

Original Article

Hypoadiponectinemia: A useful marker of dyslipidemia in women with polycystic ovary syndrome[☆]

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Abstract

Objective: Adiponectin plays a role in obesity, lipid metabolism, and anti-inflammation. Women with polycystic ovary syndrome (PCOS) are also at risk for dyslipidemia. Therefore, we investigated the association between adiponectin levels and the lipid profile including high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TGs) in women with PCOS and contemplated what role adiponectin might play in dyslipidemia with PCOS.

Materials and Methods: We recruited 118 young Taiwanese women with PCOS. The women enrolled were not taking any medication and those with other systemic diseases of nonovarian origin, which could have affected the hypothalamic–pituitary–ovarian axis, were excluded. The serum lipid profile, metabolic and hormonal parameters, and adiponectin were measured. The lipid profile and adiponectin were analyzed and adjusted for age, body mass index (BMI), homeostasis model assessment–insulin resistance (HOMA-IR), and sex hormone-binding globulin (SHBG).

Results: In a simple linear regression, adiponectin was significantly inversely related to LDL-C and TGs, but positively related to HDL-C (all $p < 0.001$) after logarithmic transformation. In the multiple linear regression, adiponectin was significantly related to HDL-C ($p < 0.001$) independent of age, BMI, HOMA-IR, and SHBG after logarithmic transformation. Using a logistic regression, the odds ratio was 0.088 between the association of increased adiponectin and abnormal HDL-C (≤ 50 mg/dL).

Conclusions: We demonstrated that adiponectin is an independent biomarker that is positively and evidently related to HDL-C and TGs in women with PCOS. Hypoadiponectinemia may be a useful marker of dyslipidemia in women with PCOS.

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Keywords: adiponectin; dyslipidemia; high-density lipoprotein cholesterol; hypoadiponectinemia; polycystic ovary syndrome; triglycerides

Introduction

Polycystic ovary syndrome (PCOS), a syndrome of ovarian dysfunction, is associated with oligo- and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries [1]. PCOS is considered to be one of the most common endocrinopathies in fertile women [2] and even a variant of metabolic syndrome [3]. A close relationship between PCOS and insulin resistance is recognized [4,5]. Whether women with PCOS are under an increased risk of

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cardiovascular disease (CVD) is still being debated [2]. Cardiovascular risk factors including dyslipidemia, hyperandrogenemia, and markers of inflammation in women with PCOS were demonstrated [2]. As to dyslipidemia, a lower serum level of high-density lipoprotein cholesterol (HDL-C) in women with PCOS compared to those without PCOS was documented [6]. HDL-C is the best potential lipoprotein predictor of morbidity and mortality in patients with CVD [7,8].

Adiponectin is exclusively produced by adipocytes [9–12]. The adiponectin gene is located on chromosome 3q37, as is a locus for diabetes susceptibility, and encodes a secretory protein from adipose tissue, which accounts for 0.01–0.05% of the total serum protein [9,13]. In both obesity and type-2 diabetes mellitus, serum adiponectin levels are significantly lower in affected groups than in healthy groups [14]. It was also proposed that decreased adiponectin levels were related to coronary artery disease (CAD) compared to matched controls [13]. Adiponectin may play a role as an anti-inflammatory vasoprotective adipokine [15].

Recently, several studies found that serum adiponectin levels are significantly decreased in PCOS groups compared to control groups [16,17]. However, no further study on the relationship between adiponectin and the lipid profile in PCOS was published. In the present study, we comprehensively explored the association between adiponectin and HDL-C in young Taiwanese women with PCOS prior to treatment.

Materials and methods

Participants

From October 2004 to May 2006, we recruited 118 young Taiwanese women with PCOS who had received no medication for 6 months prior to enrollment in this study. They visited our reproductive endocrinology clinic and presented with irregular menstrual cycles and/or clinical hyperandrogenism. The present study was approved by the Institutional Review Board of National Taiwan University Hospital, and the patients and/or their parents all signed an informed consent form prior to data collection. All women with PCOS enrolled in this study were diagnosed with two of the three criteria proposed at the Rotterdam revised consensus meeting [4], including oligomenorrhea or amenorrhea, clinical hyperandrogenism and/or hyperandrogenemia, and polycystic ovaries as visualized by pelvic ultrasonography (US), as described in our previous study [18].

