CEOG Clinical and Experimental Obstetrics & Gynecology

Association of CD36 gene single nucleotide polymorphism with gestational diabetes mellitus in Chinese Han population

Y. Yang, B.R. Luo, M. Hu, D.M. Zhao, W.J. Jing

West China Second University Hospital, Sichuan

Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education (China)

Summary

Introduction: It is generally believed that gestational diabetes mellitus (GDM) and type 2 diabetes mellitus (T2DM) share similar genetic susceptibility and pathogenesis, which is characterized by insulin resistance and impaired insulin secretion. Thus it is believed that the two suffer from the same genetic pathogenic background. A variety of studies have confirmed that *CD36* gene single nucleotide polymorphisms (SNP) are significantly associated with T2DM. In this context, this study aims to discover the correlation between the two SNPs in *CD36* gene and GDM in Chinese Han population. *Materials and Methods:* 424 Chinese pregnant women in Han population were analyzed according to clinical parameters. Out of them, 215 normal glucose tolerance (NGT) and 209 GDM patients were genotyped for two SNPs namely rs1761667 (G > A) and rs1527479(C > T) in the *CD36* gene using Taqman allelic discrimination assay followed by statistical analysis. *Results:* The distribution of genotype frequency and allele frequency of rsl527479 and rs1761667 between GDM group and NGT group showed no statistical significance ($p > 0.05$). In GDM group, the differences of fasting plasma glucose (FPG), zero-hour plasma glucose (PG) in oral glucose tolerance test (OGTT), body weight (BW) increment, homeostasis model assessment for insulin resistance (HOMA-IR), triglyceride (TG) among three genotypes of rs1761667 indicated statistical significance ($p < 0.05$). The differences of FPG, zero-hour PG in OGTT, BW increment, total cholesterol (TC), TG, HOMA-IR among three genotypes of rs1527479 displayed statistical significance ($p < 0.05$). In NGT group, there were no statistical significance between any genotypes of the two SNPs. *Discussion:* The genotype and allele frequency distribution of *CD36* gene SNPs(rs 1761667 and rs1527479) were not associated with the risk of GDM. However, the authors observed significant differences between the clinical and biochemical index in different genotypes. *Conclusion:* Therefore, *CD36* gene SNPs (rs1761667 and rs1527479) demonstrated a certain correlation with some metabolic index and phenotypes of GDM.

Key words: Gestational diabetes mellitus; CD36 gene; Single nucleotide polymorphism.

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. In recent years, the incidence of GDM has been increasing [2, 3]. It may have many adverse effects on pregnant women and fetus [4, 5]. However, the specific pathogenesis of GDM is still unknown. It is generally believed that GDM and Type 2 diabetes mellitus (T2DM) have similar genetic susceptibility and pathogenesis, which is characterized by insulin resistance and impaired insulin secretion. From this, many believe the two have the same genetic pathogenic genes [6-8]. Some studies have found that *CD36* gene is associated with insulin resistance, dyslipidemia as well as atherosclerosis and elevated triglyceride (TG) levels, which often proceed with T2DM [9-14]. Many studies abroad have also confirmed that some *CD36* gene single nucleotide polymorphisms (SNPs) (e.g. rs1761667, rs1527479, and -178A/C) are related with type 2 diabetes mellitus (T2DM) [15-17]. Therefore, the authors propose that the *CD36* gene SNP may increase the risk of GDM.

The *CD36* gene is located on chromosome 7q11.2 and is comprised of 15 alternatively spliced exons that are differentially regulated by several upstream promoters [18, 19]. In the human *CD36* gene, 1,372 single nucleotide polymorphisms (SNPs) have been reported up to now; however most of these findings were reported in European populations. Since there have been some studies on the association of genetic variants in the *CD36* gene with T2DM [15–17], the authors proposed to investigate two probable *CD36* gene polymorphisms that might have an important role in GDM and related complications. Therefore, the present study selected two SNPs, rs1761667 and rs1527479 from Chinese Han in Chengdu as candidate SNPs to evaluate the genetic and functional effects of *CD36* gene polymorphisms on GDM and related complications. This is perhaps the first report of CD36 gene polymorphism study in GDM patients in Chinese Han population.

