European Review for Medical and Pharmacological Sciences 2017; 21: 5702-5710

Expression of C1q/TNF-related protein-3 (CTRP3) in serum of patients with gestational diabetes mellitus and its relationship with insulin resistance

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Abstract. – OBJECTIVE: In this study, the changes of insulin resistance (IR) and pancreatic β-cell function in GDM patients were observed; changes of CTRP3 level in fasting serum and relationships with plasma glucose (PG) and pancreatic β-cell function were explored at the same time, and the correlation between serum CTRP3 and body mass index (BMI) was preliminarily discussed, providing a new way to identify the pathogenesis of GDM.

PATIENTS AND METHODS: Data of women from 24 to 28 weeks of pregnancy were collected. 100 women were selected to form gestational diabetes mellitus (GDM) group and another 100 women were chosen to constitute normal glucose tolerance (NGT) group according to the results of oral glucose tolerance test (OGTT). They were divided into GDM overweight/obesity (GDM + OW) group, GDM non-overweight/obesity (GDM + NW) group, simple overweight (OW) group and normal body weight (NW) group, according to whether the progestational body mass index (BMI) was higher than 24 kg/m^2 before pregnancy. General information of all subjects, for example, age, last menstrual period, parity, diet, weight and height, were collected, and blood samples were taken from all subjects for use in detections of total cholesterol (TC), triglyceride (TG), very low-density lipoprotein (VLDL), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and serum C1q/tumor necrosis factor-related protein-3 (CTRP3).

RESULTS: The levels of FPG, 1 h PG, 2 h PG, fasting CP (FCP), fasting insulin (FINS), homeostasis model assessment of IR (HOMA-IR), TG and VLDL-C in the GDM group, were significantly higher than those in the NGT group. TC and LDL-C in the GDM group were greater than those in the NGT group. Compared with that in the NGT group, homeostasis model assessment of β (HOMA-β) index was lower in the GDM group. From the NGT group to the GDM group, FPG, 1 h PG, 2 h PG, FINS and FCP had rising tendencies, and the differences were of statistical significance. Pearson correlation analysis indicated that HOMA-IR was positively correlated with pre-pregnancy BMI, FPG, 2 h PG, FINS, 1 h INS, 2 h INS, FCP, 1 h CP and 2 h CP in the GDM group, HOMA-β was negatively related to FPG. In the NGT group, there was a positive correlation between HOMA-IR and pre-pregnancy BMI. The level of CTRP3 in fasting serum of the GDM group was distinctly lower than that of the NGT group. Pearson correlation analysis revealed that in the GDM group, fasting serum CTRP3 had positive correlations with HOMA-β and HDL-C, but negatively associated with pre-pregnancy BMI, FPG, 1 h PG, 2 h PG, FCP, HOMA-IR, TG and VLDL-C. In the NGT group, the fasting serum CTRP3 was negatively correlated with pre-pregnancy BMI. Multiple linear stepwise regression analysis showed FPG was an independent influencing factor for fasting serum CTRP3.

CONCLUSIONS: With the increase of FPG, the progression of GDM IR patients is increased, and pancreatic β-cell function progressively declines. The decrease of CTRP3 level in fasting serum in GDM patients plays a metabolic role in the pathogenesis of GDM.

Key Words:
GDM, CTRP3, Insulin resistance, BMI, Ð-cell function.

Introduction

Gestational diabetes mellitus (GDM) is the most common metabolic disease during pregnancy. In recent years, with the development of economy and improvement of living standards, GDM is more and more common, and coupled with more and more elderly parturient women and less reasonable dietary pattern and lifestyle of pregnant woman. GDM morbidity is also increasing year by year. World Health Organization (WHO) had predicted that China would be

