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An observational study of post prandial hypertriglyceridemia is a reliable predictor for coronary artery disease

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***Abstract*---**Introduction: Hypertriglyceridemia is recognized as a high-risk factor for coronary artery disease. It remains unclear whether fasting or postprandial hypertriglyceridemia is more informative for predicting the risk of coronary artery disease. Recent studies recommended postprandial Hypertriglyceridemia as a useful predictor of cardiovascular disease risk. This study was conducted to find the correlation between postprandial Hypertriglyceridemia in patients with coronary artery disease. Materials and Methods: This was an observational study on 100 patients diagnosed with coronary artery disease from 14/10/2017 to 10/09/2018. In patients diagnosed with coronary artery disease based on ECG changes or TMT, changes were included in the study. Fasting lipid profile, FBS, and 2-hour postprandial Triglyceride were done. All statistical data were analyzed using frequency, percentages, and ratios. A chi-square test is used to study the associations among different variables. Results: Among the 100 cases included in the study, 68 were males, and 32 were females. Postprandial Hypertriglyceridemia was found in 71% of patients, 48% had high BMI, 80% of Patients had high Waist Hip ratio, and 64 % of patients had diabetes mellitus. There is a statistically significant correlation between postprandial Triglyceride and coronary artery disease with a relative risk of 1.45. Conclusion: Coronary artery disease patients with normal fasting triglycerides levels have postprandial Hypertriglyceridemia. So postprandial Hypertriglyceridemia is a better and reliable predictor of coronary artery disease.

***Keywords*---**hypertriglyceridemia, myocardial infarction, coronary artery disease, atherosclerosis.

Introduction

Triglyceridemia is an independent risk factor for coronary artery disease irrespective of total cholesterol and LDL cholesterol or low HDL cholesterol.[1] ATP III guidelines2 suggest at least 9 hours fasting before estimating lipid profile. Many studies did not agree with this practice. Although this association is not entirely certain, it does raise into question the requirement for obtaining fasting lipoprotein measurements.[2,3] Coronary artery disease (CAD) due to atherosclerosis is the leading cause of death and disability in the developed world. Diabetes, Hypertension, Obesity, Sedentary lifestyles are known risk factors for CAD. The role of blood triglycerides levels in predicting CAD independently remains unclear. In addition, it remains to be determined whether fasting or nonfasting levels are informative for CAD risk. In practice, triglycerides are routinely measured in the fasting state.

However, postprandial lipids may play an important role in the pathogenesis of CAD because postprandial triglyceride-rich remnant lipoproteins can penetrate the endothelial cell layer and reside in the subendothelial space and contribute to the formation of foam cells, a hallmark of early atherosclerosis. Elevated postprandial levels of triglycerides via higher peak concentrations or delayed clearance also might represent an abnormal response to an oral fat load that reflects insulin resistance and predispose an individual to CAD· Heart Disease is responsible for more deaths and disability among the Western Population, both male and female, than any other killer disease, and it is quickly establishing itself as the leading cause of death and disability among Indians as well.

This sudden increase in the incidence of Heart disease is seen in our people, as they have adopted a more sedentary westernized lifestyle together with the intake of high- fat, high-salt diet and processed food. Researchers are noticing that Diseases prevalent in the western hemisphere are now becoming more and more prevalent causes of death in Asia. The most important cause of Coronary Artery Disease is Atherosclerosis. The risk factors for atherosclerosis are smoking, diabetes mellitus, dyslipidemia, sedentary lifestyle, positive family history, hypertension, and obesity. The association between atherosclerotic diseases and elevated fasting plasma LDL-C and reduced fasting plasma HDL-C is well established.

However, many individuals without fasting lipid abnormalities develop atherosclerotic diseases, and several lines of evidence suggest that nonfasting lipid measurements may be more relevant to atherogenesis. Typical diets are associated with measurable postprandial lipemia over 18 hours of the day. A major source of circulating triglycerides is dietary fat, which undergoes hydrolysis into free fatty acids and glycerides and is transported through the intestinal villi, absorbed by enterocytes, where these particles are synthesized into chylomicron-associated Triglycerides for entry into the blood compartment and ultimately storage in adipose tissue.

Postprandial lipids and their associated partially hydrolyzed chylomicron remnants, small LDL particles appear to promote early atherogenesis and adversely affect endothelial function. They correlate with both pro-thrombotic and

proinflammatory biomarkers, including factor VII, plasminogen activator inhibitor-1, and C-reactive protein. Thus measurement of postprandial Triglycerides - particularly because the peak 3-4 hr after ingestion of a fat-rich meal-might well provide more relevant information on vascular risk than measurements based on fasting concentrations. Diabetic patients have delayed clearance of Triglyceride from the blood. Most type2 diabetic patients have postprandial triglycerides above optimal concentrations for several hours after meals. Moreover, optimal fasting concentrations are not always a good predictor of postprandial triglycerides.