Oligomenorrhea was defined as fewer than eight spontaneous menstrual cycles per year and with an interval of greater than 45 days between cycles. The definition of hyperandrogenism was an elevated serum total testosterone level of >0.8 ng/mL with persistent acne or hirsutism (a Ferriman and Gallwey score of >8). Visualized polycystic ovaries meant more than 12 follicles, 2–9 mm in diameter, per ovary by transvaginal US or an ovarian volume of 10 cm^3 by transabdominal US with a distended bladder in virginal women. Exclusion of other etiologies of nonovarian origin included hyperprolactinemia, thyroid

dysfunction, Cushing's syndrome, congenital adrenal hyperplasia, adrenal tumors, virilizing ovarian tumors, autoimmune diseases, malignancies, central nervous system diseases, a current or previous pregnancy in the past year, and prescription of oral contraceptives or other medications that could affect the hypothalamic–pituitary–ovarian axis within the previous 6 months.

Data collection

Blood samples were collected from these women under spontaneous menstrual cycles between the 3rd and 7th days and between 08:00 and 10:00 after an overnight fast. In women without menstruation for longer than 3 months, blood samples were collected without hormone-induced withdrawal bleeding under pelvic US detection, and the serum progesterone level was also determined. If the serum estradiol level exceeded 150 pg/mL, the serum progesterone exceeded 2 ng/mL, or a dominant follicle was present on US, the sampled blood was discarded. Patients whose blood samples had been abandoned were then asked to measure their basal body temperature in order to detect if spontaneous ovulation had occurred in this discarded cycle. We subsequently collected blood samples again during the next cycle in 2–3 weeks following menstruation.

Blood samples were processed within 30 minutes of collection. Blood glucose and insulin samples were kept at 4°C and analyzed on the day of sampling. Prior to the assay, serum and plasma were separated into aliquots and frozen at -70°C . Anthropometric, pelvic US, and blood-pressure measurements were performed on the day of venipuncture. The body mass index (BMI) was calculated by the weight (in kilograms) divided by the height (in meters) squared.

Assay methods

We used an autoanalyzer (Toshiba TBA-120FR Chemistry Analyzer; Tokyo, Japan) to measure plasma glucose levels. We measured serum concentrations of total cholesterol, low-density lipoprotein cholesterol (LDL-C), HDL-C, and triglycerides (TGs) with a biochemical autoanalyzer (Toshiba TBA-200FR). We measured insulin levels by a microparticle enzyme immunoassay using an AxSYM system (Abbott Laboratories, Dainabot, Tokyo, Japan). The degree of insulin resistance [homeostasis model assessment–insulin resistance (HOMA-IR) = $(\text{glucose} \times 0.05551) \times \text{insulin}/22.5$] was estimated, where the levels of insulin and glucose are expressed in $\mu\text{U/mL}$ and mg/dL , respectively [19].

We used chemiluminescence (Vitros Eci; Ortho-Clinical Diagnostics, Rochester, NY, USA) to measure directly the concentrations of serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and progesterone. We measured the levels of serum sex hormone-binding globulin (SHBG) by electrochemiluminescence (Elecsys 2010; Roche Diagnostics, Mannheim, Germany). We measured levels of serum total testosterone and dehydroepiandrosterone sulfate (DHEA-S) by a radioimmunoassay (RIA; Diagnostic Systems

Table 1

Clinical and hormonal characteristics of 118 Taiwanese women with polycystic ovary syndrome.