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one of the countries with the largest proportion of increase in prevalence of DM within the next 30 years since 1995, and GDM prevalence would rise accordingly at the same time. Studies[1-3] have shown that about 16-20% of GDM women have severe adverse outcomes during perinatal period, including polyhydramnios, premature delivery, stillbirth, fetal macrosomia, pulmonary dysmaturity, and neonatal jaundice. After delivery, plasma glucose (PG) levels of some GDM patients can return to normal, but with a little bit of poor prognosis. It is reported that GDM women get an approximate 17-63% chance of developing into type 2 DM within 5-16 years after childbirth[4,5]. In addition, GDM patients usually have no polyuria, dry mouth, polydipsia, weight loss and other clinical uncomfortable symptoms, and merely detecting elevated PG in the screening is easy to cause delayed diagnosis and missed diagnosis, increasing the mortality of perinatal infant and maternal, and raising the neonatal complications. Therefore, GDM is a serious threat to maternal and neonatal health, and the study on GDM pathogenesis is particularly important. With the continuous research and exploration, it is currently considered that the risk factors of GDM are not only related to insulin resistance (IR) caused by increases in levels of hormones such as estrogen, human placental lactogen, growth hormone and cortisol of pregnant women during pregnancy[6], genetic factors, adipokines. Inflammatory factors are also involved in the occurrence and development processes of GDM[7-9]. Nevertheless, the specific pathogenesis of GDM is still unclear. Reports have proven that adipokines can lower the sensitivity of insulin and may be involved in the occurrence and development of GDM[10]. At the same time, reports have indicated that transformations in some adipokines are likely to affect pancreatic β-cell function in pregnant women[11]. The family of C1q/tumor necrosis factor-related proteins (CTRPs) recently identified, has homologous structure with adiponectin (APN) and owns 15 members. Among them, C1q/tumor necrosis factor-related protein-3 (CTRP3) is deemed as an anti-inflammatory adipokine, which is able to inhibit inflammatory responses caused by lipopolysaccharide, Toll-like protein 4 and fatty acid, and can promote the release of APN and resistin mouse adipocytes[12]. Animal experiments have suggested that CTRP3 also has the effect of inhibiting hepatic glycogen output, lowering PG and so on[13]. APN is one of the most familiar members of the CTRPs superfamily, closely linked to IR, and considered as a biomarker and therapeutic target for metabolic diseases such as obesity. Functions of CTRP3 and APN in the CTRPs family are closest, and there are no reports on changes of CTRP3 in GDM and its relationship with IR to this day. In our work, the changes of IR and pancreatic β-cell function in GDM patients were observed, changes of CTRP3 level in fasting serum and relationships with PG and pancreatic β-cell function were explored at the same time, and the correlation between serum CTRP3 and body mass index (BMI) was preliminarily discussed, providing a new way to identify the pathogenesis of GDM.

Patients and Methods

Patients

Information on women from 24 to 32 weeks of pregnancy who went to the Endocrinology Laboratory of our hospital and received oral glucose tolerance test (OGTT) from January 20 to January 2017 were collected. According to OGTT results, 100 women were chosen to comprise gestational diabetes mellitus (GDM) group, and another 100 women were selected to compose normal glucose tolerance (NGT) group. The GDM patients were given low-sugar and low fat diet intake without any anti-diabetic drugs to achieve euglycemia. Furthermore, the GDM group was divided into GDM overweight/obesity (GDM + OW) group, with 34 cases, and GDM non-overweight/obesity (GDM + NW) group, with 66 cases, based on whether body mass index (BMI) before pregnancy was greater than 24 kg/m^2. The NGT group was divided into simple overweight (OW) group having 30 cases and normal body weight (NW) group having 70 cases in the same way. GDM diagnostic criteria used was the standard stipulated by American Diabetes Association (ADA) in 2012. 75 g OGTT were conducted from 24 to 28 weeks of pregnancy to detect fasting PG (FPG) level as well as 1 h PG and 2 h PG levels. GDM was confirmed if any one of the following was met: FPG $\geq$ 5.1 mmol/L, 1 h PG $\geq$ 10.0 mmol/L, or 2 h PG $\geq$ 8.5 mmol/L. Diagnosis standard for overweight referred to recommendations of Working Group of Obesity in China on recommended criteria for overweight and obesity classification of Chinese adults: BMI < 18.5 kg/m^2 = emaciated, 18.5 kg/m^2 < BMI < 23.9 kg/m^2 = normal, 24 kg/m^2< BMI <27.9 kg/m^2 = overweight, and BMI $\geq$ 28 kg/m^2 = obese. All subjects were free from progestational abnormal glucose toler-

ance, hypertension, polycystic ovary syndrome, hyperthyroidism and other endocrine diseases, infection during the study, plus heart, liver, kidney or other organ diseases during pregnancy, did not take medicines affecting glucose metabolism recently, and had no diet preference during pregnancy. All women signed the informed consent. Both GDM and NST groups were given the same basic MedDiet recommendations, but with restrict consumption of dietary fat and sugar according to Chinese dietary guidelines. They were also recommended to walk ≥ 30 min/day. This investigation was approved by the Ethics Committee of Hebei Cangzhou Central Hospital.

