Serum level of A-kinase anchoring protein 1, negatively correlated with insulin resistance and body mass index, decreases slightly in people with newly diagnosed T2DM

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Running title: serum AKAP1 with T2DM and obesity

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Abstract

Introduction: At present, the number of people suffering from diabetes and obesity is increasing in China, and also all over the world. Researchers found that decreased expression of A-kinase anchoring protein 1 (AKAP1), which was thought to regulate the function and structure of mitochondria, might be related to these two diseases. However, as far as we know, there is no study about the changes of serum AKAP1 protein in these two diseases. Hence we conducted this experiment to study the relationship between serum levels of AKAP1 with T2DM and obesity.

Material and methods: There were 261 subjects involved in the experiment, including 130 patients with newly diagnosed T2DM and 131 individuals with normal glucose tolerance (NGT). They were further divided into four groups as follows. Subjects with NGT and normal weight (NW) were assigned to the NGT+NW group, those with NGT but with overweight (OW) or obesity (OB) were assigned to the NGT+OW/OB group, and so on; the rest were divided into the T2DM+NW group and the T2DM+OW/OB group. Serum AKAP1 levels were tested by ELISA method and compared by T-test. Linear regression was applied to discuss independent factors of AKAP1. Multiple logistic regression was used to analyse the relationship between

AKAP1 and the prevalence of T2DM.

Results: Serum AKAP1 in the NGT+NW group was 1.74 ± 0.42 ng/mL, higher than that in the NGT+OW/OB group, at 1.59 ± 0.41 ng/mL (t = 2.114, p = 0.036), and the T2DM+OW/OB group, at 1.52 ± 0.36ng/ml (t = 3.219, p = 0.002). A-kinase anchoring protein 1 in 130 subjects with T2DM was lower than that in subjects with NGT, 1.57 ± 0.35 ng/mL vs. 1.67 ± 0.42 ng/mL, t = 2.036, p = 0.043. Liner regression showed that insulin resistance (IR) and body mass index (BMI) were independent factors negatively related to AKAP1: β = -0.019 and -0.032, respectively. Compared to the highest tertile of AKAP1, the prevalence of T2DM was higher in the other two tertiles; OR was 2.207 (1.203, 4.050) and 2.051 (1.121, 3.753), respectively.

Conclusions: Serum AKAP1 level decreases slightly in patients with T2DM and obesity. Subjects with lower leve1s of serum AKAP1 are susceptible to T2DM.

Key words: A-kinase anchoring protein 1; type 2 diabetes mellitus; obesity

Introduction

According to the data released by the International Diabetes Federation, there were more than 114 million Chinese people suffering from diabetes in 2017 [1]. And in 2014, the number of obese people in China was 90 million [2]. Diabetes, of which T2DM comprises the majority, and obesity have brought a heavy burden to Chinese society and families. At present, it is believed that T2DM and obesity are collectively caused by many factors, such as environment, diet, exercise, heredity, etc. A growing number of studies have confirmed that mitochondrial dysfunction is closely related to T2DM and obesity [3].

The A-kinase anchored proteins (AKAPs) family is a group of proteins with different structures but similar functions. It is named because of its binding property with protein kinase A (PKA). A-kinase anchoring protein 1, located in the outer membrane of mitochondria (OMM), which plays an important role in maintaining the normal metabolism and survival of cells, can maintain the functional activity of mitochondrial respiratory chain and regulate the mitochondrial dynamics [4]. Previous studies showed that decreased expression of AKAP1 was related to maladjustment of

peroxisome proliferator-activated receptor (PPARγ), further damaging the lipolysis caused by catecholamine and leading to obesity [5]. The expression of AKAP1 mRNA decreased in obese subjects [6]. Akap1−/− mice were vulnerable to impaired glucose tolerance and insulin resistance [7]. The above studies showed that AKAP1 might play an important role in the occurrence and development of diabetes and obesity. However, few studies are related to serum level of AKAP1 protein in obese individuals and patients with diabetes. Hence, we designed this experiment to study the changes of serum level of AKAP1 protein in the above population.

