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Association Between Serum Levels of Adipocyte Fatty Acid-binding Protein and Free Thyroxine

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Abstract: Adipocyte fatty acid-binding protein (AFABP) has been shown to be a biomarker of body weight change and atherosclerosis. Changes in thyroid function are associated with changes in body weight and risks of cardiovascular diseases. The association between AFABP and thyroid function status has been seldom evaluated.

The aim of this study was to compare the serum AFABP concentrations in hyperthyroid patients and those in euthyroid individuals, and to evaluate the associations between serum AFABP and free thyroxine (fT4) levels.

For this study, 30 hyperthyroid patients and 30 euthyroid individuals at a referral medical center were recruited. The patients with hyperthyroidism were treated with antithyroid regimens as clinically indicated. No medication was given to the euthyroid individuals. The body weight, body mass index, thyroid function, serum levels of AFABP, and biochemical data of both groups at baseline and at the 6th month were compared. Associations between AFABP and fT4 levels were also analyzed.

At the baseline, the hyperthyroid patients had significantly higher serum AFABP levels than the euthyroid individuals (median [Q1, Q3]: 22.8 [19.4, 30.6] ng/mL vs 18.6 [15.3, 23.2] ng/mL; $P = 0.038$). With the antithyroid regimens, the AFABP serum levels of the hyperthyroid patients decreased to 16.6 (15.0, 23.9) ng/mL at the 6th month. No difference in the AFABP level was found between the hyperthyroid and the euthyroid groups at the 6th month. At baseline, sex (female vs male, $\beta = 7.65$, $P = 0.022$) and fT4 level ($\beta = 2.51$, $P = 0.018$) were significantly associated with AFABP levels in the univariate regression analysis. At the 6th month, sex and fT4 level ($\beta = 8.09$, $P < 0.001$ and $\beta = 3.61$, $P = 0.005$, respectively) were also significantly associated with AFABP levels. The associations between sex and fT4 level with AFABP levels remained significant in the stepwise multivariate regression analysis, both at baseline and at the 6th month.

The patients with hyperthyroidism had higher serum AFABP levels than the individuals with euthyroidism. In the patients with hyperthyroidism, the serum AFABP concentrations decreased after the antithyroid treatment. In this study, the serum AFABP concentrations were positively associated with female sex and the serum fT4 level.

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Abbreviations: AFABP = adipocyte fatty acid-binding protein, BH = body height, BMI = body mass index, BW = body weight, FABPs = fatty acid-binding proteins, FPG = fasting plasma glucose, fT4 = free thyroxine, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, TRAb = TSH receptor autoantibody, TSH = thyroid-stimulating hormone.

INTRODUCTION

Fatty acid-binding proteins (FABPs) are expressed in almost all mammalian tissues. Tissues with a higher rate of fatty acid (FA) metabolism have higher FABP levels.[1] By regulating FA transport in the nuclear and extranuclear compartments of the cells, FABPs modulate intracellular lipid metabolism and influence systemic energy homeostasis.[2] Adipocyte FABP (AFABP), also named FABP-4, is a cytosolic protein of mature adipocytes and macrophages. This protein is well documented to be an important regulator of systemic insulin sensitivity, as well as of lipid and glucose metabolism.[3–4] In macrophages, AFABP modulates inflammatory cytokine production and cholesterol ester accumulation.[5] Serum AFABP level has been shown to be a biomarker of body weight (BW) change,[6–8] atherosclerosis,[9–10] metabolic syndrome,[10–13] nephropathy, and macrovascular complications in type 2 diabetes.[14] The association between serum AFABP levels and left ventricular function has been reported in patients with coronary artery disease[15] and in morbidly obese patients.[16] In patients with critical illnesses, serum AFABP levels are associated with insulin resistance and prediction of mortality.[17] Pharmacological agents that modify AFABP functions may become a new class of medicines for diseases such as obesity, diabetes, and atherosclerosis.[18] As a result, AFABP stands out among the other members of the FABP family and has attracted huge attention from endocrinologists.

