Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

Prevalence and Risk Factors of Plasma Adiponectin Deficiency: A Cross-Sectional Study in a Physical Examination Cohort from Southwest China

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Background: Numerous studies have investigated adiponectin in disease populations, but no study has focused on the plasma adiponectin level, adiponectin deficiency, and its influencing factors in the population who have not yet developed disease symptoms.

Methods: The data of physical examination subjects who completed adiponectin detection in our hospital from 2020 to 2024 were included. The adiponectin levels in different age, genders, and subgroups were analyzed, and the indicators under adiponectin deficiency (<4 μg/mL in men and <5 μg/mL in women) were compared. The factors that might affect adiponectin deficiency were further included in multivariate logistic regression analysis. The odds ratio (OR) and 95% confidence interval (CI) were calculated to understand the possible risk factors for adiponectin deficiency.

Results: A total of 11829 subjects were included in the study, and the overall rate of adiponectin deficiency was 12.06%. The adiponectin level was generally higher in women; however, there were no significant differences among the subgroups of hypoproteinemia, low HDL-C, and anemia. Besides, hyperglycemia (OR: 2.02, 95% CI: 1.64–2.50), obesity (OR: 2.34, 95% CI: 1.87–2.91), hypertriglyceridemia (OR: 2.17, 95% CI: 1.89–2.48), low HDL-C (OR: 2.09, 95% CI: 1.66–2.65), increased PLT count (OR: 2.57, 95% CI: 1.57–4.50) and elevated ALT (OR: 1.48, 95% CI: 1.24–1.76) are associated with higher adiponectin deficiency. However, no significant associations were observed between adiponectin deficiency and gender, blood pressure, or elevated LDL-C.

Conclusion: The adiponectin level is generally higher in women than in men except for subjects with anemia, hypoproteinemia, and low HDL-C. Overweight/obesity, hypertriglyceridemia, low HDL-C, hyperuricemia, hyperglycemia, elevated ALT, and increased PLT count may be the risk factors for adiponectin deficiency. When these risk factors are present, targeted adiponectin testing is recommended.

Keywords: adiponectin, adiponectin deficiency, physical examination population, risk factors

Introduction

Adiponectin is the most abundant adipokine in human plasma and its monomer consists of a carboxyl (COOH) terminal globular domain, a collagen-like domain, a variable region, and an amino (NH2) terminal signal peptide.[1] The biological functions of adiponectin are multifaceted. Recent epidemiological evidence underscores that adiponectin deficiency correlates strongly with insulin resistance (IR),[2–4] dyslipidemia,[5] and systemic inflammation[6,7] across diverse populations. Patients with nonalcoholic steatohepatitis (NASH)[8,9] and central obesity exhibit severe hypoadiponectinemia, which exacerbates hepatic inflammation and fibrosis by worsening IR and dyslipidemia. Additionally, adiponectin may possess the preventive and protective properties against individual breast cancer,[10–12] while exhibiting a positive correlation with cognitive function.[13,14] These observations suggest that the reduction of adiponectin level is closely related to the risk of a variety of major diseases and poor prognosis, and it is an important biomarker reflecting the metabolic health and inflammatory state of the body.

Received: 16 February 2025
Accepted: 1 August 2025
Published: 20 August 2025

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Previous investigations on adiponectin have predominantly focused on individuals with preexisting conditions.[15,16] There are few reports on the plasma adiponectin level, adiponectin deficiency and its influencing factors in the population who have not yet developed disease symptoms. Therefore, this study focused on the physical examination population, and addressed the above doubts through the analysis on the large-scale physical examination data. By identifying individuals at high risk for adiponectin deficiency, this study facilitates early warning and lays the groundwork for elucidating potential pathophysiological mechanisms and formulating individualized prevention and intervention strategies.

Methods

Study Design and Participants

The data of subjects who completed adiponectin detection in the Department of Health Management of the First Affiliated Hospital of Army Medical University from 2020 to 2024 were screened. The following data were collected: body mass index (BMI), waist circumference (WC), blood pressure (BP), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), uric acid (UA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), creatinine (Cr), blood urea nitrogen (BUN), platelet (PLT), hemoglobin (HGB), and white blood cell (WBC). The subjects with incomplete data were excluded. A total of 12517 subjects completed adiponectin detection. After screening, 11829 subjects were finally included in the statistical analysis. As all data were retrospectively analyzed in an anonymous form, the written informed consent from subjects was waived. This study was approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University (Ethical Approval Number: KY2024139) and strictly complied with the ethical standards of the Declaration of Helsinki.