Collection of General Information

Age, last menstrual period, parity, diet custom, literacy and family history of diabetes of the subject were collected, and the weight within one month before pregnancy was recorded. Current height (m) and body weight (kg) were measured, of which height was required to be accurate to 1.0 cm and weight was required to be precise to 0.5 kg. Gestational age was calculated according to the last menstrual period. Pre-pregnancy BMI and post-pregnancy BMI were calculated according to the formula: BMI = body weight (kg)/ height^2 (m^2). Pre-pregnancy BMI was subtracted by post-pregnancy BMI to get BMI increase during pregnancy.

Collection, Detection and Preservation of Blood Samples

All subjects were required to have an overnight fasting for 8-10 h, and went to the Endocrinology Laboratory of our hospital for collecting fasting venous blood samples at 8 am on the second day. After fasting, blood samples were taken, 75 g powdered anhydrous glucose were added to 300 mL water, and the subjects were asked to drink up it within 5 min. Blood samples were taken at 1 h and 2 h after drinking up the glucose water, and PG, insulin, and C-peptide (CP) levels were detected at each time point. Another 5 mL fasting non-anticoagulant blood specimens taken during the course of OGTT were stood at room temperature for 2 h and then centrifuged for 15 min at 2-8°C in a 1000*g centrifuge. Serum was collected and stored in a refrigerator at -80°C, used for detecting total cholesterol (TC), triglyceride (TG), very low-density lipoprotein (VLDL), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and serum C1q/ tumor necrosis factor-related protein-3 (CTRP3).

Statistical Analysis

Statistical Product and Service Solution 19.0 statistical software (SPSS 19.0, IBM, Armonk, NY, USA) was used for relevant analysis. Measurement data were expressed as $\bar{x}\pm s$, using *t*-test for comparison of means between the two groups. Pearson correlation analysis was employed for correlation between one dependent variable and single independent variable, and multiple linear stepwise regression analysis was applied for relationship between one dependent variable and multiple independent variables. $p<0.05$ suggested that the difference was statistically significant.

Results

Comparisons of Clinical Data

There were no statistical differences between the GDM group and the NGT group in age, parity, gestational age, pre-pregnancy BMI, BMI increase during pregnancy and HDL-C. The levels of FPG, 1 h PG, 2 h PG, FCP, fasting insulin (FINS), homeostasis model assessment of IR (HOMA-IR), TG and VLDL-C in the GDM group were significantly higher than those in the NGT group. TC and LDL-C in the GDM group were greater than those in the NGT group. Compared with that in NGT group, homeostasis model assessment of β (HOMA-β) index was lower in the GDM group ($p<0.05$) (Table I). Age, parity, BMI increase during pregnancy, FPG, 1 h PG, 2 h PG, FINS, HOMA-IR, HOMA-β, TC and LDL-C between the GDM + OW group and the GDM + NW group showed no statistical differences. Compared with GDM + NW group, the GDM + OW group had clearly higher VLDL-C ($p<0.05$) and overtly lower HDL-C ($p<0.05$) (Table II). No statistical differences were found between the NW group and the GDM + OW group in parity, gestational age, BMI increase during pregnancy, HOMA-β, TC and LDL-C. Age, pre-pregnancy BMI, FPG, 1 h PG, 2 h PG, FCP, FINS, HOMA-IR, TG and VLDL-C in the GDM + OW group were higher than those in the NW group ($p<0.05$), while HDL-C of the GMI + OW group was lower than that of the NW group ($p<0.05$) (Table III).

Comparisons of Trends of Changes in PG, Insulin, and CP in OGTT Between the GDM Group and the NGT Group

FPG, 1 h PG and 2 h PG showed increasing trends from the NGT group to the GDM group, and the differences were statistically significant

Table I. Comparisons of clinical parameters between GDM and NGT groups.