Changes in thyroid function are associated with marked changes in BW and energy expenditure.[19] Patients with hyperthyroidism usually have BW loss. After antithyroid treatment, they usually regain BW. Thyroid hormone is an important regulator of lipid metabolism.[20] Relationships between lipid profile and/or various adipokines and thyroid hormones have been investigated in literatures.[21] Thyroid hormone is also an important regulator of cardiac function. Risks of cardiovascular disease and cardiovascular mortality increase in patients with hyperthyroidism.[22–24]

Both AFABP and thyroid hormone levels have been associated with BW change and risks of cardiovascular disease.[6–8,17,19,22–24] However, serum AFABP levels in patients

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with different thyroid function statuses have never been discussed in literatures. In this study, we compared the serum AFABP concentrations in hyperthyroid and euthyroid patients. We also evaluated the association between serum AFABP and free thyroxine (fT4) levels.

METHODS

Patients

This is a prospective observational study. The study was approved by the research ethics committee of the National Taiwan University Hospital in accordance with the Declaration of Helsinki. First-visit patients to the endocrinology clinics of the National Taiwan University Hospital between the years 2010 and 2011 were identified. Patients who had ever been diagnosed with thyroid disorders and those with other comorbidities or under medications were excluded. Consent was obtained from each of the 62 patients after providing them with a full explanation of the purpose, nature, and procedures of the study.

Data Collection, Thyroid Function Status

Basic data such as sex; age; body height (BH); BW; concentrations of fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), AFABP, fT4, thyroid-stimulating hormone (TSH), and TSH receptor autoantibody (TRAb); and thyroid sonography findings were collected. The reference fT4 and TSH levels used in our hospital were 0.6–1.75 ng/dL and 0.1–4.5 μIU/mL, respectively. *Hyperthyroidism* was defined as an fT4 level >1.75 ng/dL and a TSH level <0.1 μIU/mL. *Subclinical hyperthyroidism* was defined as a TSH level <0.1 μIU/mL, with an fT4 level within the reference range. *Euthyroidism* was defined as both fT4 and TSH levels within their reference ranges. *Subclinical hypothyroidism* was defined as a TSH level >4.5 μIU/mL, with an fT4 level within the reference range. *Hypothyroidism* was defined as a TSH level >4.5 μIU/mL, with an fT4 level <0.6 ng/dL.

Trained staffs measured height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (m^2).

Biochemical Assay

Blood samples were drawn with minimal trauma from an antecubital vein in the morning after a 12-hour overnight fast. FPG level was measured by using the Olympus AU series 680 with the hexokinase method (Beckman Coulter, Nyon, Switzerland). Serum TC, TG, HDL-C, and LDL-C levels were measured by using the Olympus AU series 5800 with the cholesterol oxidase phenol 4-aminoantipyrine peroxidase method, glycerophosphate oxidase-phenol aminophenazone method, accelerator selective detergent, and liquid selective detergent, respectively (Beckman Coulter). TSH and fT4 levels were measured by using Siemens DPC Immulite 2000 (Siemens, Erlangen, Germany). Thyroid function values outside the laboratory measurement range (fT4 level >5.4 ng/dL or TSH level <0.004 μIU/mL) were recorded as an fT4 level of 5.4 ng/dL or a TSH level of 0.004 μIU/mL, respectively. Serum AFABP concentrations were determined by using the enzyme-linked immunosorbent assay (ELISA) method (human FABP4 ELISA kit, BioVendor, Heidelberg, Germany). TRAb levels were determined by using the radioimmunoassay method (TSH receptor autoantibody coated tube kit, RSR, Cardiff, UK). A percentage inhibition of TSH binding <10% was recorded as negative; >15% as positive; and 10% to 15% as borderline positive. All the assays were performed following the manufacturers' instructions.

Thyroid Ultrasound

All of the participants received thyroid ultrasonographic examination at baseline. The sonographic examination was performed by an endocrine specialist by using the Toshiba Aplio Ultrasound System (SSA-790) with a PLT-805AT probe. Aspiration cytological examination was performed as clinically indicated. None of the patients had malignant lesions.