	No. (%)	Mean \pm SE	Range
Age (y)		24.78 \pm 0.43	15–37
15–19	11 (9.32)		
20–24	47 (39.83)		
25–29	43 (36.44)		
30–34	12 (10.17)		
35–37	5 (4.24)		
BMI (kg/m ²)		24.23 \pm 0.55	15.43–40.70
<18.50	21 (17.80)		15.43–18.49
18.50–23.99	48 (40.68)		18.75–24.88
24.00–26.99	11 (9.32)		25.07–29.43
≥ 27.00	38 (32.20)		30.08–40.70
FSH (mIU/mL)		5.56 \pm 0.11	8.87–2.44
LH (mIU/mL)		11.99 \pm 0.62	34.50–1.61
Estradiol (pg/mL)		42.53 \pm 3.55	413.00–15.42
DHEA-S (μ g/dL)		286.11 \pm 6.36	627.00–62.70
Fasting glucose (mg/dL)		84.52 \pm 1.12	66–132
Fasting insulin (μ U/mL)		13.76 \pm 1.20	0.2–62.5
HOMA-IR		3.09 \pm 0.32	0.04–20.20
LDL-C (mg/dL)		106.96 \pm 2.72	44–193
HDL-C (mg/dL)		47.24 \pm 4.35	27–94
Total cholesterol (mg/dL)		190.86 \pm 3.17	114–281
Total triglyceride (mg/dL)		87.24 \pm 4.71	28–336
SHBG (nmol/L)		38.1 \pm 2.1	9.9–124.0
Total testosterone (ng/mL)		1.00 \pm 0.03	0.4–2.1
Adiponectin (μ g/mL)		1.95 \pm 0.09	0.61–6.02

BMI = body-mass index; DHEA-S = dehydroepiandrosterone sulfate; FSH = follicle-stimulating hormone; HDLC = high-density lipoprotein-cholesterol; HOMA-IR = homeostasis model assessment of insulin resistance; LDL-C = low-density lipoprotein cholesterol; LH = luteinizing hormone; SE = standard error; SHBG = sex hormone-binding globulin.

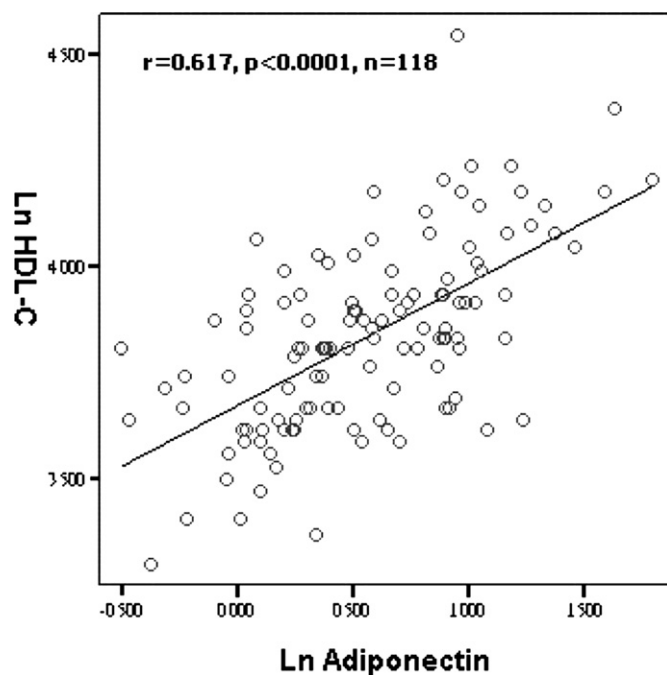


Fig. 1. Linear regression curve of logarithmically transformed (Ln) HDL-C as the dependent variable in Taiwanese women with polycystic ovary syndrome ($r = 0.617$, $p < 0.0001$). HDL-C = high-density lipoprotein cholesterol.