Materials and Methods

The authors investigated Chinese Han pregnant women who gave birth in West China Second University Hospital in Chengdu

Revised manuscript accepted for publication August 1, 2016

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLV, n. 2, 2018
doi: 10.12891/ceog3844.2018

7847050 Canada Inc.
www.irog.net

from August to December in 2014. All these women without a previous diagnosis of glucose intolerance were routinely screened for GDM between 24 and 28 weeks of gestation with the recommendation of the diagnosis of GDM by international DM and pregnancy group (IADPSG) in 2010 [20]. They were divided into gestational diabetes mellitus (GDM) group and normal glucose tolerance group (NGT). The authors studied 424 pregnant women, 209 of them with GDM and 215 with NGT.

The subjects' clinical and biochemical data were acquired from these women's medical records that included age, height, weight, gestational weight gain (GWG), systolic blood pressure and diastolic blood pressure, the family history of T2DM, and history of gestation. Body mass index (BMI) before gestation (pre-BMI) was calculated as body weight (kg) divided by the square of height (m^2). Biochemical data consisted of fasting plasma glucose (FPG), fasting plasma insulin (FPI), lipid profile (total serum cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and serum triglycerides), hepatitis B surface antigen (HbsAg), white blood count (WBC), hemoglobin (Hb), platelets (PLT), alanine transaminase (ALT), aspartate transaminase (AST), albumin (ALB), and blood urea nitrogen (BUN). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated by (FPI in mU/L×FPG in mmol/l)/22.5 while homeostasis model assessment of beta-cell function (HOMA-B) was calculated by (FPI in mU/L×20)/(FPG in mmol/l -3.5) with HOMA indices [21].

Blood samples were taken for these participants during their childbirth. Genomic DNA was obtained from a human whole blood kit. CD36 gene (rs1761667 and rs1527479) SNPs were genotyped by the Taqman allelic discrimination assay. The genotyping results were verified by direct sequencing test. During data analysis the quality value was set as 95% and the Sequence Detection System version 2.4 software was used. Genotyping quality control was performed in 10% of the samples by duplicate checking (rate of concordance in duplicates > 99%).

Written informed consent was obtained from each participant, and the study was approved by the Institutional Review Board of West China Second University Hospital.

The quantitative variable with normal distribution was given as mean ± standard deviation (SD). The continuous data (HOMA-B, HOMA-IR, total cholesterol, triacylglycerol, LDL-cholesterol, and HDL-cholesterol) was log-transformed to approximate normal distributions. Quantitative data with normal distribution or log-transformed variables was analyzed by Student's *t*-test. The authors tested each polymorphism for deviation from Hardy-Weinberg-Equilibrium (HWE) by using chi-square test and they also used chi-square to test differences in allele, genotype between NGT and GDM. Genotypes were given codes of 0, 1, and 2, and the odds ratio (OR) was expressed per difference in the number of risk alleles. The ORs with 95% confidence intervals (CIs) were presented. Comparisons of different variables between groups were done by one-way ANOVA. A two-sided *p* value, 0.05 was considered statistically significant. The statistical analyses were performed by SPSS 17.0.

Results

The clinical and biochemical parameters of the NGT and GDM groups are presented in Table 1. The differences of age, body weight (BW) increment, systolic blood pressure (SBP), diastolic blood pressure (DBP), TG, TC, HDL-C, LDL-C, FPG, zero-, one-, and two-hour OGTT, fasting insulin (FINS), HOMA-IR, HOMA-β showed statistical significance ($p < 0.05$).

Taqman SNP genotyping results showing the pattern of genotypes for the two SNPs (rs1527479 and rs1761667) in the *CD36* gene are represented in Figures 1a−d. The allele and genotype frequency distribution of *CD36* gene polymorphisms among 215 NGT and 209 GDM are shown in Table 2. In case of both SNPs, the allele and genotype frequencies in NGT and GDM groups are in Hardy–Weinberg Equilibrium (HWE). For both C/T and G/A polymorphism, no allelic and genotypic associations are observed in the present study ($p > 0.05$).