So there should be some association between postprandial lipid Metabolism and atherosclerosis, which remains to be proved. Two articles recently published in the Journal of the American Medical Association directly address these issues by comparing fasting with nonfasting (Postprandial) triglycerides with respect to the prediction of future cardiovascular events. In an Asia Pacific cohort studies, a collaborative study that included data from 26 cohorts showed postprandial triglyceride concentrations were a more potent predictor of vascular events than were fasting triglycerides. Our study is aimed at establishing the association between postprandial Hypertriglyceridemia and atherosclerosis.

Objectives

- To study the association of postprandial Hypertriglyceridemia in patients with coronary artery disease.
- To study the association between risk factors for atherosclerosis and postprandial triglyceride levels in patients with coronary artery disease.

Materials and Methods

This was an observational study on 100 patients diagnosed with coronary artery disease from 14/10/2017 to 10/09/2018

Source of data

The data is collected from all patients aged above 18 years attending OPD or admitted at Father Muller Medical College Hospital who are diagnosed to have coronary artery disease on the basis of history of angina pain or with electrocardiogram changes or with significant TMT changes with fasting serum triglycerides less than 150mg/dl. This study is approved by the Ethical Committee of the Institute. An informed consent was taken from the patients and the following information documented – name, age, occupation and the place of residence.

A history of the predisposing factors, occupation, past history of diabetes, hypertension, family history, habits of smoking and alcohol was noted and the presenting complaints are elicited followed by a general physical examination and cardiovascular systemic examination. Blood pressure measurements were performed with a mercury sphygmomanometer in a standardized fashion. Height measured in standing position without shoes with a standard tapemeter.

Body mass index was calculated with formula of B.M.I = wt(kg)/Ht (m^2)
Classification of obesity was done as per the National Institutes of Health Definition:
Normal range: 18.5-24.9
Overweight: 25-29.9
Obesity: Class I - 30-34.9 Class II - 35- 39.9 Class III - > 40

Waist circumference was measured at the umbilical level. Hip circumference was measured at maximum girth at the hip. Waist hip ratio cut off points > 1.0 for male and > 0.85 for female was considered.

ECG

Recording of ECG was done with 12 leads recording in standard fashion with B.P.L machine. ECG showing ST segment depression or elevation in two consecutive chest or limb leads were taken for study. The patients fulfilling the "Inclusion" and "Exclusion" criteria are included in the study using the purposive sampling technique.

Inclusion criteria

Patients having a history of angina pain, Electrocardiogram changes of CAD, Significant TMT changes suggestive of CAD.

Exclusion Criteria

Patients on lipid lowering agents, Case of Rheumatic heart disease. Patients on oral contraceptive pills, or other hormone therapy, Patients on anti thyroid drugs.

Statistical Analysis

All statistical data were analysed using statistical package for social sciences and frequency, percentage and ratios were analysed from the data, Chi-square test and student "t" test was used to assess the statistical significance of the findings. The significance of the test was decided on the basis of P-value. Two tailed P-values < 0.05 were considered significant.

Data analysis done in order of

A. Profile of Patients
B. Segregation of patients into two groups according to
    1. Postprandial Triglyceride levels: Normal: up to 160 mg%, High: > 160mg%.
    2. According to the presence or absence of Diabetes Mellitus.
    3. Obese and non-obese.
    4. According to Waist-Hip ratio.
    5. According to the presence or absence of hypertension.

Results

Table - 1: Distribution according to age andsex, body mass index and gender & waist-HIP ratio and sex

Distribution of patients according to	Male	Female	Total
1. Age & Sex			
35-45	3	1	4
46-55	40	20	60
56-65	22	8	30
>66	3	3	6
Total	68	32	100
2. BMI & Gender			
Normal	6	2	8
Over weight	32	12	44
GR – I Obesity	20	8	28
GR – II Obesity	6	6	12
GR – III Obesity	4	4	8
Total	68	32	100
3.Waist- Hip Ratio and Sex			
Normal	12	8	20
High	56	24	80
Total	68	32	100

In this study, there were total of 100 patients, out of whom 68 were male and 32 were female. Only 1 female patient is aged less than 45 years. There were 60 patients in the age group 46-55 out of which 40 were male, and 20 were female. In the age group 56-65 years, 22 were male and 8 were female, while only 3 males and3 females were in the age group of >66 years. (Table-1) In this study, 44 patients were overweight among them 32 were male (72.7%) and 12 were female (27.2%). 48 were obese among them 30 males (62.5%) and18 females (37.5%). 8 patients had normal weight among them 6 were male (75%) and 2 females (25%).(Table-1)