Definition of Positivity

In this study, the high-molecular-weight adiponectin level was analyzed by latex particle-enhanced turbidimetric immunoassay (LTIA), the kits were produced by IPROCOM Inc. Recognizing the significant population and regional variations in adiponectin levels, we established the adiponectin deficiency threshold (<4 μg/mL in men and <5 μg/mL in women) for this study based on the analysis of a healthy cohort from Chongqing. The criteria for dyslipidemia included any of the following conditions: TG >1.73 mmol/L, TC >5.7 mmol/L, LDL-C >3.1 mmol/L or HDL-C <0.9 mmol/L. Other definitions were below: abnormal FBG: FBG ≥ 6.1 mmol/L; hyperuricemia: UA > 428 umol/L; abnormal ALT: ALT >42 IU/L; abnormal AST: AST >42 IU/L. The criteria for anemia were as follows: HGB <120 g/L for men, HGB <110 g/L for women. The reference range of certain indices were as follows: WBC 3.5×10^9/L-9.5×10^9/L, PLT 125×10^9/L-350×10^9/L, ALB 38–51 g/L, Cr 45–84 mmol/L, and BUN 1.7–8.3 mmol/L. Based on BMI, the subjects were classified into three types: underweight (BMI <18.5 kg/m^2), normal (18.5 kg/m^2≤BMI <24.0 kg/m^2), overweight (BMI ≥ 24.0 kg/m^2), and obesity (BMI ≥ 28.0 kg/m^2). Central obesity in adults was defined as WC ≥ 90 cm for men and ≥85 cm for women. Abnormal blood pressure: systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg.

Statistical Analysis

The quantitative data of normal distribution were presented as mean ± standard deviation (SD) (x ± SD) and analyzed in a pairwise form using the independent sample *t* test. The categorical variables were expressed as a number (percent), and the intergroup comparison was performed with the x^2 test. Pearson correlations were used for normally distributed data, while Spearman correlations were used for abnormally distributed data. The OR and 95% CI were calculated using multivariable logistic regression to determine the relationship between adiponectin and different influencing factors. Only the subjects with complete data in all variables were considered in the model. Covariates include age, sex, BMI, WC, blood pressure, blood lipid, FBG, blood lipid, Cr, BUN, uric acid, ALT, AST, ALB, HGB, WBC, and PLT. All statistical analyses in this study were conducted using SPSS 23.0 software and the significance level was two-sided α=0.05.

Results

Plasma Adiponectin Level in the Physical Examination Population

A total of 11829 participants were included in the study, comprising 5726 women and 6103 men. Adiponectin levels show a U-shaped change with age, and the turning point occurs around the age of 40 ($P < 0.05$). The same trend was observed in different genders. The overall prevalence of adiponectin deficiency was found to be 12.06%. Notably, the highest occurrence rate of adiponectin deficiency was observed in men aged 30–40 years and women aged 40–50 years. Furthermore, there was a gradual decline of adiponectin level in the normal weight, overweight and obesity groups compared to the underweight group ($P < 0.001$). In addition, the adiponectin level exhibited a progressive reduction with the increase of FBG ($P < 0.001$). The adiponectin level showed a tendency to increase with the rise of SBP, particularly in hypertension grade 2 and grade 3 ($P < 0.05$). However, there was no significant alteration observed with the change of DBP (Figure 1).