The authors analyzed the association between three genotypes of each SNP and clinical and biochemical parameters in the research (as shown in Table 3). In GDM group, the differences of FPG, 0hPG in OGTT, BW increment, HOMA-IR, and TG among three genotypes of rs1761667 showed statistical significance ($p < 0.05$). The differences of FPG, 0hPG in OGTT, BW increment, TC, TG, HOMA-IR among three genotypes of rs1527479 displayed statistical significance ($p < 0.05$). In NGT group, there is no statistical significance between any genotypes of the two SNPs.

Table 1. Clinical characteristics of the study participants.

Variables	GDM (n=209) ($\bar{x}\pm s$)	NGT (n=215) ($\bar{x}\pm s$)	*t*	*p*
Age (years)	32.99±4.49	31.36±4.24	3.849	<0.001
Weight (kg)	69.10±7.50	68.98±8.44	0.157	0.875
Height (cm)	159.66±4.48	160.42±4.56	-1.729	0.084
Pre-BMI (kg/m^2)	21.95±2.76	21.09±2.80	3.146	0.002
GWG (kg)	14.60±3.75	13.14±4.87	3.483	0.001
SBP (mmHg)	116.2±11.90	113.4±10.51	2.878	0.004
DBP (mmHg)	73.85±10.48	71.57±9.51	2.669	0.008
WBC ($\times10^9$/L)	9.09±2.22	8.99±2.35	1.829	0.068
PLT ($\times10^9$/L)	159.06±49.34	158.10±49.44	0.199	0.842
Hb (g/L)	121.10±14.23	118.84±13.53	1.845	0.066
ALT (IU/L)	19.38± 8.60	19.23±7.33	0.843	0.400
AST (IU/L)	21.75± 5.85	21.60±6.50	0.205	0.838
TC (mmol/L)	5.69±1.07	5.16±1.11	6.145	<0.001
TG (mmol/L)	3.68±1.93	2.86±0.80	6.077	0.006
HDL-C (mmol/L)	1.67±0.33	1.83±0.42	-3.350	0.001
LDL-C (mmol/L)	3.23±0.59	2.82±0.84	4.142	<0.001
75gOGTT0hBG (mmol/l)	4.95±0.58	4.51±0.39	8.865	<0.001
75gOGTT1hBG (mmol/l)	10.13±2.78	7.56±1.28	11.451	<0.001
75gOGTT2hBG (mmol/l)	8.97±1.61	6.77±0.99	15.978	<0.001
FPG (mmol/L)	4.83±0.92	4.51±0.74	4.004	<0.001
FPI (μU/mL)	13.36±5.51	10.78±4.87	5.073	<0.001
HOMA-IR	2.91±1.02	2.22±0.98	2.970	0.003
HOMA-β	252.03±172.51	273.6±213.74	-1.974	0.049

Two variables (HOMA-B, HOMA-IR) are log-transformed to approximate normal distributions and are analyzed by Student's *t*-test. The other variables are the quantitative variables with normal distribution and are given as means ± standard deviation.

Table 2. — *Genotype and allele distributions and corresponding odds ratios for GDM.*

		GDM (%)	NGT (%)		
SNP	Genotype	n=209	n=215	*p*-value	OR (95% CI)
rs1527479	TT	85 (40.7)	96 (44.7)	Ref.	
	CT	99 (47.3)	102 (47.4)	0.654	0.912 (0.610-1.364)
	CC	25 (12.0)	17 (7.9)	0.142	0.602 (0.304-1.191)
	TT	85 (40.7)	96 (44.7)	0.407	0.850 (0.578-1.249)
	CC/CT	124 (59.3)	119 (55.3)		
	Allele				
	T	269 (65.1)	294 (68.4)	0.216	0.835 (0.626-1.111)
	C	149 (34.9)	136 (31.6)		
rs1761667	GG	88 (42.1)	98 (45.6)	Ref.	
	AA	22 (10.5)	15 (7.0)	0.177	0.612 (0.299-1.254)
	AG	99 (47.4)	102 (47.4)	0.703	0.925 (0.621-1.379)
	GG	88 (42.1)	98 (45.6)	0.471	0.868 (0.591-1.275)
	AA/AG	121 (57.9)	117 (54.4)		
	Allele				
	G	275 (65.8)	298 (69.3)	0.275	0.852(0.639 -1.136)
	A	143 (34.2)	132 (30.7)		