	GDM Group	NGT Group	*t*-value	*p*-value
Age (year)	31.52 ± 3.67	29.84 ± 4.17	1.742	0.062
Number of pregnancies	1.34 ± 0.6	1.42 ± 0.7	-0.326	0.715
Gestational Age (week)	28.13 ± 2.48	28.34 ± 2.42	-0.386	0.704
Pre-pregnancy BMI (kg/m^2)	23.26 ± 2.97	22.27 ± 2.53	1.218	0.189
The increased BMI (kg/m^2)	4.17 ± 1.53	4.38 ± 1.65	-0.772	0.417
FPG (mmol/L)	5.46 ± 0.58	4.87 ± 0.34	8.142	<0.0001
1 h PG (mmol/L)	10.21 ± 2.17	7.18 ± 2.02	6.244	<0.0001
2 h PG (mmol/L)	8.58 ± 2.51	6.73 ± 1.02	6.015	<0.0001
FINS (mU/L)	16.19 ± 7.42	11.26 ± 4.08	4.422	<0.0001
FCP (ng/mL)	2.12 ± 0.67	1.56 ± 0.43	4.887	<0.0001
HOMA-IR	4.11 ± 1.95	2.39 ± 0.74	5.074	<0.0001
HOMA-β	172.3 ± 77.68	204.15 ± 93.94	-2.213	0.032
TC (mmol/L)	5.53 ± 1.07	5.02 ± 1.05	2.327	0.030
TG (mmol/L)	2.92 ± 1.36	2.51 ± 0.79	2.712	0.006
HDL-C (mmol/L)	1.62 ± 0.51	1.53 ± 0.37	0.758	0.448
VLDL-C (mmol/L)	1.08 ± 0.49	0.95 ± 0.33	2.63	0.005
LDL-C (mmol/L)	3.11 ± 0.92	2.86 ± 0.87	2.117	0.045

(p<0.01). PG values at 1 h were the highest in both groups. From the NGT group to the GDM group, FINS and FCP had rising tendencies, and the differences were of statistical significance (p<0.01) (Figure 1).

Analyses of Correlations Between IR Indexes and Various Indicators

Pearson correlation analysis indicated that HOMA-IR was positively correlated with pre-pregnancy BMI, FPG, 2 h PG, FINS, 1 h INS, 2 h INS, FCP, 1 h CP and 2 h CP in the GDM group, and it had no significant correlation with 1 h PG; HOMA-β was negatively related to FPG. In the NGT group, there was a positive correlation between HOMA-IR and pre-pregnancy BMI (Figure 2).

Comparisons of Serum CTRP3 Levels in Each Group

The level of CTRP3 in fasting serum of the GDM group was distinctly lower than that of the NGT group. The fasting serum CTRP3 in the GDM + OW group was significantly lower than that in the GDM + NW group. The fasting serum CTRP3 in GDM + OW group was clearly lower than that in the NW group. The fasting serum CTRP3 in GDM + NW group was overtly lower than that in the NW group. The fasting serum

Table II. Comparisons of clinical parameters between GDM+OW and GDM+NW groups.

	GDM+OW	GDM+NW	*t*-value	*p*-value
Age (year)	31.64 ± 3.35	29.89 ± 3.72	1.678	0.079
Number of pregnancies	1.45 ± 0.62	1.38 ± 0.56	0.867	0.334
Gestational Age (week)	27.08 ± 2.54	28.16 ± 2.41	-0.398	0.663
Pre-pregnancy BMI (kg/m^2)	26.78 ± 2.35	21.09 ± 1.74	9.896	<0.0001
The increased BMI (kg/m^2)	3.69 ± 1.86	4.38 ± 1.29	-1.315	0.211
FPG (mmol/L)	5.73 ± 0.49	5.37 ± 0.54	1.756	0.09
1 h PG (mmol/L)	10.56 ± 1.94	9.98 ± 2.26	1.828	0.063
2 h PG (mmol/L)	9.23 ± 3.27	8.84 ± 1.97	1.123	0.287
FINS (mU/L)	19.12 ± 8.21	14.93 ± 7.34	1.913	0.058
FCP (ng/mL)	2.42 ± 0.97	1.84 ± 0.68	2.539	0.013
HOMA-IR	4.57 ± 1.86	3.68 ± 1.73	1.935	0.071
HOMA-β	178.87 ± 93.13	167.11 ± 81.15	0.332	0.708
TC (mmol/L)	5.41 ± 0.93	5.79 ± 1.08	-1.014	0.221
TG (mmol/L)	3.52 ± 2.28	2.36 ± 1.05	2.911	0.006
HDL-C (mmol/L)	1.34 ± 0.48	1.76 ± 0.41	-2.808	0.007
VLDL-C (mmol/L)	1.33 ± 0.84	0.91 ± 0.22	2.813	0.007
LDL-C (mmol/L)	2.98 ± 0.77	3.19 ± 0.93	-0.814	0.437

Table III. Comparisons of clinical parameters between GDM+OW and NW groups.

