

Correlation of Postprandial Lipemia with Postprandial Hyperglycemia and Poor Glycemic Control Among Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction: Postprandial lipemia characterized by a rise in triglyceride-rich lipoproteins after eating, is associated with increased risk of cardiovascular disease. Among diabetic patients, postprandial lipemia is often overlooked once fasting lipid parameters are within target. The aim of the study is to determine the correlation of glycemic control and postprandial hyperglycemia with postprandial lipemia among patients with type 2 diabetes mellitus (DM). The result of the study may have important implications on how dyslipidemia should be completely addressed.

Methodology: A clinic-based retrospective chart review of 102 patients with recorded fasting and postprandial blood measurements was performed. Subjects included adult patients with type 2 DM whose fasting lipid parameters were controlled with diet and/or medications. Plasma glucose and glycosylated hemoglobin (HbA1C) were independent variables while triglyceride, total cholesterol, low density lipoprotein (LDL) and high density lipoprotein (HDL) were dependent variables. Pearson correlation was used to determine the strength of relationships among the variables mentioned. A p-value <0.05 was considered significant.

Results: Of the 102 patients, 52.9% and 47.1% were achieving their target HbA1C and two-hour postprandial plasma glucose, respectively. The postprandial level of plasma glucose, mean triglyceride, total cholesterol, LDL and HDL were 196.39 mg/dL, 189.06 mg/dL, 177.07 mg/dL, 122.40 mg/dL and 34.83 mg/dL, respectively. HbA1C has strong positive correlation with postprandial lipemia (Pearson's $r=0.40$) while the two-hour plasma glucose has moderate positive correlation (Pearson's $r=0.34$) with postprandial lipemia. Both relationships were considered significant (p-value <0.05).

Conclusion: A significant correlation of glycemic control and postprandial hyperglycemia with postprandial lipemia was observed. Our data suggest that despite achievement of optimal fasting lipid parameters, poor control of diabetes is positively correlated with abnormal elevation of postprandial triglyceride. Addressing both postprandial hyperglycemia and lipemia may improve cardiovascular outcome.

Keywords: postprandial lipemia, postprandial hyperglycemia, diabetes mellitus

Introduction

People spend most of their waking hours in the postprandial state, yet glucose and lipids are systematically monitored in the fasting state.^{1,2} Epidemiologic data indicate that a postprandial state characterized by abnormally increased levels of glucose and lipids is an independent predictor of future cardiovascular events. Postprandial hyperglycemia and lipemia increases oxidative stress which triggers a series of inflammation, endothelial dysfunction, hypercoagulability and sympathetic hyperactivity.^{3,4}

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Compared to normal individuals, patients with type 2 diabetes mellitus (DM) have a slower clearance of chylomicrons from the blood after dietary fat. Liver is the major site of remnant lipoprotein clearance which may be aided by apoprotein E and hepatic lipase. The latter may be reduced in diabetes.⁵

Several studies have shown that a fasting glucose of 90 mg/dl can be associated with a two-hour postprandial glucose level >200 mg/dl. Postprandial hyperglycemia can cause macrovascular and microvascular complications and the level correlates with risk of cardiovascular death and all-cause mortality. The risk of postprandial hyperglycemia begins to increase at levels >80 mg/dl. By 140 mg/dl, cardiovascular risk is already increased by 58%.^{6,7}

Postprandial lipemia is considered an important risk factor for cardiovascular disease among patients with type 2 DM. It is characterized by elevated levels of triglycerides, chylomicron remnants and free fatty acids. Fasting triglycerides <150 mg/dl is considered

to be the optimal fasting triglyceride concentration for which cardiovascular risk is expected to be lower. However, optimal fasting lipid concentrations are not always a good predictor of postprandial triglycerides. Despite normal fasting triglyceride levels, elevated postprandial triglycerides may be an independent risk factor for early atherosclerosis in type 2 DM. Carotid intima media thickness was also greater in patients with postprandial elevation of triglyceride levels.⁸

Objective and Significance of the Study

The aim of the study is to determine the correlation of glycemic control and postprandial hyperglycemia with postprandial lipemia among patients with type 2 DM. Postprandial lipemia may independently potentiate the adverse effects of postprandial hyperglycemia by augmenting oxidative stress and inflammation. The result of the study might have important implications on how dyslipidemia among diabetic patients should be properly addressed.