Discussion

The role of *CD36* gene in insulin resistance and T2DM prompted the present authors to investigate its SNP association with GDM in their Chinese population. Researchers have found that polymorphisms of *CD36* gene may affect glucose and lipids metabolism and some *CD36* gene SNPs are seen to be related with T2DM in several studies [9-17].

A genetic study of the *CD36* gene in a French diabetic population indicated that A/C-178 in the promoter, A/G-10 in intron 3 and (GGGTTGAGA) insertion in intron 13 were equally frequent in diabetic subjects and controls. However, adiponectin levels, a marker for insulin sensitivity, were significantly linked with the -178 A/C promoter variant allele ($p = 0.003$). Thus, the -178 A/C SNP promoter mutation in the *CD36* gene represents a putative genetic marker for insulin-resistance in the French population, although it does not appear to contribute to the genetic risk for T2DM [15]. Another study in North Indian population demonstrated that the GA heterozygous genotype of a promoter polymorphism (rs1761667) in the *CD36* gene was more common in the T2DM patients and had association with diabetes. The presence of the minor allele A of rs1761667 in the-31118 promoter region of the *CD36* gene seemed to contribute greatly to increasing the risk of developing T2DM [17]. A similar correlation between a promoter polymorphism (rs1527479) in the *CD36* gene with insulin resistance and T2DM was discovered in the Caucasian population at risk for metabolic syndrome (MetS) [16]. It was reported that T2DM was more prevalent in the TT genotype than in the CC genotype. This was most pronounced in women and in subjects with a high BMI (> 27 kg/m^2). In addition, within the group of diabetic patients, the TT genotype was more common in subjects with increased HOMA-IR. This suggests that the regulatory region of the gene is responsible for the varied expression of the *CD36* gene in normal and diseased conditions since a variant located in the *CD36* upstream promoter determines the binding site for transcription factors. It is indicated from a study in African Americans that five SNPs of *CD36* gene associated with increased odds for the MetS and *CD36* variants may be related to insulin resistance that may impact MetS pathophysiology and HDL metabolism, which are both the predictors of heart disease and type 2 diabetes [12]. A recent study in Boston and Puerto Rican adults also revealed an association with metabolic syndrome that can increase the risk of cardiovascular disease and T2DM [22].

In the study presented here the authors failed to find an association between polymorphisms of the rs1761667 and rs1527479 SNPs in the *CD36* gene and GDM. For both C/T and G/A polymorphism, no allelic and genotypic associations were observed in the present study ($p > 0.05$). This result is in conflict with the research on North Indian population [17]. However when comparing the clinical and biochemical index among genotypes in the two SNPs, it is seen that part of the indicators has statistical significance, especially in GWG, FPG, TG, and IR. It indicates that the genotypes of *CD36* gene SNP are associated with certain metabolic index and its phenotype of GDM, which may lead to insulin resistance, TG concentrations, and weight growth, etc. However, the specific mechanism is not very clear.

Population genetics studies demonstrate that different genotypes may cause different phenotypes which are the result of the combination of genotype and environment. *CD36* gene encodes *CD36* proteins that affect some of the signs and symptoms of disease. It suggests that it may help