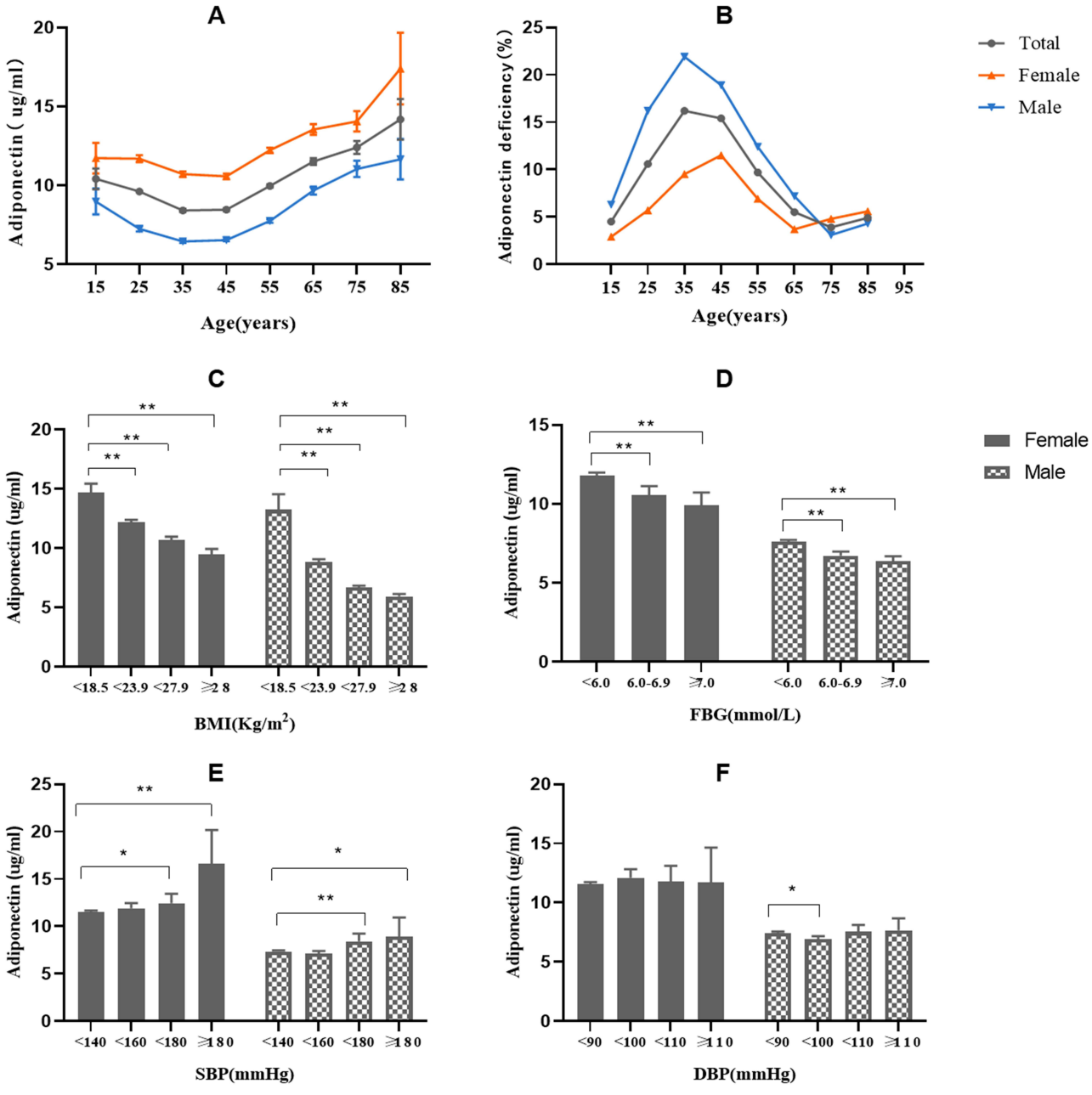

Figure 1 Plasma adiponectin levels in different groups. (**A**) Adiponectin levels in different age groups; (**B**) Adiponectin deficiency in different age groups; (**C**) Adiponectin levels in different BMI groups; (**D**) Adiponectin levels in different glucose groups; (**E**) Adiponectin levels in different systolic blood pressure groups; (**F**) Adiponectin levels in different diastolic blood pressure groups. *P<0.05, **P<0.001.

https://doi.org/10.2147/DMSO.S522521

The subjects with central obesity, hyperuricemia, hypertriglyceridemia, and low HDL-C exhibited a significantly lower plasma adiponectin level ($P < 0.001$). Conversely, the subjects with hypercholesterolemia demonstrated a higher adiponectin level ($P < 0.001$), while men with high LDL-C had a decreased adiponectin level ($P < 0.001$). In most subgroup analyses, women exhibited a significantly higher adiponectin level compared to men ($P < 0.001$). However, no significant differences were observed among the subgroups characterized by low HDL-C, low ALB, and anemia. The adiponectin level was found to be lower in the group with elevated ALT and AST compared to the normal liver function group, while a positive correlation was observed between adiponectin level and WBC ($P < 0.001$) or PLT ($P < 0.05$) (Table 1).

The Correlations Between Physical Examination Data and Adiponectin Level

There were no significant correlations between adiponectin level and TC, BUN, or SBP. However, correlation analysis revealed a positive correlation between adiponectin level and HDL-C ($r = 0.46$, $P < 0.001$), a negative correlation between adiponectin level and WC ($r=-0.35$, $P < 0.001$), BMI ($r = -0.33$, $P < 0.001$) and HGB ($r = -0.34$, $P < 0.001$) (Figure 2).