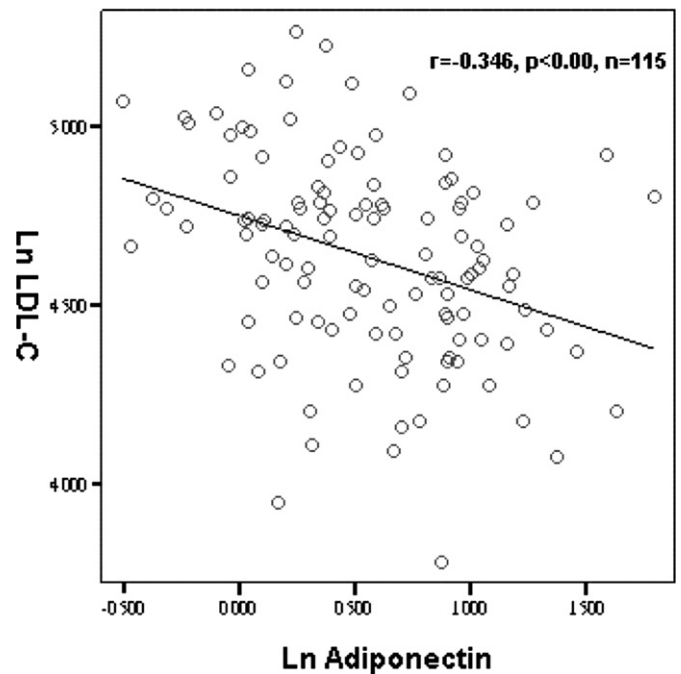


Fig. 2. Linear regression curve of logarithmically transformed (Ln) LDL-C as the dependent variable in Taiwanese women with polycystic ovary syndrome ($r = -0.346$, $p < 0.001$). LDL-C = low-density lipoprotein cholesterol.

Laboratories, Webster, TX, USA). We used a commercial enzyme-linked immunosorbent assay (ELISA) (Human Adiponectin ELISA Kit, B-Bridge International, Sunnyvale, CA, USA) according to the manufacturer's instructions to measure levels of serum adiponectin [20]. The intra- and interassay coefficients of variation of the aforementioned assays were all $<10\%$.

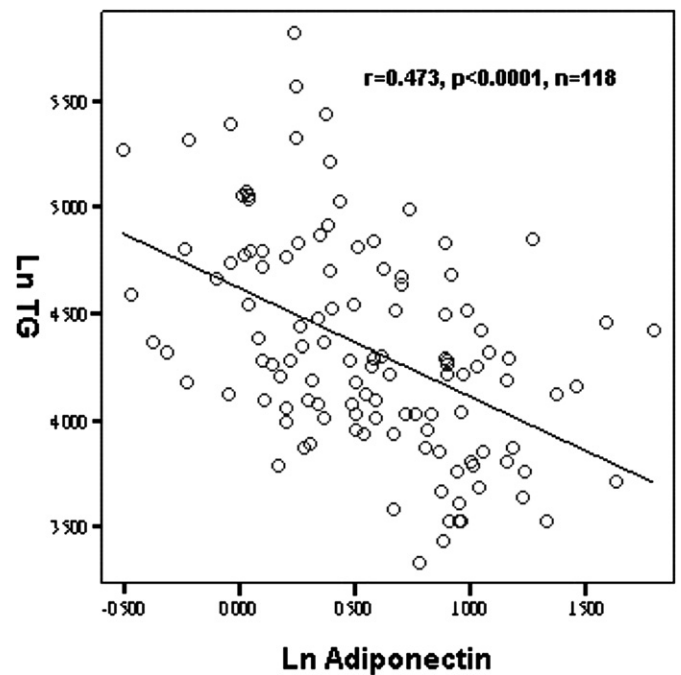


Fig. 3. Linear regression curve of logarithmically transformed (Ln) TGs as the dependent variable in Taiwanese women with polycystic ovary syndrome ($r = -0.473$, $p < 0.0001$). TG = triglyceride.

Table 2

Regression of logarithmically transformed (ln) lipid levels with age and ln HOMA-IR, adiponectin, SHBG, and BMI among 118 Taiwanese women with polycystic ovary syndrome.

	ln HDL-C			ln LDL-C			ln TG		
	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>
Age	0.008	0.004	0.928	0.406	0.005	<0.0001	0.327	0.009	<0.001
ln BMI	−0.478	0.076	<0.0001	0.412	0.105	<0.0001	0.525	0.170	<0.0001
ln HOMA-IR	−0.398	0.019	<0.0001	0.371	0.025	<0.0001	0.567	0.039	<0.0001
ln SHBG	0.536	0.028	<0.0001	−0.224	0.043	0.016	−0.396	0.071	<0.0001
ln adiponectin	0.617	0.034	<0.0001	−0.346	0.053	<0.001	−0.473	0.088	<0.0001

BMI = body-mass index; HDL-C = high-density lipoprotein cholesterol; HOMA-IR = homeostasis model assessment-insulin resistance; LDL-C = low-density lipoprotein cholesterol; SE = standard error; SHBG = sex hormone-binding globulin; TG = total triglyceride.