In this study, 56 male patients out of 68 males have a high waist-hip ratio (82.3%) and 24 female patients out of 32 female patients (75%) had a high waist-hip ratio.(Table-1)

Table - 2: Presence of diabetes mellitus & hypertension

Presence Of	Male	Female	Total
1. Diabetes Miletus			
Presence	46	18	64
Absence	22	14	36
Total	68	32	100
2. Hypertension			
Presence	50	22	72
Absence	18	10	28
Total	68	32	100

In this study, out of 68 males 46 (67.6%) were suffering from diabetes mellitus. While 18 females out of 32 were (56.2%) diabetic. So out of 100 patients, 64 patients were suffering from diabetes. In this study, 72 patients were hypertensive. 50 male patients out of 68 male patients were hypertensive (73.5%) and 22 female patients out of 32 patients (68.5%) were hypertensive. (Table-2)

Table - 3: Distribution according to PP2TG & F.HDL

Distribution According To	Male	Female	Total
1. PP2TG			
Normal	19	10	29
High	49	22	71
Total	68	32	100
2. HDL			
Low	41	20	61
Normal	27	12	39
Total	68	32	100

In this study, out of 100 patients, 71 patients showed S.triglyceride levels >160 mg% after two hours of a meal. 49 out of 68 male patients (72.6%) and 22 out of 32 females (68.7%) showed postprandial Hypertriglyceridemia. (Table-3) In this study, 61 patients had a low fasting HDL level. 41 out of 68 males (60.2%) and 20 out of 32 females (62.5%) had low fasting HDL level. (Table-3)

Figure-1 : Baseline characteristics

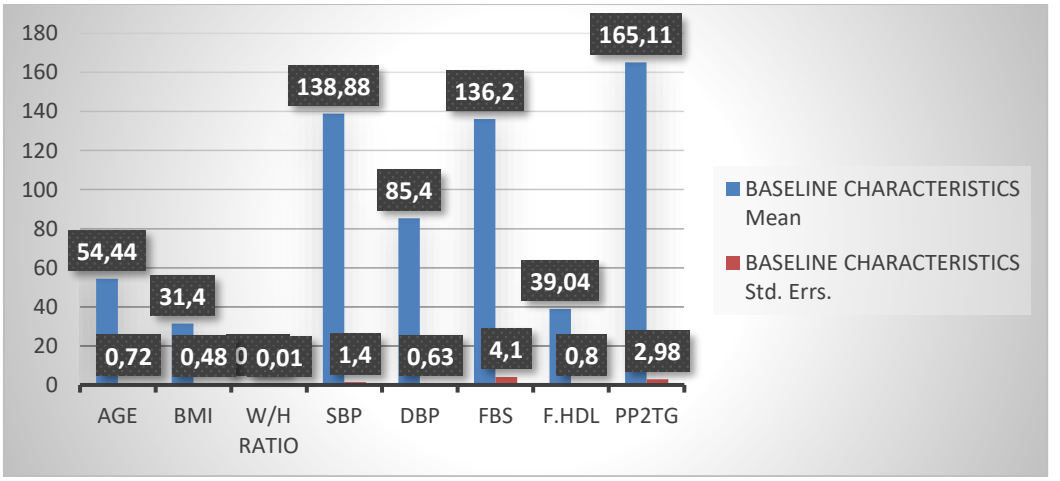

Table – 4: Distribution according to age, waist-HIP ratio, BMI, diabetes hypertension and PP2TG

Distribution According to	Normal PP2TG	High PP2TG	Total
1. Age			
35-45	0	4	4

46-55	18	42	60
56-65	10	20	30
>66	1	5	6
Total	29	71	100
2. W-H Ratio			
Normal	16	4	20
High	13	67	80
Total	29	71	100
3. BMI			
Normal	5	3	8
Overweight	10	34	44
High	14	34	48
Total	29	71	100
4. Diabetes			
Absent	24	12	36
Present	10	54	64
Total	34	66	100
5. Hypertension			
Absent	10	18	28
Present	24	48	72
Total	34	66	100

In this study, postprandial Hypertriglyceridemia was found in all 4 patients (100%)in the age group 35-45, 42 patients out of 60 patients (70%) in the age group 45-55, 20 out of 30 patients (66.6%) in the age group 55-65, and 5 patients out of 6 (83.3%) in the age group above 66 years. (Table-4) In our study, out of 80 patients having a high waist-hip ratio, 71(86.5 %) had high postprandial triglyceridemia. Out of 20 patients having a normal waist-hip ratio, 4 had high postprandial triglyceride levels, while 16 had normal postprandial triglyceride levels. The calculated P-value was < 0.05 suggesting an association between High waist-hip ratio and High PP2TG level. (Table-4)

