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CORRELATION OF LIPID PROFILE WITH INTERLEUKIN-12 IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Dyslipidemia is one of the common disorders in the diabetes mellitus (DM) patients causes cardiovascular disorders. Interleukin-12 (IL-12) is an important inflammation cytokine and elevated in type 2 DM (T2DM) which may contribute to inflammation of atherosclerotic plaque formation. Hyperglycemia, hyperlipidemia, hyperinsulinemia and oxidative stress that lead to endothelial dysfunction of atherosclerotic. The aim of this study to determine the correlation of lipid profile with IL-12 in T2DM. This study was an analytical study with cross-sectional design in 30 patients T2DM meet the inclusion and exclusion criteria and conduct blood tests at the Central Laboratory Installation of Dr.M.Djamil Hospital Padang in September 2016-August 2017. Level of lipid profile performed by the enzymatic colorimetric method. Sandwich ELISA used to measure the level of IL-12 in Biomedical Laboratory Medical Faculty of Andalas University. Spearman correlation was used, significant if $p < 0.05$. The mean levels of total cholesterol, high-density lipoprotein (HDL), triglycerides and low-density lipoprotein (LDL) in T2DM were 204.2 ± 42.8 mg/dL; 46.8 ± 9.3 mg/dL; 57 ± 53.4 mg/dL; 132.97 ± 41.0 mg/dL. The mean level of IL-12 in T2DM is 160.15 ± 99.05 pg/mL. Spearman correlation test of total cholesterol, (HDL), triglycerides and (LDL) with IL-12 are $r = 0.228$ ($p = 0.225$); $r = -0.234$ ($p = 0.212$); $r = 0.415$ ($p = 0.031$); $r = 0.215$ ($p = 0.291$) and analysis linear regression showed a moderate correlation between the levels triglycerides and IL-12 with $r = 0.512$ and $p < 0.05$. There is a moderate positive correlation between triglycerides, weak between total cholesterol and LDL with IL-12 and negative correlation between HDL with IL-12 in T2DM.

Key words: Interleukin-12, lipid profile, type 2 diabetes mellitus

INTRODUCTION

Dyslipidemia is one of the common disorders in diabetes patients, which causes cardiovascular disorders.^{1,2} Dyslipidemias are characterized by isolated increase in low-density lipoprotein (LDL-C ≥ 130 mg/dL), triglycerides (TG ≥ 150 mg/dL), both LDL-C and TG, or by the reduction in high-density lipoprotein (HDL-C < 40 mg/dL).^{3,4} Abnormal serum lipids are likely to contribute to the risk of coronary artery disease in diabetic patients and its consideration in people with diabetes as a standard of diabetes care.² Dramatic increase in the incidence and prevalence of diabetes in people with genetic susceptibility to diabetes were resulted by changed in the human environment, behavior, and lifestyle.^{1,2} Institution of proven treatment modalities including good glycemic control, reduction in the blood pressure, control of dyslipidemia and modification of abnormal risk factors among others.¹

Interleukin-12 (IL-12) is an important cytokine produced by antigen-presenting T cells, such as dendritic cells, macrophages, and natural killer cells and it also plays a critical role in cell-mediated immunity, and its concentration elevated in people

with type 2 diabetics, contributes to atherosclerotic plaque formation and macrovascular complications.⁵ Increased systemic inflammatory activity in patients with CAD (coronary artery disease) is associated with a prominent Th1 response. Interleukin-12 plays a critical role in the changes in the blood of patients with type 2 diabetes remains unclear.⁶ Atherosclerosis is a chronic inflammatory disease triggered by lipid retention in the arterial wall.⁷

Therefore, the present study was undertaken to assess the correlation of lipid profile with interleukin-12 in type 2 diabetes mellitus.

METHODS

The study was conducted in September 2016 – August 2017 using a cross-sectional design and samples were taken consecutively. Subjects consisted of patient type 2 diabetic without cardiovascular disease, renal disease, liver, carcinoma in Outpatients of Internal Medicine, Dr. M. Djamil Hospital Padang. Lipid profile (total cholesterol, LDL, HDL, and triglycerides) were checked in Central Laboratory Dr. M. Djamil Hospital Padang. Level of lipid profile performed by the

enzymatic colorimetric method. Sandwich ELISA used to measure the level of IL-12 in Biomedical Laboratory Medical Faculty of Andalas University.

Statistical analysis was performed using a computer program. Alteration in variables of all groups was assessed by analysis of variance (ANOVA). The Spearman correlation test compared the correlation between two continuous variables. Multivariate linear regression was used to determine which of the analyzed independent variables primarily affects serum IL-12 concentrations. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The characteristic criteria of subjects were sex and age, without knowing other therapy of subjects. The subjects in this study consisted of (12) 40% male and 18 (60%) female. They were aged between 46-78 years, with normal distribution and mean age of 61.5 ± 8.6 years (Table 1).