Material and methods

Study subjects

From October 2019 to February 2020, a total of 261 subjects were involved in the study, including 130 patients with newly diagnosed T2DM from the endocrinology department of the First Affiliated Hospital of Soochow University, and 131 individuals with normal glucose tolerance (NGT) from the physical examination centre of the hospital. All participants underwent an oral glucose tolerance test (OGTT) in which 75 g glucose was dissolved in the appropriate amount of water, and all subjects drank it within 5 min. Diabetes was diagnosed as fasting blood glucose (FBG) $\geq$ 7.0 mmol/L and/or 2 h OGTT $\geq$ 11.1 mmol/L, while NGT was diagnosed as FBG < 6.1 mmol/L and 2 h OGTT < 7.8 mmol/L. Height (H) and weight (W) of the participates were measured by skilled nurses. Body mass index (BMI) was calculated by W/H^2: BMI < 25 kg/m^2 was defined as normal weight (NW), BMI $\geq$ 25 kg/m^2 and < 30 kg/m^2 defined as overweight (OW), and BMI $\geq$ 30 kg/m^2 defined as obesity (OB). According to the results of OGTT and BMI, the subjects were divided into four groups: subjects with NGT and NW were assigned to the NGT+NW group, those with NGT but overweight (OW) or obesity (OB) were assigned to the NGT+OW/OB group, and so on; the rest were divided into the T2DM+NW group and the T2DM+OW/OB group. Exclusion criteria: T1DM; age less than 25 or more than 70 years; BMI $\geq$ 35 kg/m^2 or < 18.5 kg/m^2; Cushing's syndrome; thyroid disease; acute and chronic heart, liver, and kidney disorders; acute complications; pregnancy and lactation; cancer;

smoking; and alcohol intake over 140 g per week (male) or 70 g per week (female). In addition, patients who had received hypoglycaemic treatment were not enrolled in the study, and neither were those who had taken antihypertensive and lipid-lowering drugs. However, patients with hypertension or dyslipidaemia but with no history of taking medicine were not excluded. The study was approved by the Ethics Committee of the hospital; and all the participants were informed and agreed.

Data collection

Body mass index was obtained as described above, waist circumference (WC) and hip circumference (HC) were measured, and the waist/hip ratio (WHR) was calculated as WC divided by HC. After sitting for 15 minutes, the blood pressure was measured twice on the right upper arm. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined by the mean level of the two measurements. Venous blood samples were taken after overnight fasting for more than 10 hours. After blood centrifugation, serum levels of glutamic-pyruvic transaminase (ALT), creatinine (Cr), FBG, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were determined by a Hitachi 7600 analyser (Tokyo, Japan). Glycosylated haemoglobin (HbA_{1c}) was tested by high-performance liquid chromatography method. Insulin (INS) concentration was checked by an automated immunoassay analyser (AIA-2000ST). IR was estimated by the following formula: IR = INS * FBG / 22.5. Serum AKAP1 levels were measured by using ELISA method (reagents provided by Elabscience Biotechnology, Wuhan, China, with a sensitivity of < 0.1 ng/mL. The intra-CV and inter-CV were < 10%).

Data analysis

Continuous variables were tested by Kolmogorov-Smirnov test to determine whether the data conformed to normal distribution, and they were expressed as mean ± S.D. or median (P25, P75). T-test or Mann-Whitney U test was used for comparison between two groups, while ANOVA or Kruskal-Wallis test was used for comparison between multiple groups. Chi-square test was used to compare categorical variables among

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groups. Pearson correlation was adopted to analyse the correlation between AKAP1 and other indicators, and stepwise linear regression was adopted to investigate the independent risk factors of AKAP1. Before correlation or regression analysis, skew distribution data were log-transformed. Multiple logistic regression analysis was used to evaluate the association between AKAP1 and the prevalence of T2DM. All analyses were performed by SPSS 22.0. $p < 0.05$ (two sides) was adopted as the level of statistical significance.

