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Original Research Article

Correlation of adiponectin, body mass index and waist-to-height ratio with the risk of developing gestational diabetes mellitus in hypertensive patients

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Abstract

Purpose: *To analyze the effects of abnormalities in adiponectin (APN), body mass index (BMI) and waist height ratio (WHtR) on the risk of a combination of gestational diabetes mellitus (GDM) and hypertensive disorders complicating pregnancy (HDCP).*
Methods: *The clinical data of 62 patients with GDM who visited Ningbo Beilun District People's Hospital between January 2018 and June 2020 were assigned to the GDM group, and the clinical data of 38 patients with GDM and HDCP during the same period were assigned to the combination group. Blood lipid levels were measured with a fully automated biochemical analyzer. APN level was determined using double antibody sandwich enzyme immunoassay kit.*
Results: *The combination group had higher BMI, WHtR, family history of diabetes and hypertension, levels of hyperlipidemia, triglycerides (TG), as well as very low-density lipoprotein cholesterol (VLDL-c), and lower APN levels than the GDM group ($p < 0.05$) Multifactorial logistic regression results revealed that BMI, WHtR, APN, TG and VLDL-c levels may be risk factors for the occurrence of a combination of HDCP and GDM ($OR > 1$, $p < 0.05$).*
Conclusion: *BMI, WHtR and APN are closely related to the risk of HDCP in patients with GDM, Thus, these indicators may be used to predict, evaluate and diagnose the disease.*

Keywords: *Adiponectin, Gestational diabetes mellitus, Hypertensive disorders complicating pregnancy, Risk factors*

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INTRODUCTION

Gestational diabetes mellitus (GDM) refers to an abnormal glucose tolerance during pregnancy, which is mostly related to low insulin levels, and is due to an increase in anti-insulin-like substances such as estrogen, placental lactogen, progesterone, and placental insulinase in pregnant women [1,2]. Abnormal blood glucose in patients with GDM is associated with increased blood viscosity which stimulates the vascular wall, causes hypertrophy and hyperplasia, increases luminal resistance, and induces HDCP [3,4]. The combination of GDM and hypertensive disorders complicating pregnancy (HDCP) is a challenge worldwide, and

is difficult to cure, as it induces adverse pregnancy outcomes such as hyperhydramnios, fetal distress, prematurity, and even endangering maternal and infant health in severe cases [5]. Therefore, effective indicators should be investigated to determine pregnant women who are at a high risk of GDM combined with HDCP, so as to improve maternal and infant outcomes.

Patients with GDM and HDCP are in a state of disorder in glucose and lipid metabolism disorder, and obese people have abnormal fat cell function. The release of many adipose-derived factors can cause disorders of glucose and lipid metabolism as well as insulin resistance, thus increasing the risk of atherosclerosis. Therefore, obesity is a risk factor for GDP and HDCP [4,6]. BMI and WHtR can be used as indicators of obesity. Neonatal complications and pregnancy complications are strongly associated with maternal weight gain and BMI during pregnancy, and a reasonable BMI control is helpful to optimize perinatal outcomes [7]. WHtR has a higher predictive advantage than BMI and waist circumference (WC) in predicting obesity-related dyslipidemia, diabetes and cardiovascular disease risk [8]. APN, a protein hormone secreted by adipocytes, has been associated with insulin resistance, hypertension, obesity, and abnormal lipid metabolism. However, there are few clinical reports on the role and association of these three indicators in the progression of HDCP combined with GDM. The current research retrospectively analyzed the clinical data for 62 patients with GDM and 38 patients with GDM combined with HDCP to investigate the correlation between BMI, WHtR, APN and the risk of GDM combined with HDCP, and thus, provide a reference for clinical improvement.

METHODS

Patients

A total of 62 patients with GDM who visited Ningbo Beilun District People's Hospital between January 2018 and June 2020 were enrolled in a GDM group, while 38 patients with GDM combined with HDCP over the same period were enrolled in a combination group.

Inclusion criteria

Patients in the GDM group met the diagnostic criteria of the Guidelines for the Diagnosis and Treatment of Gestational Combined Diabetes (2014 edition) [9] as follows: At 24 - 28 weeks gestational age, patients underwent 75 g oral glucose tolerance test (OGTT). Blood glucose levels were lower than 5.1 mmol/L before drinking the glucose solution, lower than 10.0 mmol/L one hour after drinking, and lower than 8.5 mmol/L two hours after drinking, and any blood glucose level reaching or exceeding these criteria was regarded as GDM; The GDM combined with the HDCP group met the diagnostic criteria of the Guidelines for the Diagnosis and Treatment of Gestational Combined Diabetes (2014 Edition), and Guidelines for the Diagnosis and Treatment of Hypertensive Disorders in Pregnancy (2015) [10]; Age 20 - 35 years; gestational week 24 - 28 weeks; no pre-pregnancy diabetes or hypertension; singleton pregnancy; complete clinical data.