Statistical analyses

All statistical analyses were performed using the statistical software SPSS version 12.0.1C (SPSS Inc., Chicago, IL, USA). Numeric variables are shown as the mean \pm standard error (SE) and range, unless indicated otherwise. Due to positively skewed distributions about the BMI, HOMA-IR, HDL-C, LDL-C, TG, SHBG, and adiponectin, we first logarithmically transformed those data and then used a simple linear regression to calculate the regression coefficient between the logarithmically transformed lipid profile parameters and other parameters, including age, logarithmically transformed BMI (ln BMI), ln HOMA-IR, ln SHBG, and ln adiponectin.

We used ln HDL-C, ln LDL-C, and ln TGs as the dependent variables, and anthropometric and metabolic factors and ln adiponectin as independent variables to perform forward stepwise multiple linear regression models. We introduced a multivariate regression analysis to assess the respective relationships of ln HDL-C, ln LDL-C, and ln TGs with ln adiponectin after adjusting for anthropometric and metabolic factors. In the multiple linear model, age, ln BMI, ln HOMA-IR, ln SHBG, and ln adiponectin were diagnosed by values of the variance inflation factor (VIF) to avoid collinearity. A *p* value of <0.05 was considered statistically significant.

Results

The mean age of the total 118 participants was 24.78 ± 4.69 (range, 15–37) years. The basic characteristics

of these participants are summarized in Table 1. Under a simple linear regression, levels of ln adiponectin were significantly correlated with that of ln HDL-C ($p < 0.0001$, Fig. 1), ln LDL-C ($p < 0.001$, Fig. 2), and ln TGs ($p < 0.0001$, Fig. 3) (Table 2).

Considering possible confounding factors to adiponectin, we used multiple linear regression analyses and found that the adiponectin level after logarithmic transformation was only significantly related to the ln HDL-C level ($p < 0.0001$) compared to LDL and TGs after adjusting for age, ln BMI, ln HOMA-IR, and ln SHBG (Tables 3–5, model 1). As to the analysis of collinearity in the multiple linear model to predict levels of HDL-C, values of the VIF for age, ln BMI, ln HOMA-IR, ln SHBG, and ln adiponectin were 1.103, 2.625, 2.101, 1.798, and 1.615, respectively. Therefore, adiponectin had no interactions with age, BMI, HOMA-IR, or SHBG. After a forward stepwise multiple linear regression with ln HDL-C as the dependent variable, we found that only ln SHBG and ln adiponectin were significant in the multiple regression model (Table 3, model 2). Consequently, we noted that the HDL-C level was essentially dependent on both adiponectin and SHBG levels.

With LDL-C as the dependent variable, age and ln BMI were significant in the forward stepwise multiple linear regression after adjusting for ln HOMA-IR, ln SHBG, and ln adiponectin (data not shown). We then used a multiple linear regression with LDL-C as the dependent variable, and found that the LDL level was dependent on only age and adiponectin did not affect the LDL level at all (Table 4, model 1). Although only age and ln BMI were significant after the forward

Table 3

Multiple regression analysis of ln HDL levels (mg/dl) with age, logarithmically transformed (ln) BMI, ln HOMA-IR, ln SHBG, and ln adiponectin among 118 Taiwanese women with polycystic ovary syndrome.

Variable	Model 1			Model 2			Model 3		
	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>
Age (y)	0.139	0.003	0.054				0.126	0.003	0.074
ln BMI (kg/m ²)	−0.102	0.104	0.360						
ln HOMA-IR	0.067	0.022	0.497						
ln SHBG (nmol/L)	0.283	0.033	0.003	0.314	0.028	<0.001	0.305	0.028	<0.001
ln adiponectin (μg/mL)	0.489	0.041	<0.0001	0.467	0.036	<0.0001	0.498	0.037	<0.0001
<i>R</i> ²	(0.690) ² = 0.476			(0.676) ² = 0.457			(0.687) ² = 0.472		

BMI = body-mass index; HDL = high-density lipoprotein; HOMA-IR = homeostasis model assessment-insulin resistance; SE = standard error; SHBG = sex hormone-binding globulin.