	GDM+OW	NW	*t*-value	*p*-value
Age (year)	31.64 ± 3.35	28.03 ± 4.46	3.102	0.004
Number of pregnancies	1.45 ± 0.62	1.31 ± 0.81	0.902	0.384
Gestational Age (week)	27.08 ± 2.54	28.31 ± 2.32	-0.442	0.667
Pre-pregnancy BMI (kg/m^2)	26.78 ± 2.35	20.92 ± 1.89	10.137	<0.0001
The increased BMI (kg/m^2)	3.69 ± 1.86	4.45 ± 1.78	-1.389	0.186
FPG (mmol/L)	5.73 ± 0.49	4.71 ± 1.42	6.535	<0.0001
1 h PG (mmol/L)	10.56 ± 1.94	7.29 ± 1.37	8.294	<0.0001
2 h PG (mmol/L)	9.23 ± 3.27	6.31 ± 0.96	3.782	0.001
FINS (mU/L)	19.12 ± 8.21	10.91 ± 3.68	3.193	0.001
FCP (ng/mL)	2.42 ± 0.97	1.44 ± 0.52	4.348	<0.0001
HOMA-IR	4.57 ± 1.86	2.19 ± 0.72	4.579	<0.0001
HOMA-β	178.87 ± 93.13	192.38 ± 84.47	0.936	0.517
TC (mmol/L)	5.41 ± 0.93	5.23 ± 1.18	0.510	0.648
TG (mmol/L)	3.52 ± 2.28	2.03 ± 0.67	3.787	<0.0001
HDL-C (mmol/L)	1.34 ± 0.48	1.59 ± 0.31	-1.931	0.049
VLDL-C (mmol/L)	1.33 ± 0.84	0.79 ± 0.18	3.954	<0.0001
LDL-C (mmol/L)	2.98 ± 0.77	2.81 ± 0.94	0.629	0.548

CTRP3 in the OW group was lower than that in the NW group (Figure 3).

Analyses on Correlations of Fasting Serum CTRP3 with Various Indexes

Pearson correlation analysis revealed that in the GDM group, fasting serum CTRP3 had positive correlations with HOMA-β and HDL-C (correlation coefficients: r=0.314 and r=0.348, respectively, p<0.05), but negatively associated with pre-pregnancy BMI, FPG, 1 h PG, 2 h PG, FCP, HOMA-IR, TG and VLDL-C, and showed no significant correlations with age, parity, gestational age, BMI increase during pregnancy, FINS, TC and LDL-C (Table IV). In the NGT group, the fasting serum CTRP3 was negatively correlated with pre-pregnancy BMI, and had no obvious correlations with age, parity, BMI increase during gestation, HOMA-IR, TC, TG, VLDL-C, LDL -C and HDL-C (Table V). Multiple linear stepwise regression analysis took fasting serum as the dependent variable, and pre-pregnancy BMI, FPG, 1 h PG, 2 h PG, TG, HDL-C and VLDL-C as independent variables, and the results of the analysis conducted over the GDM group showed that FPG was an independent influencing factor for fasting serum CTRP3 (Table VI).

Table IV. Correlation analysis of serum CTRP3 and other clinical index in GDM.

	r-value	*p*-value
Age (year)	-0.218	>0.05
Number of pregnancies	-0.292	>0.05
Gestational Age (week)	-0.016	>0.05
Pre-pregnancy BMI (kg/m^2)	-0.439	<0.01
The increased BMI (kg/m^2)	0.025	>0.05
FPG (mmol/L)	-0.551	<0.01
1 h PG (mmol/L)	-0.452	<0.01
2 h PG (mmol/L)	-0.312	<0.05
FINS (mU/L)	-0.184	>0.05
FCP (ng/mL)	-0.313	<0.05
HOMA-IR	-0.292	<0.05
HOMA-β	0. 326	<0.05
TC (mmol/L)	0.258	>0.05
TG (mmol/L)	-0.302	<0.05
HDL-C (mmol/L)	0.336	<0.05
VLDL-C (mmol/L)	-0.305	<0.05
LDL-C (mmol/L)	0.266	>0.05

Table V. Correlation analysis of serum CTRP3 and other clinical index in NGT.

	r-value	*p*-value
Age (week)	-0.039	>0.05
Number of pregnancies	0.132	>0.05
Gestational Age (week)	-0.108	>0.05
Pre-pregnancy BMI (kg/m^2)	-0.432	<0.01
The increased BMI (kg/m^2)	-0.073	>0.05
HOMA-IR	-0.242	>0.05
TC (mmol/L)	0.178	>0.05
TG (mmol/L)	-0.158	>0.05
HDL-C (mmol/L)	0.194	>0.05
VLDL-C (mmol/L)	-0.163	>0.05
LDL-C (mmol/L)	0.212	>0.05

Table VI. Regression equation analysis.