Patients With Hyperthyroidism (HY group)

Thirty patients were diagnosed with hyperthyroidism. All of the hyperthyroid patients had positive examination results for TRAb. Sonograms of the hyperthyroid patients commonly revealed characteristics (hypoechoic and diffuse enlargement) compatible with autoimmune thyroiditis. The patients with hyperthyroidism were treated with antithyroid regimens (carbimazole 10 mg or propylthiouracil 100 mg three times daily) and laboratory follow-up as clinically indicated. They were followed up at the 2nd, 4th, and 6th months. The doses of the antithyroid drugs were titrated according to their improvement in thyroid function. Follow-up laboratory data were obtained at the 6th month.

Patients With Euthyroidism (EU group)

Thirty patients were in euthyroid status. All of them had negative examination results for TRAb. They were kept on follow-up without medications. Follow-up laboratory data were obtained at the 6th month.

Patients With Hypothyroidism/Subclinical Hypothyroidism (HO group)

One patient had subclinical hypothyroidism (fT4 level 0.72 ng/dL; TSH level 34.5 μIU/mL), and 1 patient had overt hypothyroidism (fT4 level 0.28 ng/dL; TSH level 55.3 μIU/mL). They were treated with thyroxine supplementation and dose titration to attain euthyroidism. Follow-up laboratory data were obtained at the 6th month.

Statistical Analyses

During the study period, only 30 patients with hyperthyroidism (HY group), 30 patients with euthyroidism (EU group), and 2 patients with overt/subclinical hypothyroidism (HO group) were enrolled. The first part of our analysis was to compare the initial data between the HY group and the EU group. Since the sample size was small, we used a nonparametric method in the statistical analysis. The data for the numerical variables were presented as median values (Q1, Q3). The Mann–Whitney *U* test was used for comparisons of numerical variables between the HY group and the EU group. Only 2 patients had overt/subclinical hypothyroidism. Their data were described, but not included in the analysis. Categorical data were expressed as percentages. Proportions and categorical variables were tested by using the Fisher exact test.

Second, we compared the follow-up data of the HY group and the EU group at the 6th month. The data for the numerical variables were presented as median values (Q1, Q3). The

TABLE 1. Characteristics of Patients With Hyperthyroidism or Euthyroidism

	Hyperthyroidism (N = 30)		Euthyroidism (N = 30)		$P^{\dagger}$	
	Initial (a)	6th Month (b)	Initial (c)	6th Month (d)	(a) vs (c)	(b) vs (d)
Male-to-female ratio	9:21		4:26		0.209	
Age (y)	37 (29, 43)		43 (32, 52)		0.110	
BH (cm)	161 (158, 170)		160 (157, 165)		0.268	
BW (kg)	56.6 (49.8, 61.0)	57.5 (54.0, 67.1)	60.5(55.0, 67.0)	60.0 (55.0, 67.0)	0.150	0.567
BMI	21.7 (19.5, 23.2)	22.7 (20.3, 23.9)	23.1 (21.2, 26.0)	23.0 (21.8, 26.0)	0.024*	0.099
fT4 (ng/dL)	3.19 (2.22, 3.92)	1.14 (0.89, 1.58)	0.99 (0.87, 1.06)	0.96 (0.86, 1.06)	<0.001*	0.024*
TSH (μIU/mL)	0.004 (0.004, 0.006)	0.006 (0.004, 1.450)	1.105 (0.651, 1.370)	0.904 (0.490, 1.420)	<0.001*	0.111
FPG (mg/dL)	88.5 (82, 93)	88 (79, 95)	86 (79, 89)	84.5 (79, 89)	0.047*	0.269
TC (mg/dL)	146.5 (121, 171)	181.5 (158, 207)	194 (182, 228)	191 (178, 227)	<0.001*	0.139
TG (mg/dL)	80 (60, 100)	86.5 (69, 103)	79.5 (61, 125)	92 (69, 154)	0.617	0.456
HDL-C (mg/dL)	49 (40, 58)	53 (47, 63)	56 (47, 65)	51 (43, 69)	0.053	0.994
LDL-C (mg/dL)	82.8 (66, 99.8)	110.2 (88.0, 130.0)	129 (105.4, 140.6)	107.4 (89.0, 136.4)	<0.001*	0.621
AFABP (ng/mL)	22.8 (19.4, 30.6)	16.6 (15.0, 23.9)	18.6 (15.3, 23.2)	21.2 (18.5, 26.6)	0.038*	0.149

Numerical data were presented as median (Q1, Q3).