Exclusion criteria

Patients with thyroid diseases, autoimmune diseases, hematological diseases, mental disturbance, consciousness disorders, acute and chronic infectious diseases, communication disorders, abnormalities of heart, brain, liver, kidney and other vital organs, fetal malformations, chromosomal abnormalities, and tumors were excluded.

Ethical approval

The research was implemented with the approval from Ethics Committee of Ningbo Beilun District People's Hospital (approval no. 2023LP006) and followed the ethical principles of Declaration of Helsinki [11].

Data acquisition

Clinical information on the patients was acquired, such as age, BMI, WHtR, OGTT blood glucose level, family history of diabetes and hypertension, history of infection during pregnancy, hyperlipidemia, smoking, and alcohol consumption. BMI is calculated as weight (kg) divided by height squared (m^2), with BMI < 18.5 kg/m^2 as underweight, 18.5 - 23.9 kg/m^2 as normal, 24 - 27.9 kg/m^2 as overweight, and over 27.9 kg/m^2 as obesity. WHtR = waist circumference/height, if WHtR ≥ 5 is abnormal (abdominal obesity).

Evaluation of parameters/indices

An aliquot (3mL) of fasting venous blood was collected from each patient avoiding celiac blood and hemolysis, and placed in vacuum tubes without anticoagulant, coagulated at room temperature, centrifuged for 10 min (radius = 6 cm, 3000 r/min). Serum was separated and

refrigerated at -80 ^{0}C in an ultra-low temperature refrigerator pending its use in tests.

Blood lipid level

A fully automated biochemical analyzer (Atellica CH930, Shanghai Jumu Medical Devices Co., Shanghai, China) was utilized to measure triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), and high-density lipoprotein (HDL-C).

APN

APN level was determined using double antibody sandwich enzyme immunoassay kit (Shanghai Pharmacell Biological Engineering Co. Shanghai, China). All the above operations were conducted following the kit manufacturer's instructions.

Severity of HDCP

Mild: Blood pressure ≥ 140/90 mmHg, urine protein (-), no edema, 24 h urine protein < 0.5 g.

Moderate: Diastolic blood pressure (DBP) 90 - 110 mmHg, systolic blood pressure (SBP) 140 - 160 mmHg, urine protein (+), mild edema, 24 h urine protein ≥ 0.5 g.

Severe: DBP > 110 mmHg, SBP > 160 mmHg, urine protein (++), obvious edema, 24 h urine protein ≥ 0.5 g.

Statistical methods

Data analysis was processed using SPSS 24.0 software. Measurement data were analyzed by t-test and expressed as mean ± SD, while one-way ANOVA was applied for multi-group comparison. Count data (%) were compared by χ^2 test. Pearson correlation analysis was used to determine correlations, while multivariate logistic regression model was employed for analyzing the related factors affecting the combination of GDM and HDCP. Differences were deemed to be statistically significant at $p < 0.05$.

RESULTS

Baseline profile of patients

Two groups exhibited no statistically significant differences in terms of age and 0, 1 and 2 h OGTT glucose levels, history of smoking, alcohol consumption, and infection during pregnancy ($p > 0.05$). The combination group had higher BMI, WHtR, family history of diabetes and hypertension, as well as a higher proportion of hyperlipidemia than the GDM group ($p < 0.05$). This showed that BMI, WHtR, family history of diabetes and hypertension, and hyperlipidemia may be associated with the occurrence of HDCP and GDM (Table 1 and Table 2).

Table 1: Comparison of patients' baseline data

Baseline data	GDM group (n=62)	Combination group (n=38)	t/χ^2	*P*-value
Age (years)	28.56±3.29	29.12±4.02	0.759	0.450
Gestational week (weeks)	26.25±1.06	25.94±1.37	1.268	0.208
BMI (kg/m^2)	24.81±2.91	27.14±3.06	3.811	0.000
Primigravida	22	14	0.019	0.891
Family history of diabetes	13	15	4.002	0.045
Family history of hypertension	11	14	4.584	0.032
History of infection during pregnancy	6	5	0.286	0.593
Hyperlipidemia	11	16	7.095	0.008
History of smoking	6	3	0.091	0.762
History of alcohol consumption	8	6	0.163	0.686

Table 2: Comparison of blood glucose-related indices

Index	GDM group (n=62)	Combination group (n=38)	t/χ^2	*P*-value
WHtR	0.44±0.14	0.63±0.14	6.587	0.000
OGTT 0 h blood glucose (mmol/L)	5.21±0.11	5.24±0.15	1.150	0.253
OGTT 1 h blood glucose (mmol/L)	10.21±0.24	10.32±0.36	1.834	0.070
OGTT 2 h blood glucose (mmol/L)	7.52±1.03	7.86±1.12	1.550	0.124

Biochemical indices

No significant differences were observed in TC, HDL-C and LDL-C levels between two groups ($p > 0.05$). However, combination group had lower APN level and higher TG and VLDL-C levels than GDM group ($p < 0.05$), which showed that the abnormal APN, TG and VLDL-C levels might be associated with HDCP and GDM occurrence (Figure 1).