Table 4

Multiple regression analysis of logarithmically transformed (ln) low-density lipoprotein levels (mg/dL) with age, ln BMI, ln HOMA-IR, ln SHBG, and ln adiponectin among 118 Taiwanese women with polycystic ovary syndrome.

Variable	Model 1			Model 2			Model 3		
	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>
Age (y)	0.322	0.005	<0.001	0.314	0.005	<0.001	0.347	0.005	<0.0001
Ln BMI (kg/m ²)	0.170	0.159	0.194	0.259	0.122	0.011			
Ln HOMA-IR	0.187	0.033	0.111				0.261	0.026	0.007
Ln SHBG (nmol/L)	0.048	0.050	0.657						
Ln adiponectin (μg/mL)	−0.102	0.062	0.323	−0.127	0.059	0.203	−0.134	0.057	0.164
<i>R</i> ²	(0.543) ² = 0.295			(0.528) ² = 0.278			(0.533) ² = 0.284		

BMI = body-mass index; HOMA-IR = homeostasis model assessment-insulin resistance; SE = standard error; SHBG = sex hormone-binding globulin.

stepwise multiple linear regression, we desired to see if adiponectin had any influence upon LDL-C and so added adiponectin as another independent variable after adjusting for age and ln BMI, with ln LDL-C as the dependent variable. Adiponectin, however, was still not significant in the multiple regression model (Table 4, model 2). Due to a high correlation between BMI and HOMA-IR, we replaced BMI with HOMA-IR and tried to introduce HOMA-IR to the multiple regression model. In the multiple regression model (Table 4, model 3), using ln LDL-C as the dependent variable and adding adiponectin as an independent variable after adjusting for age and ln HOMA-IR, we still found that adiponectin was not significant. Thus, adiponectin had no effect on LDL-C levels and should not be included in the regression model that is used to predict levels of LDL-C. From the results of our regression model, we understood that adiponectin had no association with the LDL-C level.

Similarly, adiponectin was not significantly related to the TG level when considering other possible confounding factors, and the TG level was mainly affected by age change and HOMA-IR level (Table 5, model 1). In order to determine whether adiponectin would affect TG, we introduced a forward stepwise multiple linear regression with ln TG as the dependent variable. Interestingly, we found that ln adiponectin was also significant in the multiple regression model (Table 5, model 3). Accordingly, adiponectin may not be a key point but still plays some role in which it accompanies age changes and HOMA-IR level in affecting the TG level. Furthermore, we found that adiponectin as another independent variable was also significant in a multiple regression model (Table 5, model 2) after adjusting for age and ln BMI, which replaced ln

HOMA-IR. If we regarded the *R*² value as a priority, model 3 in Table 5 would be a better choice than model 2 to predict TG levels. Nevertheless, adiponectin produced a larger *R*² value in the model with HDL as the dependent variable compared to that in the model with TG as the dependent variable (Tables 3 and 5). For that reason, we believe that adiponectin had a greater influence in predicting HDL-C than TG levels. Considering the relation between adiponectin and HDL-C, it was reasonable to use only adiponectin and SHBG as independent variables to predict levels of HDL, according to the results of the forward stepwise multiple linear regression (Table 3, model 2). Although age was not a significant variable in the forward stepwise multiple linear regression, we considered that age is a very important biologic character in humans and thus added it as another independent variable. We then found that age increased the *R*² value in the model with HDL as the dependent variable (Table 3, model 3). However, we still deemed that it was sufficient and logical to use only adiponectin and SHBG as independent variables to predict HDL-C levels. Additionally, we tried to perform multiple linear regression analysis in different BMI groups. Due to the small number of overweight women (24 ≤ BMI < 27), we put overweight and obese women (27 ≤ BMI) together. With ln HDL as the dependent variable, we found that ln adiponectin was still significant in the three different BMI groups (Table 6), but only ln SHBG was significant in the normal-range group.

To further investigate the effects of adiponectin on lower- and higher-HDL-C groups, we used a logistic regression to analyze the odds ratio (OR) between lower- and higher-HDL-C groups with a cutoff at 50 mg/dL, which was based on

Table 5

Multiple regression analysis of logarithmically transformed (ln) TG levels (mg/dL) with age, ln BMI, ln HOMA-IR, ln SHBG, and ln adiponectin among 118 Taiwanese women with polycystic ovary syndrome.