Table 1. The characteristics of subjects

Variables	n (%)	mean (SD)
Male	12 (40)	
Female	18 (60)	
Ages (years)		61.5 (8.6)

Type 2 diabetes mellitus mostly found in female than male because its relationship with lipid in female more than 20-25% of total body weight compared to the male that consists of lipid about 15-20% of total body weight.⁸ Ages of type 2 diabetes mellitus based on literature could happen all of the years, but the most were 40–80 years old.⁹

The mean level of total cholesterol, High Density Lipoprotein (HDL), triglycerides and Low Density Lipoprotein (LDL) in T2DM were 204.2 ± 42.8 mg/dL; 46.8 ± 9.3 mg/dL; 57 ± 53.4 mg/dL; 132.97 ± 41.0 mg/dL (Table 2).

Table 2. Lipid profile

Variable	Mean (SD)	Normal
Total cholesterol (mg/dL)	204.2 (42.8)	<200
HDL (mg/dL)	46.8 (9.3)	≥ 40
Triglycerides (mg/dL)	133.5 (53.4)	<150
LDL (mg/dL)	132.9 (41.0)	<100

Table 3. The mean level of IL-12

Variable	Mean (SD)
Interleukin -12 (pg/mL)	160.1 (99.0)

The mean level of IL-12 in T2DM is 160.15 ± 99.05 pg/mL (distribution was not normal) (Table 3).

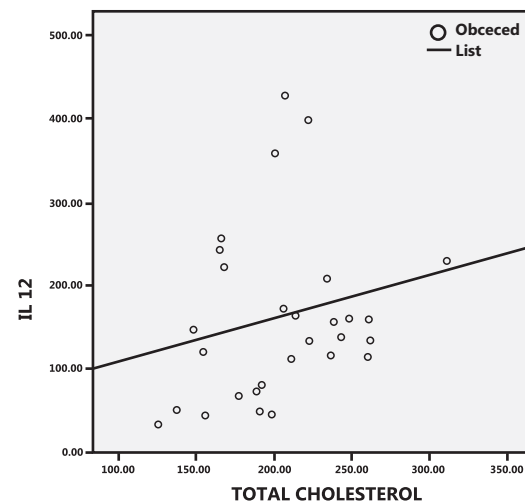


Figure 1. Correlation total cholesterol with interleukin-12 in type 2 diabetes mellitus

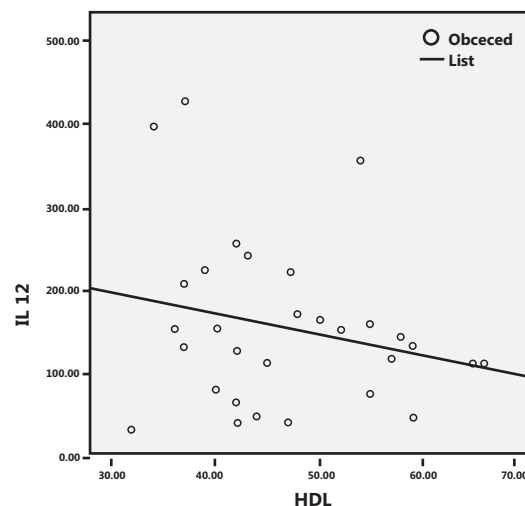


Figure 2. Correlation HDL with interleukin-12 in type 2 diabetes mellitus

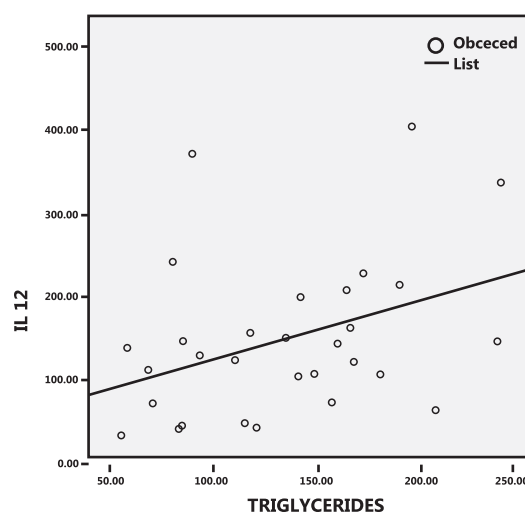


Figure 3. Correlation Triglycerides with interleukin-12 in type 2 diabetes mellitus