	β	Standardized β	*p*-value	95% CI
Pre-pregnancy BMI (kg/m^2)	-0.589	-0.246	0.075	-1.214–0.071
FPG (mmol/L)	-4.182	-0.358	0.032	-0.8116–0.292
1 h PG (mmol/L)	-0.746	-0.235	0.182	-1.803–0.337
2 h PG (mmol/L)	0.228	0.071	0.679	-0.842–1.249
TG (mmol/L)	-4.133	-0.785	0.737	-26.472–18.217
HDL-C (mmol/L)	2.352	0.153	0.338	-2.695–7.206
VLDL-C (mmol/L)	12.118	0.875	0.691	-48.773–73.458

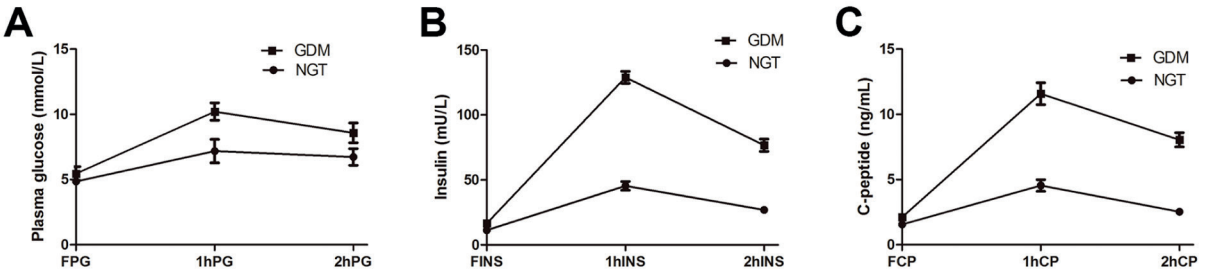

Figure 1. Comparisons of trends in plasma glucose, insulin and C-peptide during OGTT between GDM group and NGT group. ***(A)*** Plasma glucose changes during OGTT between two groups. ***(B)*** Insulin changes during OGTT between two groups. ***(C)*** C-peptide changes during OGTT between two groups.