Results

The baseline data of the participants

As shown in Table 1 WC, HC, BMI, SBP, TG, INS, and IR in OW/OB patients were higher than those in subjects with NW. Parameters: FBG, HbA_{1c}, INS, and IR in patients with T2DM were higher, while Cr was lower than that in those with NGT. Waist circumference in the T2DM+NW group was higher than that in the NGT+NW group. The lowest WHR was obtained in the NGT+NW group, and the highest in the T2DM+OW/OB group. There was no difference in WHR between the other two groups. In the T2DM+OW/OB group, TC was higher than in the NGT+NW group, LDL-c was higher than in the two NGT groups, and ALT was higher than in the other groups. TG in the NGT+OW/OB group was higher than that in the T2DM+NW group, while it was lower than that in the T2DM+OW/OB group. High-density lipoprotein cholesterol in people with NGT was higher than that in the two T2DM groups, of which the T2DM+OW/OB group had the lowest level. Glycated haemoglobin in the T2DM+NW group was higher than in the T2DM+OW/OB group. There was no significant difference in gender composition, age, and DBP between any two of the four groups.

Comparison of serum levels of AKAP1 protein among the groups

Serum level of AKAP1 protein in the NGT+NW group was 1.74 ± 0.42 ng/mL, higher than that in the NGT+NW group (1.59 ± 0.41 ng/mL, $t = 2.114$, p = 0.036) and the T2DM+OW/OB group (1.52 ± 0.36 ng/mL, $t = 3.219$, p = 0.002), while there was no

statistical difference compared with the T2DM+NW group (1.61 ± 0.35 ng/mL, $t =$ 1.891, p = 0.061). In this experiment, the AKAP1 level in 131 subjects with NGT was slightly higher than that in 130 subjects with T2DM, as shown in Figure 1 (1.67 ± 0.42 ng/mL vs. 1.57 ± 0.35 ng/mL, $t = 2.036$, p = 0.043). A-kinase anchoring protein 1 in the two NW groups was higher than in the OW/OB groups (1.68 ± 0.39 ng/mL vs. 1.55 ± 0.38 ng/mL, $t = 2.604$, p = 0.010).

Pearson correlation of the relationship between AKAP1 and other variables
As shown in Table 2, AKAP1 was negatively correlated with BMI, WHR, DBP, and TG in the NGT population. In patients with T2DM, AKAP1 was negatively related to BMI, SBP, INS, and IR.

Stepwise linear regression studying the independent influencing factors of serum AKAP1 level
From Table 3, it seems that BMI, DBP, and IR were negatively correlated with serum AKAP1 level, while HC, surprisingly, might be a positive factor.

Multiple logistic regression about the correlation between serum AKAP1 level and the prevalence of T2DM
According to the serum AKAP1 level, 261 participants were divided into three groups: T1 (< 1.44 ng/mL), T2 (1.44–1.69 ng/mL), and T3 (> 1.69 ng/mL). The prevalence of T2DM in the T3 group was 37.5%, lower than that in the T1 and T2 groups (55.2% and 57.0%), respectively (Fig. 2, chi-square test).

Multiple logistic regression showed that the risk of T2DM of T2 and T1 was significantly higher when compared to the T3 group, even after adjusting some factors including BMI and TG, as shown in model 1–3 in Table 4. However, after the adjustment for HDL-C, the prevalence of T2DM between T2 and T3 became less statistically significant, while the prevalence in T1 was still higher than in T3 (model 4 in Table 4). When further taking HC into consideration, we found that there was no significant difference of the prevalence among the three groups (model 5 in Table 4).

Discussion

Adenosine triphosphate (ATP) is mainly produced by mitochondria. Mitochondrial dysfunction affects the ATP/ADP ratio and insulin secretion [8]. Moreover, mitochondria are also the main source of reactive oxygen species (ROS). Their dysfunction produces excessive ROS, which aggravates inflammatory response and insulin resistance [9]. It is believed that mitochondrial disorder is closely related to T2DM.

