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Correlation Between Small Dense Low-Density Lipoprotein and Risk Factor Cardiovascular on Obesity

Indra Kusuma Mardia*. Santi Syafril

Department of Internal Medicine, Faculty Medicine, Universitas Sumatera Utara, Medan, Indonesia

ABSTRACT

Background: Small dense low-density lipoprotein concentration (sdLDLC) subclasses are smaller in volume than other LDL types, they have a greater propensity for endothelial penetration and subsequent atherogenesis. The objectives of the study assessed the relationship between sdLDLC and cardiovascular risk in obesity

Method: This cross-sectional study was conducted on obesity. Informed written consent was obtained after explaining the nature of the study to the patients, and ethical clearance was obtained. Body mass index (BMI) was measured using standard methods. Laboratory assessment included venous blood samples in a fasted state for the determination of components of the lipid profile [total cholesterol (TC), HDL-C, and TG], ApoB, and sdLDL. The serum glucose was measured using the glucose oxidase/peroxidase method and the lipid profile by the enzymatic colorimetric method. LDL-C was calculated from the formula of Friedewald.

Result: This study included 40 obese patients with a BMI of 33.14±5.00 kg/m2, the age of 41.75± 6.02 years old. There was a significant correlation between sdLDL with age, BMI, FPG, PPG, and TG ($p < 0.05$).

Conclusion: There is a significant between sdLDL with risk factors cardiovascular of profile lipid and profile glucose.

Keywords: sdLDL, Cardiovascular Risk, Obesity

ABSTRAK

Latar Belakang: Small-dense low-density lipoprotein (sdLDLC) lebih kecil volumenya daripada LDL, tetapi memiliki kecenderungan yang lebih besar untuk penetrasi endotel dan aterogenesis. Tujuan penelitian ini menilai hubungan antara sdLDLC dan risiko kardiovaskular pada obesitas

Metode: Studi cross-sectional ini dilakukan pada obesitas. Persetujuan tertulis diperoleh setelah menjelaskan penelitian kepada pasien. Indeks massa tubuh (BMI) diukur menggunakan metode standar. Penilaian laboratorium termasuk sampel darah vena dalam keadaan puasa untuk penentuan komponen profil lipid [kolesterol total (TC), HDL-C, dan TG], ApoB, dan sdLDL. Glukosa serum diukur menggunakan metode glukosa oksidase/peroksidase dan profil lipid dengan metode kolorimetri enzimatik. LDL-C dihitung dari rumus Friedewald.

*Corresponding author at: Department of Internal Medicine, Faculty Medicine, Universitas Sumatera Utara, Medan, Indonesia

E-mail address: indra.mardia74@gmail.com

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Hasil Penelitian: Penelitian ini melibatkan 40 pasien obesitas dengan IMT: 33,14±5,00 kg/m2, usia 41,75± 6,02 tahun. Terdapat korelasi yang signifikan antara sdLDL dengan usia, IMT, G puasa, postprandial glukosa, dan TG ($p < 0,05$).
Kesimpulan: Terdapat hubungan yang signifikan antara sdLDL dengan faktor risiko kardiovaskular lipid profil dan glukosa profil.