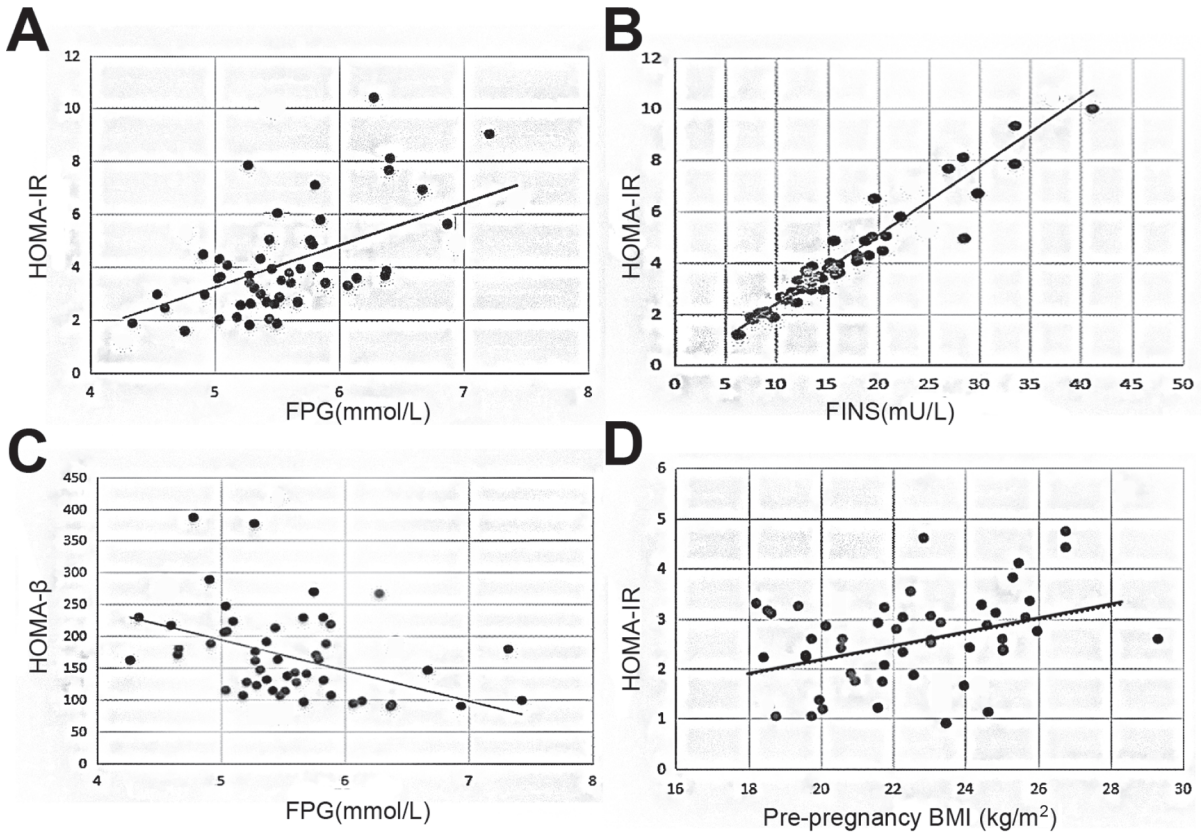

Figure 2. Analysis of the correlations between IR indexes and various indicators. ***(A)*** Relationship between HOMA-IR and FPG in GDM. ***(B)*** Relationship between HOMA-IR and FINS in GDM. ***(C)*** Relationship between HOMA-β and FPG in GDM. ***(D)*** Relationship between HOMA-IR and BMI in NGT.

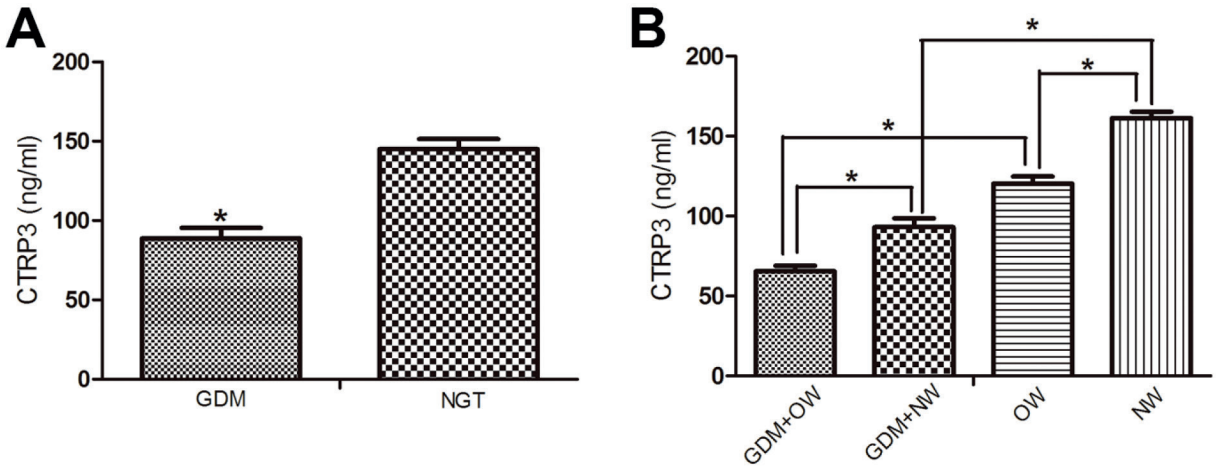

Figure 3. Comparisons of serum CTRP3 levels in each group. ***(A)*** Analysis of serum CTRP3 levels in GDM group and NGT group. ***(B)*** Analysis of serum CTRP3 levels in GDM+OW, GDM+NW, OW and NW group. * $p<0.05$.

Discussion

As the most common metabolic disease occurred during pregnancy, GDM will lead to complex pregnancy and production processes, and its main hazards are the adverse clinical maternal and neonatal outcomes and increased mortality in perinatal period, including increased risks of mother developing type 2 DM, abnormal fetal development in uterus, neonatal malformation, neonatal hypoglycemia and fetal macrosomia. A large number of studies have shown that GDM women have higher occurrence rates in acute and chronic complications than healthy pregnant women[14,15], while hyperinsulinemia can result in fetal oversize, leading to fetal trauma occurred during delivery. Therefore, the investigation of the pathogenesis of GDM is very important.