AKAP1 mediates PKA and protein tyrosine phosphatase-D1 targeting OMM, which phosphorylates important components of the oxidative respiratory chain, such as NDUFS4 and cytochrome c oxidase, further regulating oxidative respiration and ATP production [10, 11]. In addition, PKA phosphorylates and inactivates dynamic related protein 1 (Drp1), thus inhibiting mitochondrial fission [12]. It indicates that AKAP1 is critical in maintaining the function and structure of mitochondria. What is more, down-regulation of AKAP1 expression leads to mitochondrial dysfunction and increased ROS production, suggesting that AKAP1 also plays an important role in limiting the abnormal increase of ROS [13].

A previous study showed that AKAP1 deficiency would aggravate the abnormal glucose tolerance and insulin resistance, and promote liver gluconeogenesis and steatosis in high-fat fed mice. Further observation under an electron microscope revealed the notably abnormal mitochondrial structures in these mice. The mitochondria were found to be obviously swelling, the electron density became lower, and the cristae became fewer and shorter. In view of the above, AKAP1 deficiency accounting for mitochondrial dysfunction was thought to promote the development of diabetes [7]. In our experiment, the serum level of AKAP1 protein was negatively correlated with IR and slightly decreased in people with T2DM, which seemed to be consistent with the above study. Some researchers once divided obese people into a high-IR group and low-IR group, according to their levels of IR, and found no significant difference of AKAP1 mRNA expression between the two groups [5]. We did not find any significant difference in serum AKAP1 levels in OW/OB subjects

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with NGT and with T2DM in our experiment, although the levels of IR in these two groups were marked distinctively. However, further studies are needed to confirm the relationship between AKAP1 and diabetes.

It is thought that AKAP1 plays a role in fat and energy metabolism in a variety of ways: Primarily, AKAP1 may mediate PKA phosphorylation of proteins involved in lipid metabolism, including hormone sensitive lipase (HSL) and perilipin [14]. Secondly, PKA regulatory subunit IIB (prkar2b) plays an important central role in regulating energy consumption and glycolipid metabolism, and it is thought that AKAP1 mediated subcellular localisation of prkar2b is necessary for the effective transduction of signals regulating lipolysis [15]. Furthermore, AKAP1 may be a target gene of PPARγ, which is an important regulator of fat formation. PPARγ mutant causes the decrease of HSL activity and the impairment of lipolysis mediated by β-adrenergic, which may be related to AKAP1/PKA dysfunction [5]. Finally, AKAP1 can anchor protein phosphatase 1 on the lipid droplets of fat cells and mediate its role in fat metabolism [16].

Researchers found that AKAP1 mRNA decreased in adipose tissue of obese subjects [5, 6]. A-kinase anchoring protein 1 deficiency would promote fat deposition and fat cell hypertrophy in adipose tissue and aggravate obesity symptoms [7]. It seems that AKAP1 might be a negative factor in fat and energy metabolism. However, in another experiment, AKAP1−/− mice were found to have lower weight than wild-type counterparts [17]. Our results showed that there was a downward trend of serum AKAP1 level in the OW/OB population, and AKAP1 was negatively correlated with BMI. Moreover, AKAP1 was negatively related with TG in the NGT population, suggesting that AKAP1 might be involved in the regulation of fat metabolism.

A-kinase anchoring protein 1 had been confirmed before our study to regulate the cardiovascular system, including inhibiting cardiomyocyte hypertrophy, improving myocardial ischaemia and protecting the function of endothelial cell (EC) [18]. A-kinase anchoring protein 1 deficiency selectively damaged endothelium-dependent vasodilation, leading to an increase in blood pressure [19, 20]. It also seemed that there might be a negative trend between AKAP1 and blood pressure in our study. It is

generally believed that AKAP1 deficiency leads to the decrease of protein kinase B (PKB, Akt) phosphorylation, which may play a regulatory role towards EC through endothelial NO synthase (eNOS)-NO pathway [19, 20]. However, it has been confirmed that PKA can directly regulate eNOS [21]. Moreover, Akt-mammalian target of rapamycin (mTOR) signalling pathway is important for EC function, while mTOR has been proven to be the downstream target of AKAP1 in cancer [22]. It needs to be confirmed whether there are other potential mechanisms in the regulation of AKAP1 on blood vessels.