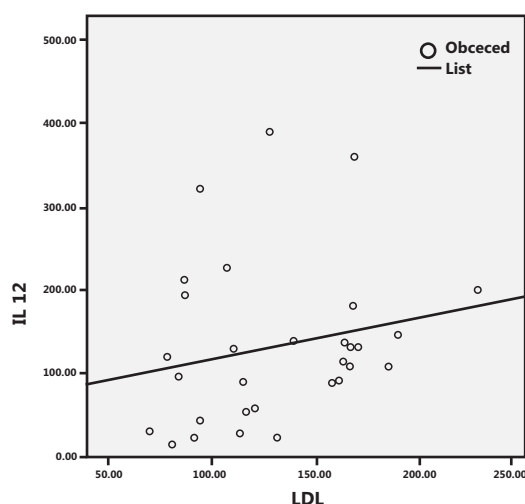


Figure 4. Correlation LDL with interleukin-12 in type 2 diabetes mellitus

Spearman correlation test of total cholesterol, (HDL), tryglicerides and (LDL) with IL-12 are $r = 0.228$ ($p = 0.225$) (Fig.1); $r = -0.234$ ($p = 0.212$) (Fig.2); $r = 0.415$ ($p = 0.031$) (Fig.3); $r = 0.215$ ($p = 0.291$) (Fig.4).

Further, the multivariate linear regression analysis was performed to investigate which one of the markers potentially influencing the serum IL-12 concentration with r -value (Table 4). LDL was not performed because of p -value > 0.5 .

Table 4. Analysis linear regression of correlation total cholesterol, HDL and triglycerides with interleukin-12

	Interleukin-12	
	r	P
Total cholesterol	0.072	0.225
HDL	-0.182	0.212
Triglycerides	0.512	0.031

The characteristic features of diabetic dyslipidemia are a high plasma triglyceride concentration, low HDL cholesterol concentration and increased the concentration of small dense LDL-cholesterol particles. The lipid changes associated with diabetes mellitus are attributed to increased free fatty acid flux secondary to insulin resistance.¹⁰ Thus, inadequate levels of HDL-C in conjunction with more atherogenic forms of LDL-C disturb this natural homeostatic process and contribute to atherogenesis.⁵ In addition to the inverse association with HDL-C, triglyceride levels are closely aligned with T2DM, even though T2DM is not always examined as a confounding factor and when it is, the diagnosis is commonly based on

history.¹¹

Diabetes was chronic hyperglycemia that associated with significant morbidity due to long-term complications, such as diabetic nephropathy, atherosclerosis, and hypertension. Endothelial dysfunction is regarded as a critical event in the development and progression of atherosclerosis and thought to be the primary cause of vascular disease due to hyperglycemia. High glucose has many toxic effects on endothelial cells, such as impaired endothelium-dependent relaxation, decreased nitric oxide release, generation of free radicals, and increased apoptosis.⁵

Within the intima, monocytes mature into macrophages under the influence of macrophage colony-stimulating factor, which is over expressed in the inflamed intima. Macrophage colony-stimulating factor stimulation also increases macrophage expression of scavenger receptors, members of the pattern-recognition receptor superfamily, which engulf modified lipoproteins through receptor-mediated endocytosis. Accumulation of cholesteryl esters in the cytoplasm converts macrophages into foam cells, i.e. lipid-laden macrophages characteristic of early-stage atherosclerosis. In parallel, macrophages proliferate and amplify the inflammatory response through the secretion of numerous growth factors and cytokines, including tumor necrosis factor and interleukin.¹²

The pathogenesis of type 2 diabetes demonstrate that a very important feature of this disease is chronic inflammation IL-12 is a pro-inflammatory cytokine, but its role in the pathogenesis and course of diabetes still is being assessed. It is well known that high levels of IL-12 in serum can stimulate T lymphocytes and NK cells proliferation and migration to atherosclerosis plaques.⁶

Till date, the mechanism that increases IL-12 levels in diabetics and cardiovascular diseases and the factor that is responsible for its increment are not fully understood. Generally, IL-12 is produced by monocytes, macrophages, dendritic cells, neutrophils and to lesser extent B cells. The increase of IL-12 in diabetics may be due to complicating interaction of insulin resistance, hsCRP, LDL-C, and HDL-C, as our subjects have visceral fat; and the adipose tissues are known for the production of different proinflammatory cytokines.⁵

CONCLUSION AND SUGGESTION

It can be stated however that the progression of atherosclerosis in type 2 diabetic patients may be

related, at least in part, to serum IL-12 concentrations and triglyceride level as CVD risk with moderate correlation and significant statistically ($r=0.512$; $p < 0.05$). Increasing triglyceride in DM 88.5 mg/dL will increase CVD disease. Further research to investigate the correlation lipid profile with interleukin-12 in controlled and uncontrolled type 2 diabetes mellitus.

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