AFABP = adipocyte fatty acid-binding protein, BH = body height, BMI = body mass index, BW = body weight, FPG = fasting plasma glucose, fT4 = free thyroxine, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, TSH = thyroid-stimulating hormone.

Column (a): hyperthyroid patients, initial data; column (b): hyperthyroid patients, data at the 6th month; column (c): euthyroid patients, initial data; column (d): euthyroid patients, data at the 6th month.

* $P < 0.05$.

† Fisher exact test for comparisons of categorical variables between hyperthyroid and euthyroid patients. Mann–Whitney *U* tests for comparisons of numerical variables between hyperthyroid and euthyroid patients.

Mann–Whitney *U* test was used for comparisons of numerical variables between the two patient groups. Categorical data were expressed as percentages. Proportions and categorical variables were tested by using the Fisher exact test.

Third, we evaluated the possible predictive factors of serum AFABP levels. We hypothesized that serum AFABP levels varied in different thyroid function statuses. We also hypothesized a positive association between fT4 and AFABP levels. The initial data of the HY group and the EU group were pooled together so that we could analyze the possible associations between serum AFABP levels and other variables. The predictive effects of demographic, anthropometric, or laboratory parameters (sex, age, and concentrations of fT4, TSH, BW, BMI, FPG, TC, TG, HDL-C, and LDL-C) for AFABP concentrations were evaluated by performing a linear regression analysis and then further tested by performing stepwise forward multivariate regression. In stepwise forward multivariate regression, variables with *P* values <0.15 remained in the model. Only variables with *P* values <0.05 were considered as statistically significant.

Fourth, follow-up data at the 6th month were used for validating our hypothesis concerning the associations between fT4 and AFABP levels. We duplicated the analysis by using the follow-up data at the 6th month. The data of the HY group and the EU group at the 6th month were pooled together. The predictive effects of demographic, anthropometric, or laboratory parameters (sex, age, and concentrations of fT4, TSH, BW, BMI, FPG, TC, TG, HDL-C, and LDL-C) for AFABP concentrations were evaluated by performing a linear regression analysis and then further tested by performing stepwise forward multivariate regression.

The normality of all the models was assessed by using the Kolmogorov–Smirnov test, and none of the models exhibited any collinearity problems. All of the analyses were performed by using the SAS version 9.1 statistical package for Windows (SAS, Cary, NC).

RESULTS

The anthropometric and laboratory characteristics of the hyperthyroid and euthyroid patients at their first visit and at the 6th-month follow-up visit are shown in Table 1. At the first visit, the hyperthyroid patients had higher fT4 and FPG levels, but lower TSH level, BMI, TC level, and LDL-C level than the euthyroid patients (Table 1, a vs c). The hyperthyroid patients apparently had higher AFABP levels than the euthyroid patients (22.8 ng/mL [19.4, 30.6 ng/mL] vs 18.6 ng/mL [15.3, 23.2 ng/mL], $P = 0.038$; Table 1, a vs c).

In the hyperthyroid patients, the fT4 level declined and the TSH level elevated significantly after the antithyroid treatment (Table 1). Among the patients in the hyperthyroid group, 10 (33.3%) attained euthyroid status, 15 (50%) had a subclinical hyperthyroid status, 4 (13.3%) remained in hyperthyroid status, and 1 (3.3%) shifted to a hypothyroid status (fT4 level 0.43 ng/dL; TSH level 59 μIU/mL) at the 6th month. All of the euthyroid patients remained in the euthyroid status at the 6th month. The mean fT4 levels in the hyperthyroid group declined, but were still higher than those in the euthyroid group at the 6th month ($P = 0.024$). The AFABP levels of hyperthyroid patients declined to 16.6 (15.0, 23.9) ng/mL at the 6th month. The anthropometric parameters, FPG level, lipid profiles, TSH level, and AFABP levels did not statistically differ between the hyperthyroid and euthyroid patients at the 6th month (Table 1, b vs d).