Table 1 Plasma Adiponectin Levels in Different Genders and Subgroups

Stratified Variable		Women		Men	
		Mean	95% CI	Mean	95% CI
WC	Normal	11.92	11.74–12.11	8.10$^{\#\#}$	7.95–8.26
	Central obesity	10.42**	10.08–10.75	6.35**$^{\#\#}$	6.21–6.48
Uric acid	<428 umol/L	11.74	11.57–11.90	8.00$^{\#\#}$	7.85–8.15
	≥428 umol/L	9.04**	8.29–9.79	6.43**$^{\#\#}$	6.29–6.57
Total cholesterol	<5.7 mmol/L	11.47	11.29–11.66	7.36$^{\#\#}$	7.24–7.49
	≥5.7 mmol/L	12.12**	11.75–12.49	7.40$^{\#\#}$	7.17–7.62
Triglyceride	<1.73 mmol/L	12.23	12.04–12.41	8.35$^{\#\#}$	8.19–8.50
	≥1.73 mmol/L	9.06**	8.76–9.36	6.01**$^{\#\#}$	5.89–6.13
LDL-C	<3.1 mmol/L	11.66	11.44–11.88	7.68$^{\#\#}$	7.51–7.85
	≥3.1 mmol/L	11.57	11.33–11.82	7.11**$^{\#\#}$	6.98–7.25
HDL-C	≥0.9 mmol/L	11.67	11.51–11.84	7.48$^{\#\#}$	7.37–7.59
	<0.9 mmol/L	6.64**	5.65–7.63	5.69**	5.31–6.07
Creatinine	<84 umol/L	11.58	11.42–11.74	7.38$^{\#\#}$	7.25–7.51
	≥84 umol/L	16.25**	14.12–18.38	7.35$^{\#\#}$	7.16–7.53
BUN	<8.3 mmol/L	11.60	11.43–11.76	7.34$^{\#\#}$	7.24–7.45
	≥8.3 mmol/L	12.74	11.37–14.11	7.99$^{\#\#}$	7.34–8.64
ALT	≤42 IU/L	11.74	11.57–11.90	7.71$^{\#\#}$	7.59–7.83
	>42 IU/L	9.47**	8.77–10.16	6.01**$^{\#\#}$	5.81–6.20
AST	≤42 IU/L	11.66	11.49–11.82	7.42$^{\#\#}$	7.31–7.53
	>42 IU/L	10.30*	9.19–11.41	6.66**$^{\#\#}$	6.22–7.09
Albumin	<38 g/l	13.48	11.29–15.67	13.92	7.22–7.43
	≥38 g/l	11.60*	11.44–11.77	7.32**$^{\#\#}$	10.83–17.01
Hemoglobin	Normal	11.60	11.43–11.76	7.33$^{\#\#}$	7.22–7.43
	Anemia	12.21	11.34–13.09	11.26**	9.25–13.28
WBC	$<3.5\times10^9$/L	13.49	12.67–14.30	8.69$^{\#\#}$	7.61–9.77
	$(3.5–9.5)\times10^9$/L	11.54**	11.38–11.71	7.37**$^{\#\#}$	7.27–7.48
	$>9.5\times10^9$/L	10.36**	8.83–11.89	6.45**$^{\#\#}$	5.89–7.01
PLT	$<125\times10^9$/L	13.69	12.74–14.64	8.62$^{\#\#}$	7.97–9.27
	$(125–350)\times10^9$/L	11.56**	11.39–11.72	7.32**$^{\#\#}$	7.21–7.43
	$>350\times10^9$/L	10.78**	9.50–12.05	7.35*$^{\#\#}$	6.29–8.40

Notes: Central obesity: waist circumference ≥90 cm for men and ≥85 cm for women; anemia: HB<120 g/l for men, HB<110 g/l for women; In the same stratified variable of the same sex, compared with the first group:* means P<0.05,** means P<0.001; In the same stratified variable, different genders were compared: $^{\#\#}$ means P<0.001.

Abbreviations: WC, waist circumference; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; PLT, platelet count; WBC, white blood cell count.