In addition, AKAP1 may control cholesterol transport by regulating the activity of steroid acute regulatory factors through a post-transcriptional mechanism [23, 24] and possibly affecting the structure of mitochondrial-associated endoplasmic reticulum membrane [23, 25]. However, no evidence in our study and others showed the relationship between AKAP1 and cholesterol.

Conclusions

In this paper, we found that AKAP1, which was negatively correlated with IR and BMI, showed a slight downward trend in patients with newly diagnosed T2DM. However, it is only a cross-sectional experiment with a small sample size. Previous studies have shown that rosiglitazone could increase the expression of AKAP1 mRNA [5], and metformin could affect the structure and function of mitochondria [26, 27]. Further studies are required, to investigate the effect of hypoglycaemic drugs on AKAP1, as well the variety of AKAP1 with prolonged course of disease.

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Table 1. Measured data of participants

Variables	NGT+NW	NGT+OW/OB	T2DM+NW	T2DM+OW/OB	p
N (M/F)	68 (36/32)	63 (34/29)	66 (36/30)	64 (35/29)	0.889
Age (year)	45.26 ± 12.33	47.06 ± 11.37	46.36 ± 11.59	43.53 ± 10.71	0.334
WC [cm]	81.00 ± 5.20	90.33 ± 7.67[a]	84.70 ± 6.48[a,b]	96.42 ± 8.18[a,b,c]	< 0.001
HC [cm]	94.85 ± 4.71	100.51 ± 6.35[a]	93.55 ± 6.21[b]	101.73 ± 8.26[a,c]	< 0.001
WHR	0.85 ± 0.05	0.90 ± 0.04[a]	0.91 ± 0.07[a]	0.95 ± 0.06[a,b,c]	< 0.001
BMI [kg/m^2]	23.09 ± 1.62	26.95 ± 1.80[a]	22.37 ± 1.74[a,b]	27.82 ± 2.44 [a,b,c]	< 0.001
SBP [mmHg]	123.63 ± 14.08	128.71 ± 14.15[a]	123.70 ± 12.59[b]	130.00 ± 12.89[a,c]	0.008
DBP [mmHg]	83.99 ± 9.14	86.91 ± 9.41	83.64 ± 7.24	86.98 ± 9.90	0.048
ALT [U/L]	20.71 ± 14.93	23.43 ± 13.41	24.39 ± 14.37	34.63 ± 18.64[a,b,c]	< 0.001
Cr [umol/L]	58.98 ± 12.99	61.95 ± 12.04	48.91 ± 11.72 [a,b]	51.57 ± 13.50[a,b]	< 0.001

FBG [mmol/L]	4.93 (4.58, 5.24)	5.04 (4.73, 5.38)	8.02 (6.42, 11.31)[a,b]	9.09 (7.64, 10.59)[a,b]	< 0.001
TC [mmol/L]	4.78 ± 0.89	5.00 ± 0.78	4.94 ± 0.98	5.21 ± 1.08[a]	0.063
TG [mmol/L]	0.97 (0.78, 1.36)	1.32 (0.91, 1.87)[a]	1.19 (0.89, 1.52)[a,b]	1.98 (1.33, 2.71)[a,b,c]	< 0.001
HDL-C [mmol/L]	1.34 (1.18, 1.58)	1.32 (1.11, 1.46)	1.05 (0.92, 1.17)[a,b]	0.91 (0.78, 1.03)[a,b,c]	< 0.001
LDL-C [mmol/L]	2.93 ± 0.80	3.10 ± 0.75	3.21 ± 0.85	3.40 ± 0.95[a,b]	0.012
HbA$_{1c}$ (%)	5.38 ± 0.25	5.41 ± 0.32	12.08 ± 2.05[a,b]	10.91 ± 1.72[a,b,c]	< 0.001
INS [mIU/L]	5.85 (3.98, 7.47)	7.65 (5.26, 9.12)[a]	10.85 (6.92, 13.03)[a,b]	13.54 (10.08, 18.56)[a,b,c]	< 0.001
IR	1.25 (0.88, 1.68)	1.63 (1.11, 2.05)[a]	3.78 (2.48, 5.72)[a,b]	5.31 (3.77, 7.57)[a,b,c]	< 0.001
AKAP1 [ng/mL]	1.74 ± 0.42	1.59 ± 0.41[a]	1.61 ± 0.35	1.52 ± 0.36[a]	0.011