At baseline, the univariate regression analysis revealed that female sex ($\beta = 7.65$, $P = 0.022$) and fT4 levels ($\beta = 2.51$,

TABLE 2. Univariate Regression Model With Concentrations of AFABP as Dependent Variables, and Demographic, Anthropometric, and Laboratory Parameters as Independent Variables in All Patients (N = 60)

	AFABP (0)		AFABP (6)	
Independent variables	**β (95% CI)**	***P***	**β (95% CI)**	***P***
Sex	7.65 (1.16, 14.14)	0.022*	8.09 (4.12, 12.06)	<0.001*
Age	−0.09 (−0.35, 0.16)	0.469	0.14 (−0.03, 0.30)	0.098
BW	−0.25 (−0.54, 0.04)	0.094	−0.15 (−0.35, 0.04)	0.125
BMI	−0.12 (−1.06, 0.82)	0.794	0.21 (−0.45, 0.88)	0.521
fT4	2.51 (0.45, 4.56)	0.018*	3.61 (1.15, 6.06)	0.005*
TSH	−3.02 (−6.36, 0.32)	0.075	−0.11 (−0.36, 0.13)	0.365
FPG	0.09 (−0.22, 0.41)	0.557	0.09 (−0.04, 0.22)	0.177
TC	−0.05 (−0.10, 0.01)	0.124	−0.01 (−0.06, 0.04)	0.569
TG	−0.02 (−0.07, 0.04)	0.536	0.01 (−0.03, 0.04)	0.823
HDL-C	−0.04 (−0.23, 0.14)	0.653	0.02 (−0.06, 0.10)	0.638
LDL-C	−0.06 (−0.14, 0.02)	0.128	−0.03 (−0.09, 0.03)	0.284

AFABP (0): levels of AFABP at baseline; AFABP (6): levels of AFABP at the 6th month.

For AFABP (0): sex, age, and anthropometric and laboratory data at baseline were used as independent variables. For AFABP (6): sex, age, and anthropometric and laboratory data at the 6th month were used as independent variables.

Sex: female vs male.

95% CI = 95% confidence interval, β = parameter estimate, AFABP = adipocyte fatty acid-binding protein, BW = body weight, BMI = body mass index, fT4 = free thyroxine, TSH = thyroid-stimulating hormone, FPG = fasting plasma glucose, TC = total cholesterol, TG = triglyceride, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol.

* Linear regression, $P < 0.05$.

$P = 0.018$) were positively associated with AFABP levels in all of the patients. At the 6th month, female sex ($\beta = 8.09$, $P < 0.001$) and fT4 levels ($\beta = 3.61$, $P = 0.005$) had a positive association with AFABP levels in the univariate analysis (Table 2).

At baseline, the stepwise multivariable regression analysis revealed that the fT4 levels ($\beta = 2.92$, $P = 0.014$) and sex (female vs male, $\beta = 8.59$, $P = 0.008$) were significantly associated with AFABP levels in all of the patients. At the 6th month, female sex ($\beta = 8.83$, $P < 0.001$), fT4 level ($\beta = 3.55$, $P = 0.002$), and BMI ($\beta = 0.58$, $P = 0.052$) were positively associated with the AFABP concentrations (Table 3).

