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Correlation between Very Low-Density Lipoprotein and Trygliseride with Glycated Hemoglobin Levels in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Patients with Type 2 Diabetes Mellitus (T2DM) have an increased prevalence of dyslipidemia, which contributes to a higher risk of dyslipidemia- related complications in T2DM such as cardiovascular disease and stroke. This study aimed to determine the correlation between TG and VLDL-C towards HbA1c levels in a person with T2DM. A retrospective study of 74 outpatients with T2DM at Sanglah General Hospital, Denpasar, who examined serum HbA1c and lipid profiles were traced for serum TG. From the obtained TG profile, a secondary calculation of VLDL was carried out using the Friedewald equation (TG/5). A correlation test was used to determine the relationship between TG and VLDL-C towards HbA1c levels. Serum TG (212.95±147.46 mg/dL) and VLDL (36.69±23.54 mg/dL) were found to be higher in the group with poor glycemic control (HbA1c > 7 mg/dL) compared to serum TG (111.00±39.56 mg/dL) and VLDL (21.05±6.13 mg/dL) in the group with good glycemic control (HbA1c ≤ 7 mg/dL) ($p < 0.05$). A positive correlation between serum TG ($r=0.512$; $p < 0.001$) and VLDL ($r=0.18$; $p <0.001$) towards HbA1c levels in T2DM patient was found. Insulin resistance increases the production of VLDL and ApoC-III in the liver and increased chylomicron absorption in the gastrointestinal tract, causing prolonged postprandial lipemia and disruption of VLDL and TG clearance, thereby resulting in increased TG and VLDL in circulation. There is a significant positive correlation between serum TG and VLDL towards HbA1c levels in a patient with T2DM.

Keywords: Lipid profile, correlation, diabetes, triglyceride

INTRODUCTION

Diabetes Mellitus (DM) is the most common metabolic disease in humans that is marked by a defect in insulin action, secretion, or both (insulin resistance).[1] Morbidity and mortality that are related to DM will increase due to the changes in lifestyle, such as an unhealthy diet, a decrease in physical activity, obesity, and smoking. Diabetes mellitus global incidence is 8.3% and estimated to be 451 million people (18–89 years old) in 2017 and will keep increasing, reaching 63 million in 2045.[2,3] The increase of DM incidence in the future will increase DM-related complications, such as coronary heart disease, peripheral artery disease, stroke and other endothelial dysfunctions that are caused by DM.[4]

Glycated hemoglobin (HbA1c) an indicator of long-term glycemic control can also predict diabetes-related complications. Dyslipidemia is a condition that often happens in patients with Type 2 Diabetes Mellitus (T2DM) that is related to poor glycemic control.[5] There is a close relationship between a patients' glycemic control and lipid profile, causing a need for monitoring these conditions to prevent DM related microvascular and macrovascular complications. Dyslipidemia is one of the risk factors for coronary heart disease.[3,4] Atherogenic activity in T2DM with dyslipidemia is marked by a low level of HDL, and a high LDL and TG level.[6]

Naqvi *et al*. found a positive significant correlation between HbA1c serum and TG serum in patients with T2DM ($r=0.278$; $p < 0.001$).[7] This explains that there is a relationship between the lipid profile and glycemic index and vice versa.[7] An improvement in glycemic-index will give a beneficial effect on lipoprotein levels in diabetes by decreasing the cholesterol and TG causing a decrease in circulating VLDL and an increase in LDL catabolism from the reduction glycation pathway and an increase in LDL receptor uptake.[8] This study aimed to evaluate the relationship between lipid profile (TG and VLDL) with HbA1c levels in T2DM patients.