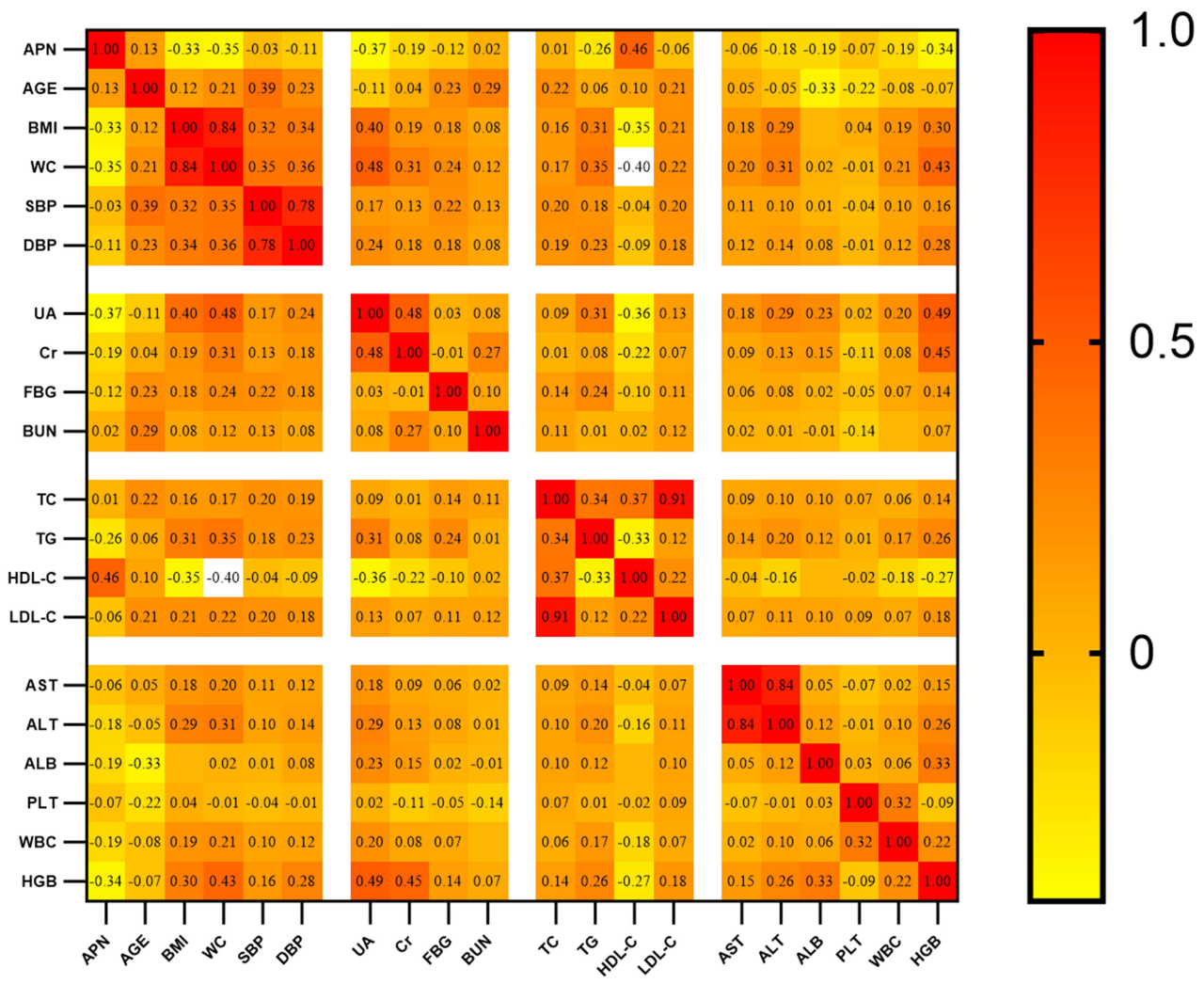

Figure 2 Correlation of APN with Health indicators. Innumerable values represent correlation coefficients close to zero.

Analysis of Physical Examination Data Based on the Adiponectin Level

In this study, the adiponectin deficiency group consisted of 1427 subjects. Compared to the normal adiponectin level group, there was a lower proportion of women (32.24% vs 50.62%) (χ^2=169.91, P < 0.001) and a younger age (43.35 ± 10.48 vs 46.03 ± 12.51) (t = 8.84, P < 0.001) in the adiponectin deficiency group. In terms of physical indicators, there were significantly higher WC (87.83 ± 9.88 vs 82.10 ± 10.24) (t = −20.45, P < 0.001), hip circumference (98.38 ± 6.38 vs 95.95 ± 11.48) (t = −7.82, P < 0.001), and BMI (26.09 ± 3.36 vs 24.02 ± 3.33) (t = −21.98, P < 0.001). Moreover, there was higher SBP (126.54 ± 16.86 vs 124.32 ± 18.03) (t=−4.62, P < 0.001) and DBP (80.48 ± 11.99 vs 77.56 ± 12.17)(t=−8.61, P < 0.001).

There were no significant differences in TC, LDL-C, and HDL-C between two groups; however, there was a lower percentage of hypertriglyceridemia in the deficiency group (21.70% vs 23.21%) (χ^2= 1.37, P < 0.001). Besides, there were higher levels of blood glucose (6.07 ± 1.73 vs 5.68 ± 1.33) (t = −8.1, P < 0.001) and UA (407.77 ± 102.3 vs 352.60 ± 93.59) (t = −19.28, P < 0.001), as well as Cr, PLT, WBC, HGB, and ALB. Furthermore, the prevalence of abnormality of ALT and AST were also higher in the deficiency group than in the normal adiponectin level group (Table 2).