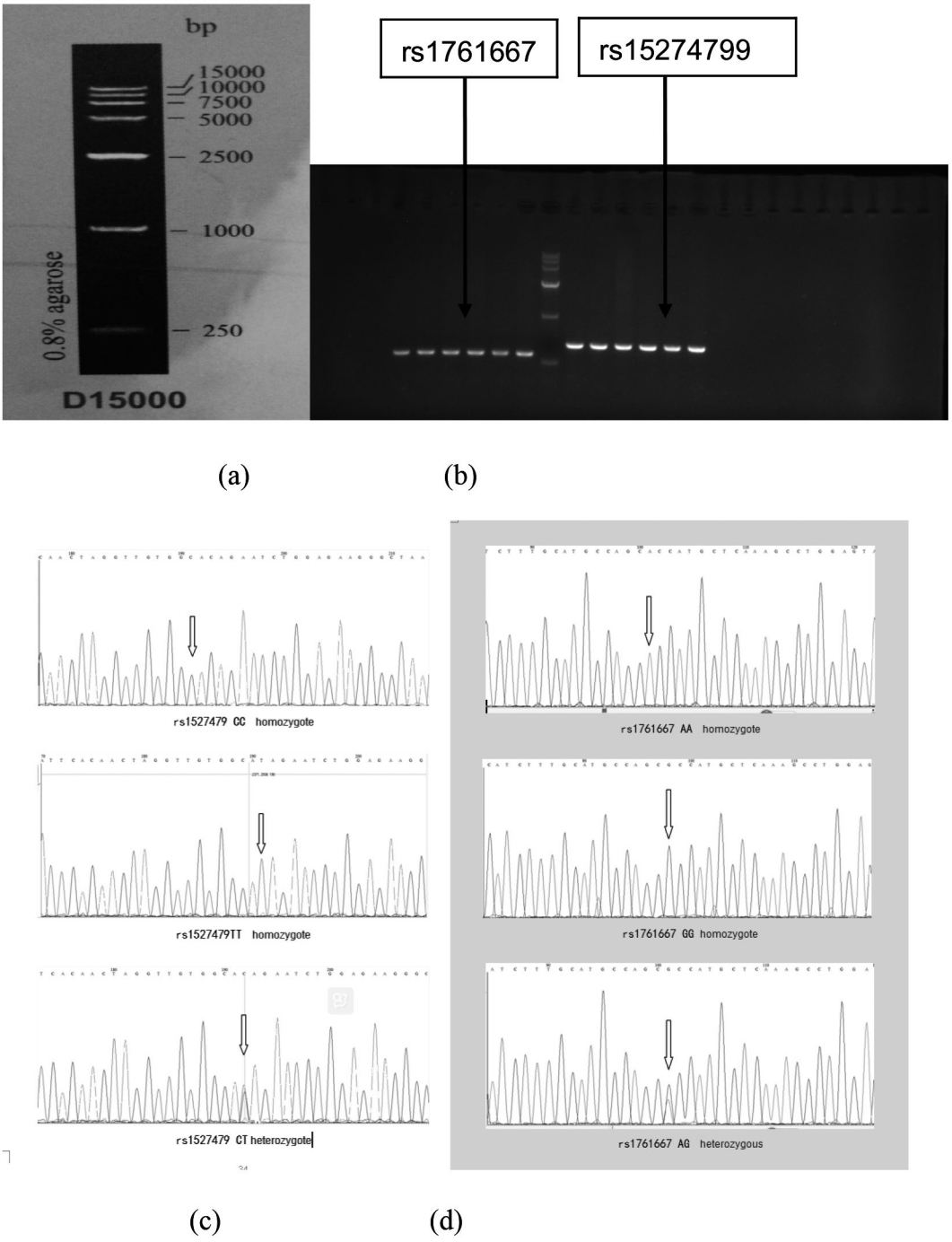

Figure 1. — The pattern of genotypes for the two SNPs (rs1527479 and rs1761667.

us identify high-risk groups and provide relevant guidance and intervention, at finally may be helpful to avoid and reduce the incidence of GDM and its complications if an early prenatal diagnosis and screening at a genetic level for pregnant women can be made. Furthermore, the screening of genes has no restrictions and is very convenient, and it can be carried out at any time during pregnancy, so it is worth recommending.

The results of the previous studies concerning *CD36* polymorphisms and the incidence of GDM contradict the data obtained from a number of studies with T2DM-patients. The reasons may be as the following. First, although GDM and T2DM seem to share similar pathophysiological pathways [23], their clinical courses may differ because of genetic variations or the functional and the phenotypical consequences, since two-allele genetic models do not fit.