IR refers to a pathological state that efficiencies of uptake and utilization of glucose promoted by insulin are declined due to various reasons and the body vicariously secretes excessive insulin to maintain a stable PG. When the woman is in normal pregnancy, the body shows a physiological IR state, with relatively elevated serum insulin and PG levels, due to regulations of insulin antagonistic hormones such as estrogen and progestin secreted by placenta, and human placental lactogen. However, IR index (HOMA-IR) in GDM women was significantly higher than that in normal pregnant women, suggesting that GDM patients have both physiological IR and pathological IR[16]. In our study, we observed that FINS and HOMA-IR in the GDM group were higher than those in the NGT group, and FINS and HOMA-IR of the GDM + NW group were greater than those of the NW group, indicating that with the growth in FPG level, insulin secretion is increased, and IR is further enhanced. The results of comparison in HOMA-β between the GDM group and the NGT group, and between the GDM + NW group and the NW group, showed that both formers had lower HOMA-β, implying that pancreatic β-cell function of the GDM patient has also been damaged. Pearson correlation analysis revealed that HOMA-IR was positively correlated with FPG, and HOMA-β was negatively correlated with FPG, insinuating that the level of FPG may affect the degrees of IR and pancreatic β-cell function damage. Obesity is a chronic metabolic disorder characterized by abnormally high percentage caused by increases in the number and volume of adipocytes in the body. A lot of studies have found that adipose tissue is equivalent to an endocrine organ that can produce and release adipokines by itself or through other means, and directly or indirectly influence the sensitivity and resistance of insulin, playing an import role in regulating glycolipid metabolism and systemic inflammation[17,18]. Due to expansion of adipose tissue and increase in the release of adipokines secreted by adipose tissue, the obese are more likely to have DM, hyperlipidemia, and a variety of cardiovascular and cerebrovascular diseases. At present, it is generally accepted that obesity is the leading cause of IR[19,20], and BMI is an important indicator used for judgment and classification of obesity. Some scholars have suggested that excessive pre-pregnancy BMI can lead to GDM, suggesting that high

BMI during pregnancy is a major risk factor for GDM. The results of this study showed that FINS and HOMA-IR in the OW group were higher than those in the NW group; Pearson correlation analysis revealed that HOMA-IR and pre-pregnancy BMI were positively correlated in the NGT group. This implied that IR was gradually aggravated along with the increase in BMI. Compared with the GDM + NW group, the GDM + OW group had obviously increased TG and VLDL-C, and significantly reduced HDL-C. This was in line with the view that the rate of dyslipidemia gradually ascends with the growth in BMI. CTRP3 is an anti-inflammatory adipose factor, cloned by Maeda et al[21] for the first time. Wurm et al[22] measured and reported human serum CTRP3 for the first time. Recent researches have suggested that CTRP3 is significantly reduced in patients with type 2 DM and is negatively correlated with PG and acute C-reactive protein (CRP)[23]. OGTT showed that 2 h postprandial CTRP3 level was significantly decreased. In patients with obesity, CTRP3 level was also overtly declined[24]. The results of our work indicated that the level of serum CTRP3 in the GDM + OW group was clearly lower than that in the GDM + NW group, and the level of circulating CTRP3 in the OW group was lower than that in the CON group, which indicated that the level of CTRP3 in fasting serum is lower than that in healthy group, no matter whether PG is normal or not. Pearson correlation analysis found that in the GDM group, NGT group, GDM + NW group and OW group, fasting serum CTRP3 was negatively correlated with pre-pregnancy BMI, which implied that BMI maybe a negative impact factor of CTRP3 regardless of whether it is affected by hyperglycemia or obesity. We found that the GDM group had significantly lower fasting serum CTRP3 level compared with the NGT group, and the same result was also observed in the comparison between the GDM + NW group and the NW group. Pearson correlation analysis showed that fasting serum CTRP3 was positively correlated with HOMA-β and negatively related to FPG, 1 h PG, 2 h PG, FCP and HOMA-IR in the GDM group. This indicated that abnormal glucose metabolism, islet cell function damage and IR can affect the level of serum CTRP3; also, it suggested that there is a relationship between serum CTRP3 and islet cell function damage. Multiple linear stepwise regression analysis revealed that FPG was an independent factor affecting the level of CTRP3, suggesting that the degree of dysglycemia maybe the most important indicator impacting the level of CTRP3. CTRP3 may play a certain role in the pathogenesis of GDM, but this does not mean that CTRP3 is the pathogenic cause of GDM IR and β-cell function damage, so the specific role of CTRP3 in GDM remains to be further studied.

Conclusions

We have observed that with the increase of FPG, the progression of GDM IR patients was increased, and pancreatic β-cell function progressively declined. The decrease of CTRP3 level in fasting serum in GDM patients may play a certain role in the pathogenesis of GDM. With the increase in BMI, the progression of IR of non-diabetic pregnant woman is severe, and the level of BMI can reflect the degree of IR to a certain extent. The level of fasting serum CTRP3 is downward in overweight/obese pregnant women, and the level of BMI plays a metabolic role on serum CTRP3 level.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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