Methodology

This is a cross-sectional single centre analytical study at an endocrine clinic at the University of Santo Tomas Hospital. Eligible subjects included adult patients with type 2 DM and dyslipidemia seen between January 2011 and December 2012. They had fasting and postprandial blood measurements as part of their regular initial or follow-up clinic visits. The sample size (184) exceeded the minimum requirement (127) for the study given the desired probability level, number of predictors, effect size and statistical power. The subjects included were adult (≥ 50 years old) Filipinos diagnosed with type 2 DM and dyslipidemia whose fasting lipid parameters were controlled with diet and/or medications which means they have most recent fasting total cholesterol < 200 mg/dl, LDL < 100 mg/dl and triglycerides < 150 mg/dl.⁹ The patients were instructed to eat a standard mixed meal that had a total energy of 9.0 kcal/kg with 60% of this energy being supplied by carbohydrate, 15% by protein and 25% by fats before their clinic visit. A special test meal is not necessary for the evaluation of postprandial hypertriglyceridemia. Blood samples were taken two hours after the meal. Serum triglyceride levels are generally increased for three to six hours after a meal.¹

Of the 164 records reviewed, 102 were included in the study. The rest were excluded because their fasting lipid concentrations were not at their optimal level after diet modification and/or medications. Second-hour plasma glucose and HbA1C were the independent variables while triglyceride (TG), total cholesterol (TC) low density lipoprotein (LDL) and

high density lipoprotein (HDL) were the dependent variables. Pearson correlation was used to determine the strength of relationships among the variables mentioned. The statistical analyses were performed using Statistical Package for the Software Sciences (SPSS). Pearson's r was interpreted as follows: > 0.70 for very high correlation, 0.40 - 0.69 for strong correlation, 0.30 - 0.39 for moderate correlation, 0.20 - 0.29 for weak correlation and 0.10 - 0.19 for negligible correlation.¹⁰ A p -value < 0.05 was considered significant.

Results

The baseline characteristics of patients included in the study were shown in Table 1. Most patients have long duration of DM (> 10 years) and with history of complications. Ninety five percent of patients were already on statin therapy. Of the 102 patients included in the study, 52.9% was achieving their target HbA1C ($< 7\%$) while 8.8% had poor glycemic control (HbA1C $> 9.0\%$) as shown in Figure 1. On the other hand, 47.1% was achieving their target postprandial plasma glucose (< 180 mg/dl) while 22.5% had postprandial glucose > 250 mg/dl as shown in Figure 2. The mean and range of postprandial lipid concentrations of patients for total cholesterol, triglyceride, low density lipoprotein (LDL) cholesterol, and high density lipoprotein cholesterol were 177.07 (100-288 mg/dl), 189.06 (60-483 mg/dl), 122.40 (41-195 mg/dl) and 34.83 (14-58 mg/dl), respectively (Table 2). Only 42 (41.2%) have postprandial triglyceride below 150 mg/dl while 12 (11.8%) have values above 300 mg/dl. The mean triglyceride-HDL cholesterol ratio was 5.55. HbA1C has strong positive correlation (Pearson's $r = 0.40$) with postprandial triglyceride. Two-hour postprandial plasma glucose has moderate positive correlation (Pearson's $r = 0.34$) with postprandial triglyceride. The p -values were considered to be significant (< 0.05). Other correlations were either weak or negligible.

Discussion

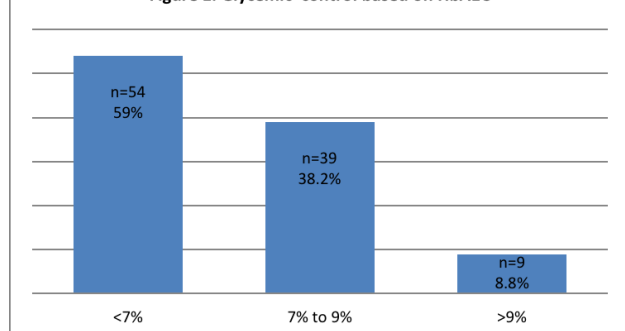
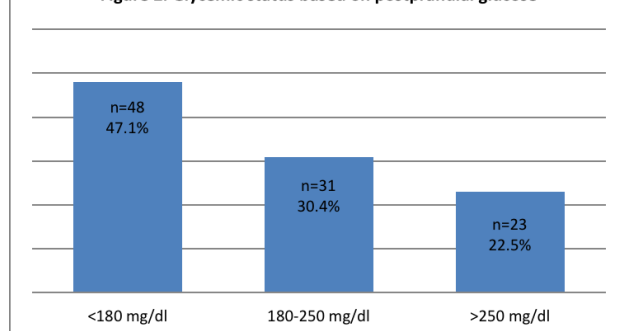
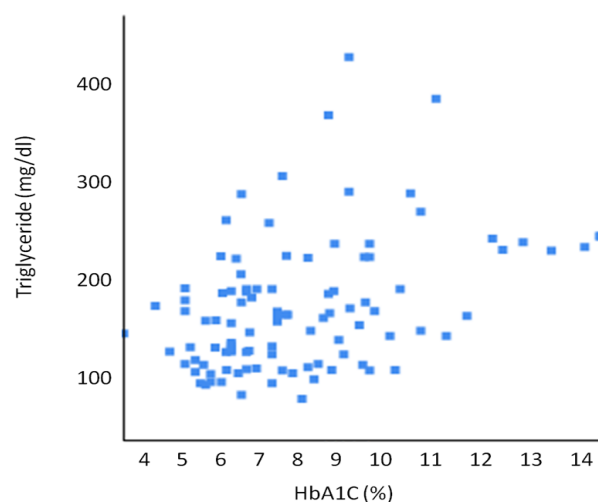
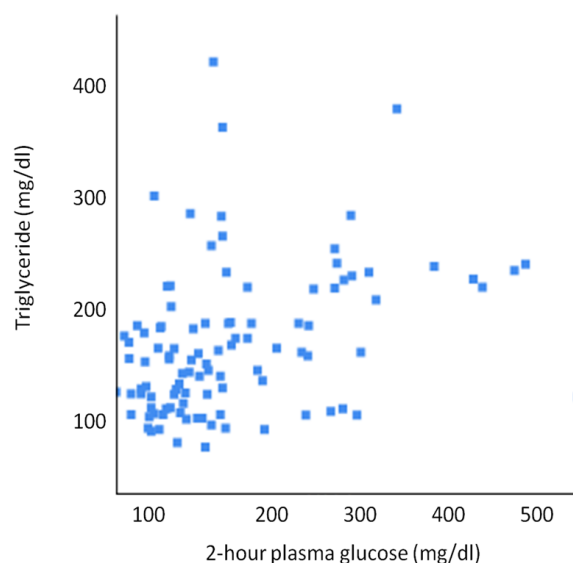
These analyses of cross-sectional data from 102 patients with DM and dyslipidemia demonstrate a clear correlation between glycemic control and postprandial lipemia. To date, this is the first study correlating HbA1C with postprandial cholesterol level. This proved even the fasting lipid concentrations are within the recommended range, there is still high likelihood of postprandial rise in triglycerides if the blood glucose is not yet controlled in reference to HbA1C and postprandial glucose. Scrutiny of the dysglycemia and dyslipidemia relationship suggests several insights from these observations.