Kata Kunci: sdLDL, Profil Lipid, Profil Glukosa Darah, Obesitas

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1 Introduction

Small dense low-density lipoprotein concentration (sdLDLC) subclasses are smaller in volume than other LDL types, they have a greater propensity for endothelial penetration and subsequent atherogenesis.[1] In addition to enhanced endothelial penetration, several other factors support the higher atherogenic profile of sdLDL-C: (i) their lower affinity with LDL receptors, causing particles to remain in circulation longer and increasing susceptibility to glycation, oxidation, and uptake by scavenger receptors,[1] and (ii) their greater susceptibility to oxidation and binding to proteoglycans, consequently leading to increased arterial thickness.[2] By these characteristics, there is an overall link between sdLDLC and arterial damage. Given their affinity for arterial penetration, and the resulting decreases in nitric oxide (NO) and enhanced foam cell production, sdLDL ultimately increases tunica intima (TI) and tunica media (TM) arterial thickness and produces the atherogenic properties attendant to cardiovascular diseases.[3] Several biomarkers are associated with elevated sdLDLC, such as Increased serum TG, TC, LDLC,[4] non-classical monocytes,[1] apolipoprotein (apo) B, the apo B glycation per se,[5] apo C,[6] and homeostatic model assessment of insulin resistance (HOMA-IR) index.[7] Importantly, apo B and apo C molecules are sensitive to glycation and compose the structure of the sdLDLC, whereas high resistin concentration induces insulin resistance as assessed by the HOMA-IR score.[8] Various diseases interplay with high sdLDLC concentrations, e.g. obesity,[1] metabolic syndrome (MetS),[2] systemic hypertension[9], and hepatic diseases,[7] to exert adverse pathophysiological effects. Low values of HDLC in postmenopausal women and men, in which the paraoxonase 1 (PON1) molecule is a precursor, are also associated with elevated sdLDL-C concentrations.[7] Obesity, whose condition may be classified as a disease, is often coupled with lipid profile dysregulation.[10] In this regard, obesity is associated with higher LDL-C and sdLDL-C/LDL- C, as well as elevated TG concentrations and TG/HDL-C ratio.[1] sdLDL-C is a surrogate biomarker strongly associated with CVD. In addition to its CV implications, sdLDL-C is also a contributory factor in the pathophysiology of several diseases and plays a damaging role in hepatic disease, metabolic syndrome, and obesity. The measurement, or even estimation, of sdLDL-C as a complement to the routine lipid profile should be considered in clinical practice to improve the management of CVD and risk factors for their progression. Taken together, clinical attention is necessary concerning the impact of pharmacological agents, therapeutic diets, and

genetic disorders on sdLDL-C concentration. However, the establishment of appropriate sdLDL-C reference ranges associated with clinical outcomes of interest is imperative to maximize the utility of its evaluation. The purpose of the study was to examine the relationship between sdLDL and profile lipid and profile glucose

2 Method

This cross-sectional study was conducted on obesity. Informed written consent was obtained after explaining the nature of the study to the patients, and ethical clearance was obtained.

This study included 40 obese patients, whereas those with a history of CVD, thyroid disorders, or currently on lipid-lowering agents were excluded. Body mass index (BMI) was measured using standard methods. Laboratory assessment included venous blood samples in a fasted state for the determination of components of the lipid profile [total cholesterol (TC), HDL-C, and TG], ApoB, and sdLDL. The serum glucose was measured using the glucose oxidase/peroxidase method and the lipid profile by the enzymatic colorimetric method. LDL-C was calculated from the formula of Friedewald.

Statistical analysis

Statistical analysis was done using the SPSS package and MS excel. Pearson correlation or Spearman correlation test and p values were calculated. P values <0.05 was considered to be significant.

3 Result

Based on table 1, there are 40 obese patients with a BMI of 33.14±5.00 kg/m2, the age of 41.75± 6.02 years old.

Table 1 Baseline data of patients

Parameters	N=40
Age (yr)	41.75± 6.02
BMI (kg/m^2)	33.14±5.00
FPG (mg/dl}	84.37 ±9.77
PPG (mg/dl)	109.95± 29.67
HbA1c (%)	5.61± 0.86
LDLC (mg/dl)	136.77 ±34.69
HDLC (mg/dl)	47.60± 12.96
TG (mg/dl)	150.17±58.38
ApoB (mg/dl)	104.25 ±19.48
sdLDL (mg/dl)	1.31 ± 0.21

Abbreviations: BMI: body mass index; FPG: fasting plasma glucose; PPG: postprandial plasma glucose; HbA1c, glycosylated hemoglobin; LDLC: low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; ApoB: apolipoprotein B, sdLDL: small dense low-density lipoprotein