Table 3. — *Comparison of clinical and biochemical data in three genotypes of rs1761667 for GDM.*

Parameter	Rs1761667 genotypes			Rs1527479 genotypes		
	AA	AG	GG	*CC*	*CT*	*TT*
weight (kg)	68.82±6.52	69.51±7.52	68.72±7.77	68.82±6.52	69.51±7.52	68.72±7.77
height (cm)	159.45±3.69	159.42±4.92	159.97±4.15	159.84±3.73	159.35±4.99	159.95±4.06
Pre-BMI (kg/m^2)	22.04±2.32	22.24±2.86	21.61±2.74	22.28±2.93	22.22± 2.67	21.54±2.80
GWG (kg)	10.68±3.26*	14.23±4.15**	13.38±4.99	11.09±3.42**	14.29±4.09	13.27±5.09
SBP (mmHg)	118.09±12.53	116.30±13.00	115.60±10.63	119.76±13.51	115.51±12.59	115.95±10.65
DBP(mmHg)	73.77±9.83	73.87±11.39	73.55±9.67	75.88±11.77	73.29±10.89	73.59±9.63
75gOGTT0hBG (mmol/L)	5.10±0.54**	4.67±0.46	4.91±0.55#	5.05± 0.54**	4.71±0.49	4.89±0.54
75gOGTT1hBG (mmol/L)	9.32±1.63	10.16±1.75	9.87±1.69	9.52±1.62	10.16±1.81	9.81±1.63
75gOGTT2hBG (mmol/L)	8.79±1.60	9.04±1.67	8.96±1.58	8.79±1.64	9.04± 1.68	8.96±1.55
FPG (mmol/L)	4.98± 2.06*	4.41± 0.64**	4.43± 0.64	4.99±1.97	4.43± 0.63	4.38±0.62
FPI (μU/mL)	14.08±11.50	13.39±12.87	14.58±23.25	16.27±16.34	12.89±11.57	14.52±23.47
WBC (×109/L)	8.59±1.23	9.08±2.50	8.99±2.43	8.70±1.42	9.00± 2.51	9.07± 2.43
PLT (×109/L)	147.14±49.54	159.65±48.73	159.11±50.42	152.31±47.62	157.48±47.89	163.31±49.08
HB (g/L)	126.64±10.60	121.42±13.49	119.20±12.17	122.75±12.28	122.16±13.42	119.23±12.09
ALT (IU/L)	16.19±8.70	20.82±9.29	19.46±8.52	15.94±8.54	20.89±9.07	19.45±8.74
AST (IU/L)	21.13±7.52	23.93± 9.26	22.11± 7.46	21.76±7.31	23.88±9.26	21.97±7.46
γ-GT (IU/L)	13.88±6.75	18.54±18.41	18.13±16.87	13.47±6.77	18.69±18.21	18.12±17.12
Cr (mmol/L)	46.25±7.11	47.47±8.60	49.81±10.24	48.12±7.61	47.24±8.72	49.71±10.17
UN (mmol/L)	3.13±0.75	3.52±1.22	3.54±1.14	3.23±0.79	3.49±1.24	3.56±1.12
Alb (g/L)	37.47±2.45	37.07±3.40	36.34±3.04	37.87±2.85	37.08± 3.29	36.18±3.03
TC (mmol/L)	5.74±0.52	5.67±0.97	5.63±1.26	4.88±1.24**	5.35±1.07	5.16±0.93
TG (mmol/L)	3.09±0.96*	3.14±1.09#	2.93±0.81	3.15±0.99*	3.19±1.06#	2.94±0.82
HDL-C (mmol/L)	1.85±0.46	1.85±0.33	1.78±0.39	1.85±0.46	1.84±0.36	1.78±0.37
LDL-C (mmol/L)	3.04±0.42	2.78±0.74	2.52±0.87	3.04±0.42	2.71±0.79	2.58±0.83
LDH (U/L)	223.19±127.19	263.59±156.04	262.79±136.91	238.12±130.60	261.05±157.50	262.37±134.58
HOMA-IR	2.01±1.39**	2.54± 2.14	2.26±1.61	1.99±1.35	2.47±1.97**	2.50±1.57*
HOMA-β	293.22±268.14	256.59±223.70	198.80±109.86	291.48±168.97	260.39±225.92	200.715±195.32

P values < 0.05 are shown in bold. *P* values are adjusted for age but not corrected for multiple comparisons.
Log transformed (log10) values are used for HOMA-B, HOMA-IR. AA *vs.* GG: *p < 0.05; AG *vs.* GG: #p < 0.05; AG *vs.* AA: ** p < 0.05. CC *vs.* TT: *p < 0.05; CT *vs.* TT: #p < 0.05; CT *vs.* CC: **p < 0.05.