Variable	Model 1			Model 2			Model 3		
	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>
Age (y)	0.229	0.008	0.003	0.197	0.008	0.013	0.237	0.008	<0.001
Ln BMI (kg/m ²)	0.096	0.250	0.408	0.345	0.199	<0.001			
Ln HOMA-IR	0.365	0.052	<0.001				0.439	0.042	<0.001
Ln SHBG (nmol/L)	−0.052	0.080	0.588						
Ln adiponectin (μg/mL)	−0.155	0.098	0.091	−0.235	0.099	0.012	−0.194	0.091	0.019
<i>R</i> ²	(0.653) ² = 0.426			(0.597) ² = 0.357			(0.647) ² = 0.419		

BMI = body-mass index; HOMA-IR = homeostasis model assessment-insulin resistance; SE = standard error; SHBG = sex hormone-binding globulin; TG = total triglyceride.

Table 6

Multiple regression analysis of logarithmically transformed (ln) HDL levels (mg/dL) with age, ln SHBG, and ln adiponectin in three different BMI groups of Taiwanese women with polycystic ovary syndrome.

Variable	BMI <18.5			18.5 ≤ BMI < 24			24 ≤ BMI		
	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>	<i>r</i>	SE	<i>p</i>
Age (y)	0.014	0.334	0.165	<0.001	0.006	0.997	0.011	0.004	0.008
Ln SHBG (nmol/L)	0.122	0.010	0.118	0.184	0.043	<0.001	−0.058	0.047	0.226
Ln adiponectin (μg/mL)	0.198	0.081	0.026	0.268	0.065	<0.001	0.212	0.053	<0.001
<i>R</i> ²	(0.645) ² = 0.416			(0.712) ² = 0.506			(0.557) ² = 0.310		

BMI = body-mass index; HDL = high-density lipoprotein; SE = standard error; SHBG = sex hormone-binding globulin.

a definition of metabolic syndrome. We found that a higher adiponectin level was associated with a lower probability of an abnormal HDL-C level (≤ 50 mg/dL), with a lower OR (0.079) [95% confidence interval (CI) = 0.015–0.412; $p = 0.003$] under multivariate logistic regression analyses after adjusting for age, ln BMI, ln HOMA-IR, and ln SHBG (Table 7, model 1). Under backward stepwise multivariate logistic regression analyses, a higher adiponectin level was still associated with a lower probability of an abnormal HDL-C level (≤ 50 mg/dL), with an OR of 0.88 (95% CI = 0.020–0.384; $p = 0.001$) (Table 7, model 2). Under consideration of health modifiers in the multivariate logistic regression analyses, we still noted that a higher adiponectin level had a lower probability of an abnormal HDL-C level (≤ 50 mg/dL), with an OR of 0.084 (95% CI = 0.019–0.381; $p = 0.001$) (Table 7, model 3).

Discussion

In the present study, we first demonstrate that a positive correlation existed between serum levels of adiponectin and HDL-C in women with PCOS. Higher levels of HDL-C were related to increased levels of adiponectin after adjusting for age, insulin resistance, BMI, and SHBG. In the stepwise multiple regression analysis, we found that increasing levels of adiponectin were prominently associated with increasing levels of HDL-C and SHBG. In addition, we also noted that adiponectin was negatively associated with increasing levels of TG to some extent. These results suggest that adiponectin may be a useful marker of the lipid status, regardless of whether SHBG is considered or not, in women with PCOS. PCOS patients with lower adiponectin levels should pay close

attention to problems of dyslipidemia. A change from a sedentary lifestyle or weight reduction may significantly elevate plasma adiponectin levels [14,21,22].

A positive correlation between serum levels of HDL-C and adiponectin was also reported in patients with type-2 diabetes, dyslipidemia, lipodystrophies, coronary heart disease, and metabolic syndrome, and in those who are overweight [23–29]. In nondiabetic men and in patients with type-2 diabetes, hypo adiponectinemia was found to be associated with increased hepatic lipase activity, which may play a role in the decreased levels of HDL-C [30]. Taken together, these possibly indicate that there is a close or direct relationship between adiponectin and HDL-C. However, the exact mechanism linking plasma adiponectin and HDL-C metabolism is still unclear [31].