DISCUSSION

Both serum AFABP and thyroid hormone levels have been reported to be associated with BW change and risks of cardiovascular disease. However, no study has discussed the serum AFABP levels in different thyroid function statuses. Our study is the first to investigate the effect of different thyroid function statuses on AFABP level. Our analysis revealed that the patients with hyperthyroidism had significantly higher serum AFABP levels than the patients with euthyroidism. The AFABP levels of the hyperthyroid patients decreased after the administration of the antithyroid regimens. Our analysis also revealed that levels of AFABP were positively associated with female sex

TABLE 3. Forward Stepwise Regression Models in All Patients (N = 60) With Levels of AFABP as Dependent Variables, and Sex, Age, Anthropometric, and Laboratory Parameters as Independent Variables

Dependent Variables	Independent Variables	Parameter Estimate	Standard Error	Partial R^2	Model R^2	*F* value	$P_r > F$
AFABP (0)							
	fT4 (0)	2.92	0.99	0.103	0.103	6.40	0.014
	Sex	8.59	3.11	0.109	0.212	7.65	0.008
AFABP (6)							
	Sex	8.83	1.95	0.256	0.256	18.23	<0.001
	fT4 (6)	3.55	1.09	0.095	0.351	7.61	0.002
	BMI (6)	0.58	0.29	0.047	0.398	3.95	0.052

Forward stepwise regression analysis, variables left in the models are significant at the levels of 0.15.

AFABP (0): levels of AFABP at baseline; AFABP (6): levels of AFABP at the 6th month; fT4 (0): fT4 at baseline; fT4 (6): fT4 at the 6th month; BMI (6): BMI at the 6th month.

Sex: female vs male.

For AFABP (0): sex, age, and anthropometric and laboratory data at baseline were used as independent variables; for AFABP (6): sex, age, and anthropometric and laboratory data at the 6th month were used as independent variables.

AFABP = adipocyte fatty acid-binding protein, BMI = body mass index, fT4 = free thyroxine.

and serum fT4 level. The association between fT4 and AFABP levels was further validated by using the follow-up data at the 6th month.

Thyroid hormones have stimulating effects on thermogenesis and energy turnover.[19] Slight changes in thyroid function were reported to be possibly important for BMI.[25] Patients with hyperthyroidism usually have increasing basal metabolic rate and loss of BW. In our series, the hyperthyroid patients had significantly lower BMI than the euthyroid control individuals. The mean BMI of the hyperthyroid patients increased after the antithyroid treatment. The difference in BMI at the 6th month between the hyperthyroid patients and the control individuals was not statistically significant.

Thyroid hormones are important regulators of glucose metabolism. Associations between hyperthyroidism and insulin resistance have been discussed in literatures.[26,27] Shoumer et al[28] reported that fasting glucose levels were significantly higher in the hyperthyroid patients than in the control individuals. After the administration of antithyroid medications, the glucose levels became similar in both the groups.[28] Similar to the data from the previous study, our data revealed that the patients with hyperthyroidism had significantly higher FPG levels than those with euthyroid at baseline. The difference in FPG levels became insignificant at the 6th month.

Thyroid dysfunction may affect adipocyte function and lipid metabolism.[21] With increasing lipolysis to more than lipogenesis, patients with hyperthyroidism usually have increased levels of plasma-free fatty acids and decreased levels of cholesterol.[19] Canaris et al[20] reported that lipid levels decreased in a graded manner as thyroid function elevated. Compared with the euthyroid controls, the patients with hyperthyroidism had lower TC and LDL-C levels. The difference in lipid profile between the 2 patient groups disappeared at the 6th month. The changes in lipid profile confirmed the effects of thyroid function on lipid metabolism.

Serum AFABP levels have been reported to be higher in women than in men.[9–13] Concurring with data from previous reports, our data revealed a sexual dimorphism, with higher AFABP levels in the women, both initially and at the 6th month. Mechanisms such as higher body fat percentage in women, sex difference in regional fat distribution, or AFABP regulation by sex hormones have been suggested for the sexual dimorphism of AFABP levels.[10] Circulating AFABP levels were reported to be associated with obesity,[7,8,11–13] dyslipidemia,[11–13] and hyperglycemia.[12–13] Our study revealed no associations between AFABP level and glycemic or lipid profiles, both initially and at the 6th month.