GDM as a polygenic hereditary disease exists genetic heterogeneity and racial differences, hence the present study may have different results due to different races. Second, *CD36* gene has multiple polymorphism loci and perhaps the sample size of this study is not enough to assess the efficient locus. In the present study, only 215 patients with GDM were genotypes, which may limit the statistical power of this analysis. Therefore, the sample size needs to be enlarged for further study on the relationship of *CD36* gene polymorphism and incidence of GDM. Third, the result may be associated with the change of GDM diagnostic standard. From 2012, the present authors have begun to use new diagnostic standard of GDM (IADPSG, 2010). With the new diagnostic criteria, the detection rate has been increasing, therefore the past negative samples may be incorporated into the present study. Furthermore, diagnostic standard is also not the same both at home and abroad and this may lead to selective bias. At last, as discussed above, an individual hereditary character does not only depend on the types of genes, but also on the gene expression patterns, namely epigenetics. Phenotype is the result of the combination of genotype and environment. Therefore it requires a further study of epigenetics to explore the pathogenesis of GDM.

In summary, this is perhaps the first study to examine the association of CD36 polymorphisms and GDM in Chinese Han population. Unfortunately, the present authors do not see an association between GDM and certain *CD36* polymorphisms. In this study, only rs1761667, rs1527479 of CD36 gene SNP were genotyped, and cannot exclude a potential influence of other CD36 genetic polymorphisms in the susceptibility on GDM. In addition, the current study may have some limitations because of study design. So more studies are required to discuss the relation of *CD36* gene SNP with GDM.

Conclusion

The genotype and allele frequency distribution of *CD36* gene SNPs were not associated with GDM, but there were

some differences between the clinical and biochemical index in different genotypes, so the present authors believe *CD36* gene SNPs have a certain correlation with some metabolic index and phenotypes of GDM.

Acknowledgements

The authors would like to thank the Public laboratory, Perinatal Medical Laboratory and Department of Obstetrics of West China Second University Hospital.

This research is supported by Science & Technology Department of Sichuan Province (No.2014JY0082).