METHODS

This is a retrospective cross-sectional study in T2DM patients that were routine Outpatients Clinic

of Sanglah Hospital, Denpasar in the January 2020–March 2020 period. This study was approved by the study Ethical Committee FK UNUD with article number 2182/UN14.2.2.VII.14/LT/2020. Data was collected from laboratory results taken from the Laboratory Information System (LIS) of Sanglah Hospital, Denpasar. Patients that examined HbA1c and lipid profile were traced for TG values, used to manually calculate the VLDL concentrations using the Friedewald (TG/5). Patients have chosen by certain characteristics such as age and gender then grouped based on their glycemic control. Inclusion criteria for this study were all male or female T2DM patients that had HbA1c and TG examinations. Exclusion criteria were if the TG levels were over 400 mg/dL, patient with an underlying disease that would affect glycemic control and lipid-like thyroid disease; chronic liver disease or malignancy, and type 1 diabetes mellitus.

The number of samples in this study was calculated using the correlation minimal sample equation, with a result of 67 samples and added 10% for preventing drop out, so in total there were 74 patients. Samples were chosen by consecutive sampling (non-random sampling) that meant all samples fulfilling the inclusion criteria would be used. The free variable in this study was T2DM, and the dependent variables were HbA1c, VLDL, and TG), the control variables were age and gender. Normal range for TG (<150 mg/dL) and HbA1c (≤7%).

This study was analyzed by SPSS version 25.0, numeric variables were shown as mean and standard deviation, categorical variables were shown in amount and percentage. Pearson correlation analysis was used to analyze the correlation between VLDL and TC with HbA1c levels, and if the data was not normally distributed, the Spearman correlation test was used. All data were deemed statistically significant if $p < 0.05$.

RESULTS AND DISCUSSIONS

This study was held during January till March 2020 with 74 T2DM patients that fulfilled the inclusion criteria. The characteristics of the samples were based on age, gender and showed no significant difference between the group with poor glycemic control and good glycemic control ($p > 0.05$) meaning that both groups had homogenous characteristics (Table 1).

Serum triglyceride (212.95+147.46 mg/dL) and VLDL (36.69±23.54 mg/dL) were significantly higher in the group with poor glycemic control (HbA1c > 7 mg/dL) compared to serum triglyceride (111.00±39.56 mg/dL) and VLDL (21.05±6.13 mg/dL) in the group with good glycemic control (HbA1c ≤ 7 mg/dL) ($p<0.05$). Correlation analysis in this study found a positive significant correlation between serum TG ($r=0.512$; $p<0.001$) with HbA1c levels, and a significant positive correlation with serum VLDL-C ($r=0.418$; $p<0.001$). These results imply that the higher the serum TG and VLDL-C the higher the HbA1c levels in T2DM patients (Table 2). The scatter plot shows a positive correlation (the line rising to the upper right region) in TG and VLDL correlations with HbA1c levels (Figure 1).

Table 1. Sample Characteristics

Characteristics	Poor Glycemic Control (HbA1c >7) (n=48)	Good Glycemic Control (HbA1c = 7) (n=26)	p
Age (years old) (mean±SD)	58.04±9.83	63.38±12.76	0.071
Gender (n, %)			
Male	27 (73%)	10 (27%)	0.144
Female	21 (56.8%)	16 (43.2%)	
TG (mg/dL) (mean±SD)	212,95±147,46	111,00±39.56	< 0.001
VLDL-C (mg/dL) (mean±SD)	36.69±23.54	21.05±6.13	< 0.001

Table 2. Correlation analysis of VLDL-C and TG towards HbA1c levels in patients with T2DM

Variable	HbA1c		
	N	R	p
VLDL-C	74	0.418	< 0.001*
TG	74	0.512	< 0.001*

*Significant ($p<0.05$); VLDL-C: Very Low Density Lipoprotein Cholesterol; TG : Triglyceride