Multivariate Logistic Regression Analysis on Influencing Factors of Adiponectin Deficiency

The indicators that exhibited differences in the above analysis were included in a logistic regression analysis to assess their impact on adiponectin deficiency. The findings revealed no association between gender and adiponectin deficiency,

https://doi.org/10.2147/DMSO.S522521

Table 2 Comparison of Various Health Indicators According to Adiponectin Group

	Total	Normal Adiponectin Level	Adiponectin Deficiency
Sex (woman/man)	5726/6136	5266/5136	460/967**
Age (years)	45.71±12.31	46.03±12.51	43.35±10.48**
WC (cm)	82.7910.37	82.10±10.24	87.83±9.88**
HC (cm)	96.24±11.01	95.95±11.48	98.38±6.38**
BMI (Kg/m^2)	24.27±3.40	24.02±3.33	26.09±3.36**
SBP (mmHg)	124.59±17.91	124.32±18.03	126.54±16.86**
DBP (mmHg)	77.91±12.18	77.56±12.17	80.48±11.99**
Hypertriglyceridemia (n/%)	2721/23.0	2412/23.2	309/21.7**
TC (mmol/L)	5.04±0.99	5.04±0.99	5.03±0.95
LDL-C (mmol/L)	3.12±0.73	3.11±0.72	3.13±0.76
HDL-C (mmol/L)	1.36±0.31	1.39±0.31	1.16±0.26
FBG (mmol/L)	5.73±1.39	5.68±1.33	6.07±1.73**
UA (umol/L)	359.26±96.38	352.60±93.59	407.77±102.37**
Cr (umol/L)	69.38±17.27	69.07±17.46	71.63±15.62**
BUN (mmol/L)	5.01±1.44	5.04±1.43	4.85±1.53**
PLT ($x10^9/L$)	213.59±57.24	212.19±56.87	223.82±58.88**
WBC ($x10^9/L$)	5.77±1.54	5.70±1.52	6.27±1.62**
HGB (g/L)	144.38±15.96	143.63±15.85	149.88±15.71**
High ALT (n/%)	1431/12.10	1118/10.75	313/21.93
High AST (n/%)	559/4.73	423/4.07	136/9.53
ALB (g/L)	44.2±2.53	44.11±2.53	44.90±2.38**

Note: (** means P<0.001).

however, the subjects aged 30–49 years had a higher risk of adiponectin deficiency compared to those aged <20 years (P < 0.05). In addition to hyperglycemia (OR: 2.02, 95% CI: 1.64–2.50), people with hyperuricemia (OR: 1.43, 95% CI: 1.24–1.66), high TG (OR: 2.17, 95% CI: 1.90–2.48), low HDL-C (OR: 2.09, 95% CI: 1.66–2.65), and obesity (OR: 2.34, 95% CI: 1.87–2.91) are more likely to have adiponectin deficiency (P < 0.001). However, there was no significant association between high LDL-C and adiponectin deficiency observed in this study (OR: 0.99, 95% CI: 0.86–1.14). The incidence of adiponectin deficiency decreased in patients with high TC (OR: 0.67,95% CI: 0.57–0.79). Besides, the subjects with elevated ALT had a higher likelihood of adiponectin deficiency (OR: 1.48, 95% CI: 1.24–1.76). The subjects with elevated PLT count (OR: 2.57, 95% CI: 1.57–4.5) were more prone to adiponectin deficiency as compared to those with thrombocytopenia; however, the change of WBC had the minimal impact (Table 3).

Table 3 Univariate and Multivariate Regression Analysis for Risk Factors of Adiponectin Deficiency

	Unadjusted			Adjusted		
	OR	95% CI	P	OR	95% CI	P
Sex (man)	2.16	1.916–2.42	<0.001	1.09	0.94–1.27	0.25
Age (years)						
<20	1.0			1.0		
20-29	2.52	0.78–8.14	0.12	3.13	0.92–10.64	0.07
30-39	4.13	1.29–13.20	0.02	4.28	1.27–14.43	**0.02**
40-49	3.87	1.21–12.38	0.02	3.78	1.12–12.76	**0.03**
50-59	2.29	0.71–7.31	0.16	2.22	0.66–7.52	0.20
60-69	1.25	0.38–4.10	0.71	1.27	0.36–4.40	0.71
70-79	0.86	0.23–3.26	0.82	0.90	0.22–3.63	0.88
≥80	1.09	0.18–6.84	0.92	1.09	0.16–7.29	0.93

(*Continued*)

Table 3 (Continued).