References

[1] "Gestational diabetes mellitus". *Diabetes Care,* 2004, *27*, S88.
[2] Ma R.C., Chan J.C.: "Pregnancy and diabetes scenario around the world: China". *Int. J. Gynaecol. Obstet.,* 2009, *104*, S42.
[3] Schneider S., Bock C., Wetzel M., Maul H., Loerbroks A.: "The prevalence of gestational diabetes in advanced economies". *J. Perinat. Med.,* 2012, *40*, 511.
[4] Metzger B.E.: "Summary and recommendations of the Third International Workshop-Conference on Gestational Diabetes Mellitus". *Diabetes,* 1991, *40*, 197.
[5] Van Lieshout R.J., Voruganti L.P.: "Diabetes mellitus during pregnancy and increased risk of schizophrenia in offspring: a review of the evidence and putative mechanisms". *J. Psychiatry Neurosci.,* 2008, *33*, 395.
[6] Lambrinoudaki I., Vlachou S.A., Creatsas G.: "Genetics in gestational diabetes mellitus: association with incidence, severity, pregnancy outcome and response to treatment". *Curr. Diabetes Rev.*, 2010, *6*, 393.
[7] Watanabe R.M., Black M.H., Xiang A.H., Allayee H., Lawrence J.M., Buchanan T.A.: "Genetics of gestational diabetes mellitus and type 2 diabetes". *Diabetes Care*, 2007, *30*, S134.
[8] Kwak S.H., Kim S.H., Cho Y.M., Go M.J., Cho Y.S., Choi S.H. *et al.*: "A genome-wide association study of gestational diabetes mellitus in Korean women". *Diabetes*, 2012, *61*, 531.
[9] Handberg A., Levin K., Hojlund K., Beck-Nielsen H.: "Identification of the oxidized low-density lipoprotein scavenger receptor CD36 in plasma: a novel marker of insulin resistance". *Circulation,* 2006, *114*, 1169.
[10] Lepretre F., Vasseur F., Vaxillaire M., Scherer P.E., Ali S., Linton K. *et al.*: "A CD36 nonsense mutation associated with insulin resistance and familial type 2 diabetes". *Hum. Mutat.*, 2004, *24*, 104.
[11] Gautam S., Agrawal C.G., Banerjee M.: "CD36 gene variants in early prediction of type 2 diabetes mellitus". *Genet. Test Mol. Biomarkers,* 2015, *19*, 144.
[12] Love-Gregory L., Sherva R., Sun L., Wasson J., Schappe T., Doria A., *et al.*: "Variants in the CD36 gene associate with the metabolic syndrome and high-density lipoprotein cholesterol". *Hum. Mol. Genet.*, 2008, *17*, 1695.
[13] Banerjee C., Moon Y.P., Paik M.C., Rundek T., Mora-McLaughlin C., Vieira J.R., *et al.*: "Duration of diabetes and risk of ischemic stroke: the Northern Manhattan Study". *Stroke,* 2012, *43*, 1212.
[14] Febbraio M., Hajjar D.P., Silverstein R.L.: "CD36: a class B scavenger receptor involved in angiogenesis, atherosclerosis, inflammation, and lipid metabolism". *J. Clin. Invest.,* 2001, *108*, 785.
[15] Lepretre F., Linton K.J., Lacquemant C., Vatin V., Samson C., Dina C., *et al.*: "Genetic study of the CD36 gene in a French diabetic population". *Diabetes Metab.,* 2004, *30*, 459.
[16] Corpeleijn E., van der Kallen C.J., Kruijshoop M., Magagnin M.G., de Bruin T.W., Feskens E.J. *et al.*: "Direct association of a promoter polymorphism in the CD36/FAT fatty acid transporter gene with Type 2 diabetes mellitus and insulin resistance". *Diabet. Med,* 2006, *23*, 907.
[17] Melis M., Sollai G., Muroni P., Crnjar R., Barbarossa I.T.: "Associations between orosensory perception of oleic acid, the common single nucleotide polymorphisms (rs1761667 and rs1527483) in the CD36 gene, and 6-n-propylthiouracil (PROP) tasting". *Nutrients,* 2015, *7*, 2068.
[18] Armesilla A.L., Vega M.A.: "Structural organization of the gene for human CD36 glycoprotein". *J. Biol. Chem.,* 1994, *269*, 18985.
[19] Rac M.E., Safranow K., Poncyljusz W.: "Molecular basis of human CD36 gene mutations". *Mol. Med.,* 2007, *13*, 288.
[20] Sladek R., Rocheleau G., Rung J., Dina C., Shen L., Serre D., *et al.*: "A genome-wide association study identifies novel risk loci for type 2 diabetes". *Nature,* 2007, *445*, 881.
[21] Matthews D.R., Hosker J.P., Rudenski A.S., Naylor B.A., Treacher D.F., Turner R.C.: "Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man". *Diabetologia,* 1985, *28*, 412.
[22] Noel S.E., Lai C.Q., Mattei J., Parnell L.D., Ordovas J.M., Tucker K.L.: "Variants of the CD36 gene and metabolic syndrome in Boston Puerto Rican adults". *Atherosclerosis,* 2010, *211*, 210.
[23] Buchanan T.A., Xiang A.H.: "Gestational diabetes mellitus". *J. Clin. Invest.,* 2005, *115*, 485.

Corresponding Author:
B. LUO, M.D.
No. 20, Section 3
Renmin Nanlu
Chengdu, Sichuan 610041
(China)
e-mail: 492049054@qq.com