In our study, the mean AFABP levels were higher in the hyperthyroid patients than in the euthyroid patients at baseline. In the hyperthyroid patients, the serum AFABP levels decreased after the treatment with antithyroid medications. Our analysis revealed positive associations between AFABP and fT4 levels, both initially and at the 6th month of follow-up. The association between fT4 and AFABP levels persisted in the multivariate stepwise regression analysis. At the 6th month, the status of one of the hyperthyroid patients became hypothyroid (fT4 level 0.43 ng/dL; TSH level 59 μIU/mL). He had an AFABP level of 24.9 ng/mL initially and 14.9 ng/mL at the 6th month. Due to the small patient number, we did not recruit patients with hypothyroidism in our analysis. However, we identified 1 newly diagnosed hypothyroid patient (fT4 level 0.28 ng/dL; TSH level 55.3 μIU/mL) and one subclinical hypothyroid patient (fT4 level 0.72 ng/dL; TSH level 34.5 μIU/mL) during our study period. Their AFABP levels increased after the treatment with levo-thyroxine (17.3 to 26.1 ng/mL and 15.7 to 30.1 ng/mL, respectively). Nakagawa et al[29] reported that hypothyroidism decreased the hepatic level of FABP and hyperthyroidism increased the hepatic FABP level in rats. Miklosz et al[30] concluded that hyperthyroidism increased lipid metabolism, especially in skeletal muscles with high capacity for fatty acid oxidation. Our data clearly demonstrated the effect of thyroid function on AFABP levels. It is plausible that thyroxine may increase the expression of AFABP. The exact mechanism merits further investigation.

In our study, the hyperthyroid patients initially had lower BMI than the euthyroid patients. The BMI of the hyperthyroid patients increased after the administration of antithyroid regimens. Some studies reported that BW reduction in obese children or adults led to reduction in AFAPB levels.[6–8] According to these studies, the BW loss in hyperthyroid patients might have decreased their AFABP levels. Our data revealed that the hyperthyroid patients had higher AFABP levels than the euthyroid patients. After the administration of antithyroid regimens, their AFABP levels decreased. This observation suggests that thyroid function status has more prominent effects than BW on AFABP levels. In our study, BMI was not associated with AFABP level in the univariate regression analysis, both initially and at the 6th month of follow-up. The association between BMI and AFABP levels was not significant in the multivariate regression analysis initially, but became borderline significant at the 6th month. Our observation suggests that thyroid function status should be considered in studies concerning the association between AFABP level and BMI.

Hyperthyroid individuals had significantly higher risks of cardiovascular diseases and mortality.[23,31] As an important regulator of insulin sensitivity and lipid metabolism,[3,4] serum AFABP level has been shown to be a biomarker of metabolic syndrome, atherosclerosis, and left ventricular function,[9–16] and a predictor of mortality in critical illness.[17] In our analysis, the fT4 levels were positively correlated with the serum AFABP levels. The link between AFABP level and cardiovascular complications of thyroid dysfunction deserves further investigation.

Our study is the first to demonstrate that thyroid function status may affect AFABP levels. However, it has several limitations. First, the patients with hyperthyroidism who were recruited had different severity or duration of thyrotoxicosis. The effects of advanced thyrotoxicosis on AFABP levels would be biased, as fT4 levels >5.4 ng/dL were recorded as 5.4 ng/dL in our analysis. Second, the effects of antithyroid medications, not changes in thyroid function, on FABP levels were not investigated in this study. Third, the clinical course varied in the hyperthyroid patients who received antithyroid medications. In hyperthyroid patients, the time and duration to achieve euthyroid status or to gain BW may affect AFABP levels. We collected initial and follow-up data at the 6th month. Whether AFABP levels fluctuated during the treatment course or not was not evaluated in this study. Fourth, due to the small patient number, the data of the patients with hypothyroidism were not included in the analysis. The association between fT4 and AFABP levels in the whole thyroid function spectrum remains to be investigated. Fifth, as our study was performed in only one medical center in Taiwan, the generalizability of this study might be limited.

In conclusion, the patients with hyperthyroidism had higher serum AFABP levels than those with euthyroidism. The serum AFABP levels of the patients with hyperthyroidism declined after the administration of antithyroid regimens.

Female sex and fT4 levels were positively associated with AFABP levels. Whether the associations between fT4 and AFABP levels persist in the whole thyroid function spectrum deserves further investigation.

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