	Unadjusted			Adjusted		
	OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
BMI (Kg/m^2)						
<24	1.0			1.0		
24-27.9	2.46	2.16–2.81	<0.001	1.94	1.66–2.27	**<0.001**
≥28	3.95	3.37–4.63	<0.001	2.34	1.87–2.91	**<0.001**
WC						
Central obesity	2.12	1.90–2.37	<0.001	0.90	0.77–1.05	0.19
Blood Pressure						
High SBP	1.18	1.03–1.35	0.02	1.07	0.88–1.30	0.52
High DBP	1.44	1.26–1.66	<0.001	0.94	0.77–1.13	0.50
FBG (mmol/L)						
<6.1	1.0			1.0		
6.1–6.9	1.70	1.45–1.99	<0.001	1.44	1.21–1.71	**<0.001**
≥7.0	2.31	1.93–2.78	<0.001	2.02	1.64–2.50	**<0.001**
Blood lipid						
Hypercholesteremia	0.92	0.80–1.05	0.20	0.67	0.57–0.79	**<0.001**
Hypertriglyceridemia	3.42	3.05–3.83	0.00	2.17	1.89–2.48	**<0.001**
High L-DLC	1.12	1.00–1.25	0.04	0.99	0.86–1.14	0.91
Low H-DLC	4.10	3.33–5.06	<0.001	2.09	1.66–2.65	**<0.001**
Hepatorenal function						
High Cr	1.30	1.13–1.49	<0.001	0.89	0.76–1.05	0.16
High BUN	1.74	1.33–2.27	<0.001	1.20	0.88–1.63	0.24
Hyperuricemia	2.72	2.42–3.05	<0.001	1.43	1.24–1.66	**<0.001**
High ALT	3.05	2.67–3.48	<0.001	1.48	1.24–1.76	**<0.001**
High AST	2.49	2.03–3.04	<0.001	1.15	0.89–1.48	0.29
Hypoalbuminemia	0.32	0.12–0.88	0.03	0.46	0.16–1.29	0.14
Blood routine examination						
Anemia	0.84	0.58–1.22	0.36	1.31	0.87–1.98	0.20
WBC<3.5×10^9/L	1.0			1.0		
(3.5–9.5)×10^9/L	1.55	1.08–2.22	0.02	0.93	0.63–1.36	0.70
>9.5×10^9/L	3.17	2.02–4.96	<0.001	1.43	0.88–2.33	0.15
PLT<125×10^9/L	1.00			1.00		
(125–350)×10^9/L	1.87	1.31–2.69	<0.001	1.80	1.21–2.66	**<0.001**
>350×10^9/L	2.89	1.72–4.87	<0.001	2.57	1.47–4.50	**<0.001**

Notes: Adjusted for age, sex, BMI, WC, blood pressure, blood lipid, FBG, Blood lipid, Cr, BUN, uric acid, ALT, AST, ALB, HGB, WBC, PLT. Data in bold indicate statistical significance with P<0.05.

Discussion

The plasma adiponectin level was observed with an initial decrease followed by an increase with advancing age. Notably, a statistically significant decline was found at an age of 30–40 years, which contrasts with the previous studies that reported a positive correlation between adiponectin level and age.[17] However, it is important to note that these earlier studies did not provide the detailed age grouping or explore the relationship between age and adiponectin level in a large-sample population. The patients under the age of 40 years were arranged to the same group without conducting a comprehensive analysis based on the specific age categories.[18] For the first time, we discovered a prevalence rate of 12.06% for adiponectin deficiency in the healthy population, and a higher risk in the subjects aged 30–50 years (OR: 3.78). The adiponectin level was consistently higher in women compared to men across all age groups and subgroups, aligning with the previous study findings.[19] The elevated adiponectin level in women might be attributed to the influence of estrogen on adipose tissue.[20] Some investigators also speculated that the gender difference might be primarily influenced by androgen level.[21] In the subgroup analysis, we observed no significant difference of adiponectin level

between men and women in the low ALB, low HDL-C, and anemia subgroups. This suggested that the impact of gender on the adiponectin level became insignificant under the condition of nutritional deficiency, necessitating further investigation into the underlying mechanisms. Although women generally exhibited a higher adiponectin level than men, a greater proportion of men presented adiponectin deficiency. However, after adjustment for influencing factors, the influence of gender on adiponectin deficiency became inconspicuous.