In recent studies, adiponectin was found to work through its adipoR2 receptor to activate the peroxisome proliferator-activated receptor (PPAR) α in mice models [32]. Activation of PPAR α was previously found to modulate the expression of proteins that participate in HDL-C metabolism, including apolipoprotein A-I (apoA-I), apoA-II, lipoprotein lipase, scavenger receptor class B type I and its human homologue (CLA-1), and adenosine triphosphate-binding cassette transporter-1 (ABCA1) [33]. Matsuura et al [34] reported that human recombinant adiponectin enhanced apoA-I secretion and ABCA1 expression in a human hepatoma cell line, suggesting that adiponectin might increase HDL assembly in the liver. In adiponectin-knockout mice, Oku et al [35] found that an adiponectin deficiency might cause impaired HDL assembly by decreasing ABCA1 expression and apoA-I synthesis in the liver. Further investigations are required to

Table 7

Multivariate logistic regression with the presence of the low serum levels of high-density lipoprotein as the dependent variable.

Variable	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Age (y)	0.956	0.841–1.087			0.982	0.872–1.107
Ln BMI (kg/m ²)	18.398	0.481–703.776				
Ln HOMA-IR	0.540	0.227–1.284				
Ln SHBG (nmol/L)	0.080*	0.020–0.325	0.087*	0.026–0.291	0.087*	0.026–0.291
Ln Adiponectin (μg/mL)	0.079**	0.015–0.412	0.088***	0.020–0.384	0.084***	0.019–0.381
Nagelkerke <i>R</i> ²		0.549		0.525		0.526

* $p < 0.001$.

** $p = 0.003$.

*** $p = 0.001$.

BMI = body-mass index; CI = confidence interval; HOMA-IR = homeostasis model assessment of insulin resistance; OR = odds ratio; SHBG = sex hormone-binding globulin; TG = total triglyceride.

clarify the exact underlying mechanism between adiponectin and HDL-C.

It was suggested that adiponectin might modulate the endothelial inflammatory response, and hypoadiponectinemia represent a risk factor for CAD [14,15,36]. Kumada et al [37] found that hypoadiponectinemia in men produced a two-fold increased risk of CAD prevalence after adjusting for other well-known CAD risk factors. HDL-C, synthesized and secreted from both the liver and the intestines, is the most important lipoprotein predictor of CAD due to its preventive effect on atherosclerosis via a major mechanism termed reverse cholesterol transport [7,8,38]. PCOS patients with lower adiponectin and HDL-C levels may have a higher risk for CVD, which deserves further investigation.

High TG levels may be an independent predictor of future risks of myocardial infarction [39] and were cited as a special elevated cardiovascular risk factor in women [40]. Although the exact mechanism between adiponectin and TG is still not well understood and unclear even in women with PCOS, we found that a negative association between adiponectin and TG might exist, which was more or less shown by our multiple regression model.

Recently, the concentration of serum adiponectin was found to be stable and not affected by hyperinsulinemia, oral glucose intake, or the fat load in the short term [41]. In addition, the concentration of serum adiponectin appeared similar on different days in both diabetic patients and normal individuals [14]. Examination of serum adiponectin levels in PCOS patients might provide information on the recent status of lipid metabolism and over a relatively longer time. Participants in our study were all Taiwanese, and the association between adiponectin and lipid profile might not be representative of women with PCOS in other ethnic groups. However, the high prevalence (64.4%) of low HDL-C levels (<50 mg/dL) in women with PCOS in our study was comparable to the prevalence (66%) documented in a recent large multicenter study [42]. The association between adiponectin levels and lipid profile deserves further studies in other ethnic groups.

In conclusion, there was a high prevalence of low HDL-C levels in young Taiwanese women with PCOS. Adiponectin levels were strongly, positively, and independently related to HDL-C levels and were also positively related to TG levels. Hypoadiponectinemia may be a useful and more stable marker for monitoring the status of dyslipidemia in young women with PCOS. Adiponectin may play a role in increasing the production of HDL-C. However, further studies are needed to clarify the exact underlying mechanism and linkage between adiponectin and the production of HDL-C and TGs.

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