 0.10; suggesting a stronger correlation of CIMT with FTG at values above 150 mg/dl.

If the subjects with normal FTG were taken to calculate correlation between PPTG and CIMT, correlation coefficient was 0.848 and if only the subjects with raised FTG were taken then the correlation coefficient was 0.735; suggesting a stronger correlation of PPTG with CIMT at normal fasting triglyceride levels.

DISCUSSION

Several studies indicate that postprandial metabolic derangements, most notably hyperglycemia and hypertriglyceridemia, are important cardiovascular risk factors since they induce oxidative stress and endothelial dysfunction, although the mechanism is unclear [11]. Measurement of carotid intima-media thickness by ultrasonography is a non-invasive and quantitative method of evaluating early atherosclerotic changes in the vasculature. It has been shown that an increase in carotid IMT is associated with an increased risk of ischemic heart disease (IHD) or cerebrovascular disease [10]. Increased thickness of intima and media of carotid artery directly increases the risk of myocardial infarction and stroke in elderly adults without a history of cardiovascular disease [12].

It is evident that postprandial dyslipidemia can induce oxidative stress and endothelial dysfunction since endothelial dysfunction is accompanied by a significant nitric oxide increase. In fact, the postprandial state as produced by ingestion of a fat-enriched meal, is associated with endothelial activation, as indicated by the increased circulating levels of the proinflammatory cytokines such as IL-1, IL-6 and adhesion molecules ICAM-1 and VCAM-1. The most common presentation of diabetes is elevated fasting blood sugar. Hyperglycemia via glycation and increase in activity of the protein kinase C pathway appears to cause oxidative stress [13]. Elevated postprandial dyslipidemia activates coagulation factor 7 and plasminogen activator inhibitor and interacts with the process of thrombosis [14].

Postprandial hypertriglyceridemia is proinflammatory and prothrombotic and severely affects endothelial functions due to oxidative stress, resulting in an atherogenic environment [12]. Studies by Gandiah P et al., [15] also confirmed that to know the risk of coronary artery disease in patients with Type II diabetes mellitus, random lipid level determination 4 hours after normal meals was an ideal way.

The present study was done on 50 North Indian Patients in the age group of 35 to 75 years, all of whom were known cases of diabetes mellitus for minimum 1 year duration. Carotid intima media thickness and fasting and postprandial triglyceride levels were estimated of all the subjects. The cases were divided into three categories for making comparisons; Normo-normo (NN) group, individuals with normal fasting and postprandial triglyceride levels; Normo-hyper (NH) group, individuals with normal fasting but high postprandial triglyceride levels and Hyper-hyper group (HH), individuals with high fasting and postprandial triglyceride levels.

In the present study the mean CIMT was highest in HH group (1.52+ 0.33mm), lowest in NN group (0.68 + 0.12mm) and intermediate in NH group (1.17 + 0.17mm) and this observed difference was statistically highly significant. In a study done by Teno et al.,[10], mean CIMT in NN group was 0.73 + 0.13mm, in NH group it was 0.86 + 0.13 and in HH group it was 0.85 + 0.12. In the study by Fiza et al.,[16] mean CIMT in NN group was 0.93 + 0.32mm, in NH group it was 1.48 + 0.54 and in HH group it was 1.79 + 0.45. In the study by Chen et al.,[17] patients with postprandial hypertriglyceridemia had carotid intima media thickness 0.90mm as compared with 0.81mm in patients with normal levels of postprandial triglycerides.

In the present study, a positive correlation was found of CIMT and hence of atherosclerosis with PPTG and FTG. PPTG levels correlated best with CIMT and level of correlation was significant at all values of PPTG. On the other hand, FTG correlated very poorly at FTG values of less than 150 mg/dl (r = 0.1039). In the study by Teno et al.,[10] CIMT correlated best with PPTG levels (r=0.414) and correlation of FTG with CIMT was weak (r=0.27) and at FTG values less than 150 mg/dl no correlation existed. In the study by Fiza et al.,[16] maximum correlation of CIMT was with PPTG (r=0.429) and level of correlation with fasting triglycerides was poor (r= 0.298). In contrast; study by Dharmalingam et al.,[18] proposed that there was a better correlation (r=0.9) between fasting triglycerides and CIMT. However they disproved any correlation between CIMT and PPTG. Ryu et al.,[19] in their study on middle aged subjects concluded that peak triglyceride response after a fat meal correlates best with CIMT (r=0.52).

CONCLUSION

The present study suggests that levels of both the fasting triglycerides and postprandial hypertriglycerides are significantly correlated with Carotid intima media thickness and hence can cause atherosclerosis in patients with Type

II Diabetes Mellitus. Thus, these investigations are must in such cases, however the correlation between increased PPTG and CIMT is even stronger and thus can be an independent risk factor of atherosclerosis. However the limiting factor in the study is that the lipid lowering effects of oral hypoglycaemic agents in such cases should also be accounted for. Also ensuring uptake of standard meal by the patients and assuring them to get the levels done within four hours is another challenge. The study advocates a need for an exhaustive study to document the correlation between various cardiovascular disease risk factors with CIMT to manage patients well and to reduce risk of such disorders.

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