Table I: Baseline characteristics of patients (N=102)

Age	59 years (39-78)
Male gender	48 (47.1%)
Duration of diabetes	22 years (6-42)
Hypertension	88 (86.3%)
Microvascular complication	76 (74.5%)
History of stroke or myocardial infarction	35 (34.3%)
On insulin alone	38 (47.2%)
On insulin and oral antidiabetic medication/s	52 (51.0%)
On oral antidiabetic medication/s alone	12 (11.8%)
On statin alone	86 (84.3%)
On statin and/or fenofibrate	11 (10.8%)

Table II: Mean and range of postprandial lipid concentrations

Total cholesterol	177.07 (100-288 mg/dl)
Triglyceride	189.06 (60-483 mg/dl)
LDL cholesterol	122.40 (41-195 mg/dl)
HDL cholesterol	34.83 (14-58 mg/dl)

Figure 1. Glycemic control based on HbA1C**Figure 1: Glycemic control based on HbA1C****Figure 2. Glycemic status based on postprandial glucose****Figure 2: Glycemic status based on postprandial glucose****Figure 3: Pearson correlation between HbA1C and postprandial triglyceride****Figure 4: Pearson correlation between second-hour plasma glucose and postprandial triglyceride**

First, measurement of fasting lipid concentrations may not be enough in patients with DM. Once optimal fasting lipid profile is achieved, clinicians must consider evaluation of postprandial lipid parameters especially serum triglycerides. Once postprandial hypertriglyceridemia occurs, it is exacerbated by the next meal and persists for the entire day. This vicious cycle may augment the oxidative damage brought by hyperglycemia.^{1,11}

Second, glycemic control in reference with the most recent HbA1C is strongly correlated for postprandial rises in triglycerides. The poorer the control of DM can lead to a greater likelihood of hypertriglyceridemia. The severe hypertriglyceridemia

can potentiate another vicious cycle of recurrent pancreatitis and insulin deficiency that can further worsen the control of diabetes. In the absence of HbA1C, a weaker yet still significant correlation between postprandial hyperglycemia and hypertriglyceridemia is observed. Monitoring postprandial glucose can be a reliable surrogate marker for occurrence of postprandial lipemia.^{2,3}

Third, serum triglyceride-HDL cholesterol ratio is an index of atherogenesis and insulin resistance. Among the patients studied, the mean ratio is 5.55. This is higher than those observed in studies correlated with insulin resistance and atherosclerosis (>3.6). This ratio is also predictive of extensive coronary artery disease among diabetic patients.¹²

In summary, our analyses in patients with DM and dyslipidemia confirm the entity of diabetic dyslipidemia or dysmetabolism. Many studies have linked postprandial dyslipidemia specifically triglyceride level with cardiovascular morbidity and mortality.¹³ The deadly duo of postprandial hyperglycemia and lipemia may be the interrelated and synergistic reason for accelerated macrovascular injury among this population.

Conclusion

A significant correlation of glycemic control and postprandial hyperglycemia with postprandial lipemia was observed. Our data suggest that despite achievement of optimal fasting lipid parameters, poor control of DM is strongly correlated with abnormal elevation of postprandial triglyceride. Addressing both postprandial hyperglycemia and postprandial lipemia simultaneously may have greater impact on the management of DM and its complications than treating them individually.

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