Data are mean ± SD or median (P25, P75). [a]*vs.* NGT+NW group, $p < 0.05$; [b]*vs.* NGT+OW/OB group, $p < 0.05$; [c]*vs.* T2DM+NW, $p < 0.05$

NGT — normal glucose tolerance; NW — normal weight; OW — overweight; OB — obesity; T2DM — type 2 diabetes mellitus; WC — waist circumference; HC — hip circumference; WHR — waist–hip ratio; BMI — body mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure ALT — glutamic-pyruvic transaminase; Cr — creatinine; FBG — fasting blood glucose; TC — total cholesterol; TG — triglyceride; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; HbA$_{1c}$ — glycosylated haemoglobin; INS — insulin; IR — insulin resistance; A-kinase anchoring protein 1; SD — standard deviation

Table 2. Correlation between serum A-kinase anchoring protein 1 (AKAP1) level and

other variables in patients with normal glucose tolerance (NGT) and patients with type 2 diabetes mellitus

AKAP1	NGT		T2DM	
	r	p	r	p
Sex	0.061	0.487	0.106	0.232
Age	–0.062	0.482	0.038	0.667
BMI	–0.182	< 0.05	–0.224	< 0.05
WC	–0.170	0.053	–0.129	0.144
HC	–0.053	0.550	–0.065	0.460
WHR	–0.203	< 0.05	–0.117	0.184
SBP	–0.163	0.062	–0.175	< 0.05
DBP	–0.201	< 0.05	–0.110	0.211
ALT	–0.095	0.283	–0.116	0.224
Cr	–0.091	0.305	–0.122	0.167
FBG	–0.035	0.689	–0.060	0.501
TC	–0.099	0.361	–0.024	0.786
TG	–0.192	<0.05	–0.103	0.243
HDL-C	0.042	0.632	0.079	0.343
LDL-C	–0.047	0.593	–0.021	0.811
HbA_{1c}	–0.085	0.337	0.095	0.281
INS	–0.163	0.063	–0.188	< 0.05
IR	–0.140	0.112	–0.202	< 0.05

BMI — body mass index; WC — waist circumference; HC — hip circumference; WHR — waist–hip ratio; BMI — body mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure ALT — glutamic-pyruvic transaminase; Cr — creatinine; FBG — fasting blood glucose; TC — total cholesterol; TG — triglyceride; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; HbA_{1c} — glycosylated haemoglobin; INS — insulin; IR — insulin resistance

Table 3. The independent influencing factors of A-kinase anchoring protein 1

(AKAP1)

Variables	Unstandardised coefficients		t	p	95% CI for β	
	β	Std. Error			Lower	Upper
Constant	2.004	0.357	5.616	< 0.01	1.3002	2.707
HC	0.010	0.005	2.206	< 0.05	0.001	0.019
BMI	–0.032	0.011	–2.842	< 0.01	–0.055	–0.010
DBP	–0.006	0.003	–2.173	< 0.05	–0.011	–0.001
IR	–0.019	0.009	–.2.237	< 0.05	–0.037	–0.002

R Square of this model is 0.089.