In the present study, out of 48 patients having a high body mass index, 34 patients (70.8%) had high postprandial triglyceride levels. While out of 44 patients having Body Mass Index in overweight range, 34 patients had (77.2%) high postprandial triglyceride levels and 3 patients out of 8 patients (37.5%) having normal Body Mass Index had high PP2TG levels. (P value < 0.05 by Chi-square method). (Table-4) In this study out of 64 diabetic patients, 54 had high PP2TG (84.3%). In 36 non diabetic patients, 12 patients had high PP2TG (33.3%).(Table-4) There was association found between Diabetes Mellitus and High PP2TG levels. Among 72 hypertensive patients, 48 patients had high PP2TG (72.7%). Among 28 normotensive patients 18 patients high PP2TG (64.2%). There was an association found between Hypertension and High PP2TG level (P value < 0.05).

Discussion

Age and gender

In the present study, 60% patients were aged less than 55 years. While 62.5% female and 58.81% male were aged less than 55 years. This shows that the majority of the patients were in the middle age group. (P value <0.05) In Hiroyasu et al study, 55% were male and 45% were female, the average age was 55.1 ± 6.3 years. In that study also the majority of patients were from the middle age group. (P value < 0.05)

Obesity and waist-HIP ratio

In our study, 44% of patients were overweight, 48% of patients were obese, according to the National Institutes of Health Definition. The mean BMI was 30.08. The mean BMI in the normal Fasting TG group was 28.96 and the high PP2TG group was 32.51, so there is a strong correlation found between High BMI and High PP2TG. In Hiroyasu et al study, the mean BMI was28.08. The mean WHR in normal Fasting TG group was 0.94 and the High PP2TG group was 1.01, so there is a correlation found between High WHR and High PP2TG. In Couillard et al[5] study, on postprandial triglyceride response in visceral obesity showed that obesity and waist hip ratio are associated with impaired postprandial TG clearance.

Diabetes mellitus In our study, 64% were diabetic of which 67.6% were male were and 56.2% were females

In Hiroyasu et al study, 52.1% of patients were diabetic. A study was done by Mette Axelsen et al[30], on postprandial Hypertriglyceridemia and type-2 diabetes showed postprandial lipid intolerance despite having normal fasting triglyceride levels and increased risk of macroangiopathy.

Triglyceride

In our study, out of 100 patients, 71 patients showed serum triglyceride level more than 160 mg% after 2 hours of meal. 49 out of 68 male patients (72%) and 22 out of 32 females (47%) showed postprandial Hypertriglyceridemia. These data revels that patient having ischemic Heart disease, even if they have normal fasting triglyceride levels, they might have impaired postprandial lipid metabolism. The mean PP2TG was 165.3 mg% (P Value < 0.05) suggest that there is an association between coronary artery disease and PP2TG levels and the relative risk was 1.45. In Hiroyasu et al study, 58% male and 64% of female patients showed postprandial Hypertriglyceridemia. (P value < 0.05).

In Borge G. Nordestgaard et al[3]study on nonfasting triglycerides and risk of Myocardial infarction, Ischemic Heart disease and Death in Men and Women showed that nonfasting triglyceride levels independently predict myocardial infarction, ischemic heart disease and death.

Hypertension

In our study 72 patients had hypertension. Among them, 66 patients had high PP2TG. The mean systolic blood pressure in normal PP2TG group was 124.1 and the high PP2TG group was 138.16 and the mean diastolic blood pressure in the normal PP2TG group was 84.18 and high PP2TG group was 85.27, so there is correlation found between hypertension and HighPP2TG. In Kolovou et al[6] study on postprandial Lipemia in Hypertension suggest that patient with hypertension have an exaggerated response and delayed clearance of plasma TGL concentration.

Conclusion

In this study with reference to patient of coronary artery disease, postprandial Hypertriglyceridemia was found in 71% patients having normal fasting triglyceride level. There is statistically a significant correlation between postprandial Triglyceride and coronary artery disease even in patients having normal fasting triglyceride level. It means that patients having high postprandial triglyceride levels have a higher risk of coronary artery disease. The relative risk is 1.45. There is statistically a significant correlation found between postprandial Hypertriglyceridemia and high waist-hip ratio, Diabetes Mellitus, BMI and hypertension.

Limitations of the study

The sample size of this study is small and the significant difference of disparity between the group of patients and equal distribution in each group is not satisfied. The fat proportion of the diet on the day of collecting blood for postprandial triglyceride level assessment needs to be formulated.

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