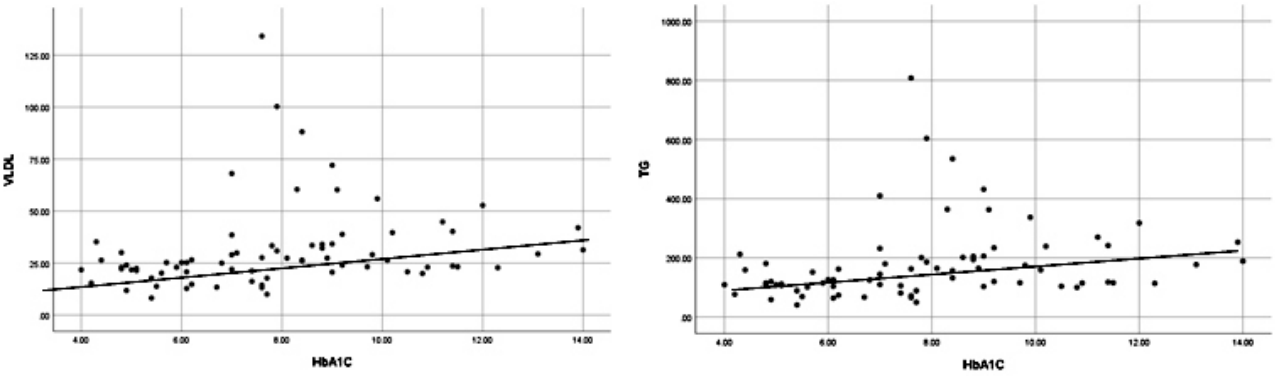

Figure 1. Correlation graph between VLDL (left) and TG (right) with HbA1c levels in T2DM patients

Diabetic condition is usually accompanied by unknown dyslipidemia, due to that matter the American Diabetes Association recommends a routine examination of the lipid profile in T2DM patients.[9] This study found that there was a higher VLDL and TG level in patients with poor glycemic control, and a positive statistically significant correlation between VLDL and TG with HbA1c levels in T2DM. HbA1c levels in a condition where hemoglobin is glycated indicating high blood glucose levels in the last three months, being the reason HbA1c is a standard in long-term blood glucose control.[10]

Artha *et al*. studied the effect of individual lipid ratio in 140 patients with T2DM in Bali and found a positive correlation between serum TG and HbA1c levels ($r=0.276$; $p<0.001$).10 Another study by Bhattaharjee *et al*. analyzed the correlation of HbA1c towards lipid profile in T2DM patients with acute myocardial infarct, finding that TG serum (170.33±1.94 mg/dL) was higher in the poor glycemic control group (HbA1c > 7 mg/dL) compared to TG levels in the good glycemic control group (HbA1c < 7 mg/dL ($p < 0.05$) also found a statistically significant positive correlation between TG and HbA1c ($r=0.560$; $p<0.05$).[11]

Insulin resistance alone can cause abnormalities in the lipid profile. A patient with insulin resistance usually has an overproduction of VLDL and ApoC-III of the liver and an increase in chylomicron uptake in the gastrointestinal tract. This causes prolonged postprandial lipemia, due to competition of VLDL and chylomicron in the same pathway mediated by lipoprotein to release TG from the circulation, postprandial lipemia causes a disruption in VLDL and TG clearance, causing a large amount of VLDL and TG to be found in circulation.[12] Dyslipidemia in T2DM patients is predicted to be caused by the activation of lipoprotein lipase due to insulin resistance. Under the influence of insulin, lipoprotein lipase has a role in helping metabolism in healthy people.[13] Type 2 diabetes mellitus, which is a condition that has relative insulin deficiency and a decrease in adiponectin levels that cause a decrease in lipoprotein lipase activity, results in a decrease of lipid metabolism causing an increase in LDL and TG while HDL decreases. Qualitative defect of LDL in T2DM is also connected to an increase in atherogenic activity triggers atherogenesis and increasing cardiovascular complications in T2DM.[13-15]

The limitations of this study are due to it being retrospective and the calculation of VLDL, which was based on secondary measurements, not directly, that contributes to the decrease in result generalization in this study towards actual happenings in the population. Data concerning DM therapy, physical activity, and diet is not available, which causes the inability to measure the influence of these variables on glycemic control.

CONCLUSIONS AND SUGGESTIONS

Patients from the poor glycemic control group had higher levels of VLDL and TG. There was a positive significant correlation between VLDL and TG with HbA1c levels in T2DM outpatients of Sanglah Hospital, Denpasar.

For further researchers, the results of this study can be used as a comparison and reference material for research, and as a consideration for further deepening further research.

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