CI — confidence interval; HC — hip circumference; BMI — body mass index; DBP — diastolic blood; IR — insulin resistance

Table 4. Correlation between A-kinase anchoring protein 1 (AKAP1) and prevalence of type 3 diabetes mellitus (T2DM)

	T3	T2		T1	
	Reference	OR (95% CI)	P	OR (95% CI)	p
Model 1	1	2.207 (1.203,4.050)	< 0.05	2.051 (1.121,3.753)	< 0.05
Model 2	1	2.413 (1.121,5.196)	< 0.05	2.196 (1.018,4.738)	< 0.05
Model 3	1	2.429 (1.033,5.949)	< 0.05	2.963 (1.197,7.332)	< 0.05
Model 4	1	2.085 (0.780,5.576)	0.143	3.104 (1.129,8.529)	< 0.05
Model 5	1	1.655 (0.601,4.559)	0.330	2.625 (0.931,7.398)	0.068

Model 1: crude; Model 2: adjusted for sex, age, ALT, Cr; model 3: adjusted for model 2 + WC, BMI, SBP, DBP, TC, TG, LDL-c; model 4: adjusted for model 3 + HDL-C; model 5:
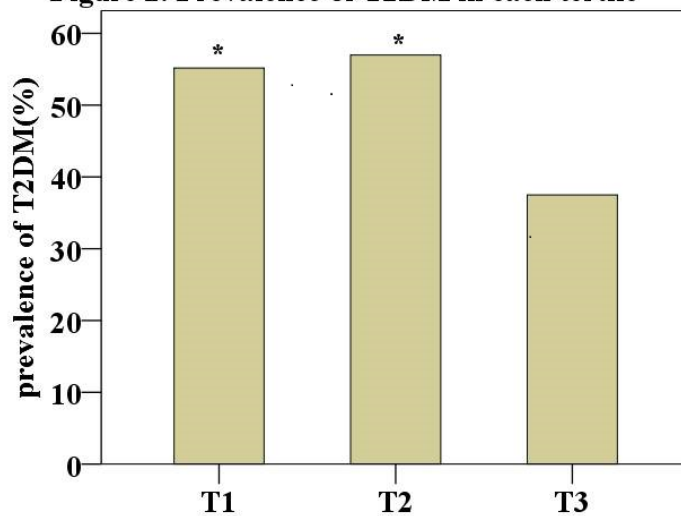
adjusted for model 4 + HC; OR — odds ratio; CI — confidence interval

Figure 1. serum AKAP1 levels in NGT and T2DM population
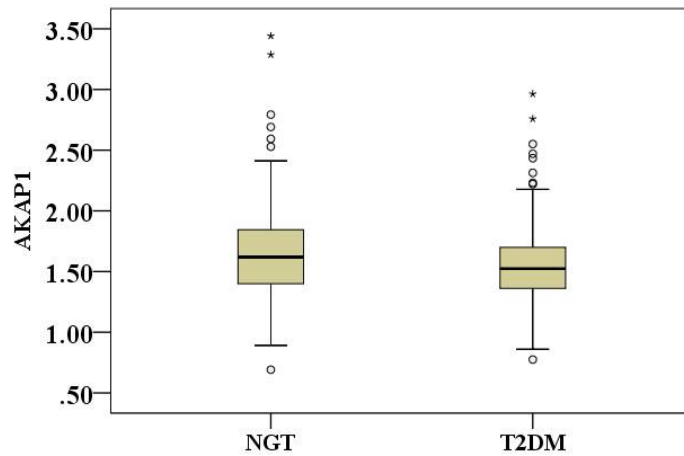
Figure 1. Serum A-kinase anchoring protein 1 (AKAP1) in people with normal glucose tolerance (NGT) vs. in people with type 2 diabetes mellitus (T2DM): 1.67 ± 0.42 vs. 1.57 ± 0.35 ng/mL (p = 0.043)

Figure 2. Prevalence of T2DM in each tertile

Figure 2. The prevalence of type 2 diabetes mellitus (T2DM) in T1, T2, and T3 groups is, respectively, 55.2%, 57.0%, and 37.5%. *represents vs. T3 groups, p < 0.05, chi-square test