Based on table 2, there was a significant correlation between sdLDL and age, BMI, FPG, PPG, and TG

Table 2 Correlation between sdLDL and Risk factors for cardiovascular

Parameter	r	p
Age (yr)	0.992	-0.002*
BMI (kg/m2)	0.956	-0.009*
FPG (mg/dl}	0.967	0.007*
PPG (mg/dl)	0.897	0.021*
HbA1c (%)	0.736	0.055
LDLC (mg/dl)	0.000	0.558
HDLC (mg/dl)	0.169	0.222
TG (mg/dl)	-0.498	0.001*
ApoB (mg/dl)	0.708	0.061

Abbreviations: BMI: body mass index; FPG: fasting plasma glucose; PPG: postprandial plasma glucose; HbA1c, glycosylated hemoglobin; LDLC: low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; ApoB: apolipoprotein B, sdLDL: small dense low-density lipoprotein

4 Discussion

CHD and links to sdLDL Concentrations of sdLDL-C may be a risk factor for CHD. In an 11- year follow-up study involving 11,419 men and women, 1158 participants who developed CHD[2] showed average sdLDL-C concentrations of 43.5 mg/dL and an sdLDL-C/LDL-C ratio of 0.35. Moreover, the increased sdLDL-C concentrations were correlated with a higher propensity for diabetes, arterial hypertension, MetS, and an increase in body mass index (BMI) and C-reactive protein (CRP) values; in other words, increased sdLDL-C was associated with a pro-atherogenic profile. Interestingly, subjects presenting with low LDL-C concentrations demonstrated an increased risk for CHD associated with increased sdLDL-C values. In a study of 294 healthy patients, 113 individuals with type 2 diabetes and no cardiac complications, and 46 diabetics with CHD, higher sdLDL-C concentrations were observed in men compared to women, as well as an association with age.[12] Importantly, diabetic subjects with CHD had elevated sdLDL-C values when compared to healthy subjects, insofar as the investigators suggested that the analysis of sdLDL-C. In a prospective study comprised of 59 men with high blood glucose or type 2 diabetes mellitus, higher concentrations of sdLDL-C were associated with age, body weight, resistin concentrations, and previous myocardial infarction; additionally, increases in sdLDL-C were associated with greater insulin resistance and increased intima-media thickness.[11] Similarly, Nakano et al. demonstrated that individuals with MetS plus type 2 diabetes mellitus had a greater association with sdLDL-C and the sdLDL-C/LDL-C ratio compared to participants with MetS alone.[4] Using multiple regression analysis, the authors reported that sdLDL-C concentrations were moderately associated with elevated LDL (R2 = 0.35606,

r = 0.5360), while TC (R2 = 0.2774, r = 0.4457), MetS (R2 = 0.1291, r = 0.3579), diabetes mellitus (R2 = 0.1267, r = 0.2777) and TG (R2 = 0.1267, r = 0.2046) demonstrated weaker associations. A related disease that may be influenced by the increase of sdLDL-C is hepatic steatosis, which is associated with the dysregulation of the biomarkers that comprise a MetS diagnosis.[13] Both Mets and hepatic steatosis, in combination or not, interplay with increases of sdLDL-C values and LDL-C/LDL-C ratio, as well as higher very low-density lipoprotein (VLDL) and TG values.[7] Among 5255 patients, including patients with hepatic steatosis, MetS, type 2 diabetes mellitus, and healthy subjects, higher sdLDL-C concentrations were reported in male patients due to aging.[14] Both sdLDL-C and sdLDL-C/LDL-C ratios were also higher for those with pre-diabetes, MetS, and hepatic steatosis, and it is worth noting that hepatic steatosis was the disease that was most related to the increase in sdLDL-C and sdLDL-C/LDL-C values.

5 Conclusion

There was a significant correlation between sdLDL and age, BMI, FPG, PPG, and TG

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