Regarding anthropometric indicators, previous studies have demonstrated a negative correlation of adiponectin level with both body weight and central obesity.[22] In the current investigation, we also observed that a higher BMI was associated with a lower adiponectin level and an increased risk of adiponectin deficiency. Notably, it is worth mentioning that there was a statistically significant decrease of adiponectin secretion in the subjects with normal BMI compared to those who were lean, which differs from the findings of a study specifically focusing on anorexia nervosa patients with low BMI.[23] In the subsequent multivariate logistic regression analysis, however, we opted not to designate BMI <18.5 kg/m^2 as a reference group; instead, due to our heightened concern regarding the impact of overweight/obesity on adiponectin deficiency in this population, we used BMI $\geq$ 24 kg/m^2 as the reference. Nevertheless, it is worth noting that adiponectin is primarily secreted by adipocytes. Therefore, why does its concentration tend to be lower in individuals who are overweight or obese? Animal studies have demonstrated that healthy adipose tissue has a greater capacity of secreting adiponectin compared to unhealthy adipose tissue.[24] In mouse models, obesity-induced endoplasmic reticulum (ER) stress could down-regulate the adiponectin level by inhibiting its expression, multimerization, and stability.[25] In addition, some studies have suggested that this phenomenon may be attributed to unhealthy lifestyle factors such as low physical activity and sedentary behavior.[26] Despite the fact that central obesity is associated with a lower adiponectin level in certain populations, it does not emerge as a risk factor for adiponectin deficiency in the context of our study population undergoing physical examinations, possibly because the effect is not obvious compared with BMI and other factors.

A low adiponectin level is associated with an increased risk of atherosclerosis.[27] Glucose and lipid metabolism disorders are closely linked to the development of atherosclerosis. In this study, we found that hyperglycemia, hyperuricemia, high TG, and low HDL-C may increase the risk of adiponectin deficiency. These findings suggest that these abnormalities may contribute to adiponectin deficiency through certain mechanisms and play a role in cardiovascular disease. Additionally, the subjects with hypercholesterolemia were found to have a lower risk of adiponectin deficiency, while LDL-C lower and blood pressure showed no association with adiponectin deficiency. Atherosclerosis is a chronic inflammatory disease affecting arterial walls. WBC and PLT are closely related to tissue damage and inflammation.[28,29] The recent studies have indicated that increased WBC and PLT count are associated with hypoadiponectinemia.[30] Our study also suggested that PLT was a risk factor for adiponectin deficiency. Although we observed a gradual decrease in adiponectin level with increasing WBC, the adjustment for multiple factors revealed no significant effect on adiponectin deficiency.

Adiponectin has two major receptors, AdipoR1 and AdipoR2, of which AdipoR2 is predominantly expressed in the liver.[22] Adiponectin deficiency predisposes individuals to hepatic steatosis,[31] and it has been demonstrated that adiponectin and its cognate receptors can mediate the amelioration of obesity-induced non-alcoholic fatty liver disease (NAFLD).[32] We observed ALT elevation, which is a risk factor for adiponectin deficiency; it is suggested that adiponectin can be detected simultaneously in people with abnormal liver function, and the improvement of liver metabolic status, such as reducing the degree of fatty liver, may increase the level of adiponectin. Adiponectin can alleviate the symptoms of ischemic renal disease by inhibiting renal cell apoptosis.[33] Several studies have reported an increased adiponectin level in patients with chronic kidney disease, particularly those with end-stage renal disease.[34] Reduced handling by the human kidney is a major factor to increase circulating APN in renal disease.[35] In this study, however, elevated Cr had the minimal impact on adiponectin deficiency. This could be attributed to the short duration and generally mild nature of renal dysfunction in the physical examination population. In the future, we will follow up this cohort of people with abnormal renal function to further study the relationship between renal function and adiponectin.

Finally, our study also has some potential limitations. First, the analysis relied on historical health examination data, which may introduce potential selection bias as participants were not randomly enrolled but self-selected for routine check-ups. Second, detailed information on key confounding variables was unavailable, including Objective

measurements of physical activity levels, specific information about the diet, Comprehensive medication use history, Detailed family histories of diabetes or cardiovascular diseases. Finally, this study was observational and retrospective in design, which prevented us from being able to draw conclusions about causal relationships between adiponectin deficiency and health outcomes. Therefore, larger prospective studies are required to establish these relationships. It is important to note that our definition of adiponectin deficiency was based on cohort in Southwest China reference ranges, acknowledging the well-documented variations in adiponectin levels across different populations.[36]

Conclusion

In conclusion, the adiponectin level exhibited a U-shaped pattern with age in the physical examination population, reaching its trough in the 30–40 age group and peaking in deficiency at an age of 30–50 years. Although women generally had a higher adiponectin level than men, there was no significant difference between women and men in some stratified subgroups. Adiponectin deficiency was associated with overweight/obesity, high TG, low HDL-C, hyperuricemia, abnormal blood glucose, elevated ALT and increased PLT. Conversely, hypercholesterolemia may be a protective factor for adiponectin deficiency, while elevated blood pressure and high LDL-C did not significantly affect adiponectin deficiency. When these risk factors are present, targeted adiponectin testing is recommended.

Acknowledgments

We thank all authors for assistance in the article preparation.

Funding

This study did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

Disclosure

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

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