Results of logistic multifactorial analysis of factors associated with the coexistence of HDCP and GDM

Logistic multifactorial results found that BMI, WHtR, APN, TG and VLDL-C levels may be risk factors affecting the occurrence of HDCP in combination with GDM (OR > 1, $p < 0.05$), indicating that abnormal BMI, WHtR, APN, TG and VLDL-C levels might raise the risk of developing co-existence of HDCP with GDM (Table 3).

***AUC* of BMI, WHtR, and APN in predicting the occurrence of HDCP and GDM**

The AUC of BMI, WHtR, and APN in predicting the co-existence of HDCP in combination with GDM was 0.712 (95% CI: 0.608 - 0.816), 0.831 (95% CI: 0.751 - 0.911), and 0.831 (95% CI: 0.754 - 0.908), separately. It indicates that BMI, WHtR, and APN all have some predictive values for the occurrence of HDCP in combination with GDM (Table 4 and Figure 2).

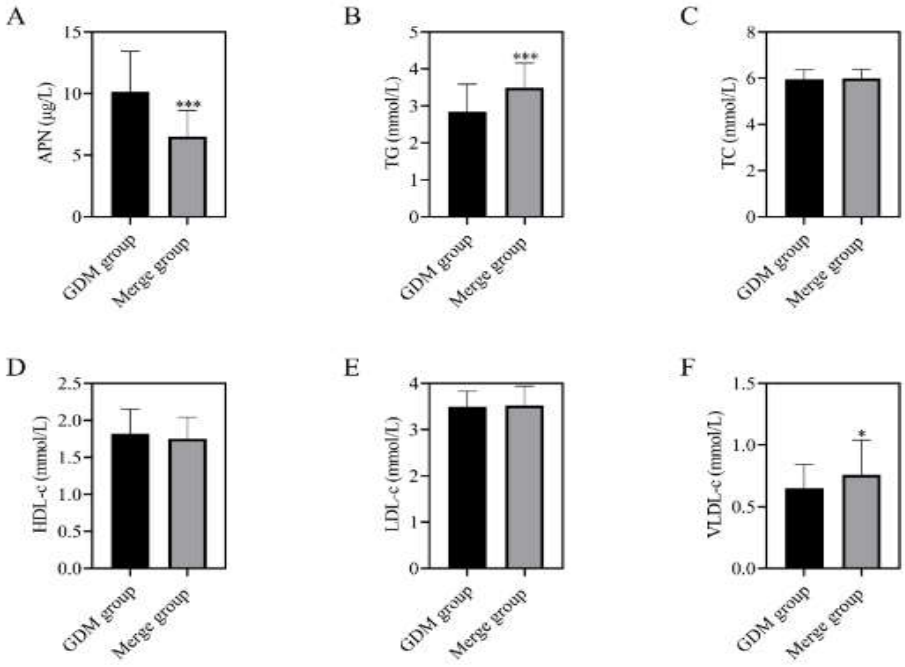

Figure 1: Comparison of biochemical indices. (A) The APN level in the combination group was lower than that in the GDM group; (B) TG level in the combination group was higher than that in the GDM group; (C) there was no significant difference between the two groups in terms of TC; (D) there was no significant difference between the two groups in terms of HDL-C; (E) there was no significant difference between the two groups in terms of LDL-C; (F) the VLDL-C level in the combination group was higher than that in the GDM group.***$P < 0.001$ and *$p < 0.05$, compared with the GDM group

Table 3: Logistic multifactor analysis of factors affecting the occurrence of HDCP in combination with GDM

Factor	B	Standard error	Wals	*P*-value	OR	95% CI
BMI	1.445	0.316	22.521	0.000	4.026	2.168-7.562
WHtR	1.034	0.448	5.319	0.021	2.812	1.168-6.768
Family history of diabetes	0.788	0.459	2.950	0.086	2.199	0.895-5.403
Family history of hypertension	0.888	0.465	3.644	0.056	2.431	0.977-6.049
Hyperlipidemia	0.805	0.450	3.199	0.074	2.236	0.926-5.400
APN	0.598	0.262	4.952	0.027	1.982	1.062-3.125
TG	0.629	0.245	5.762	0.018	1.882	1.098-3.221
VLDL-C	0.435	0.195	4.895	0.028	1.594	1.005-2.254

Table 4: Predictive roles of BMI, WHtR, and APN in co-existence of HDCP and GDM in patients

Indicator	*AUC*	Standard error	*P*-value	95% CI	Sensitivity	Specificity
BMI	0.712	0.053	0.000	0.608-0.816	0.868	0.629
WHtR	0.831	0.041	0.000	0.751-0.911	0.895	0.468
APN	0.831	0.039	0.000	0.754-0.908	0.903	0.526

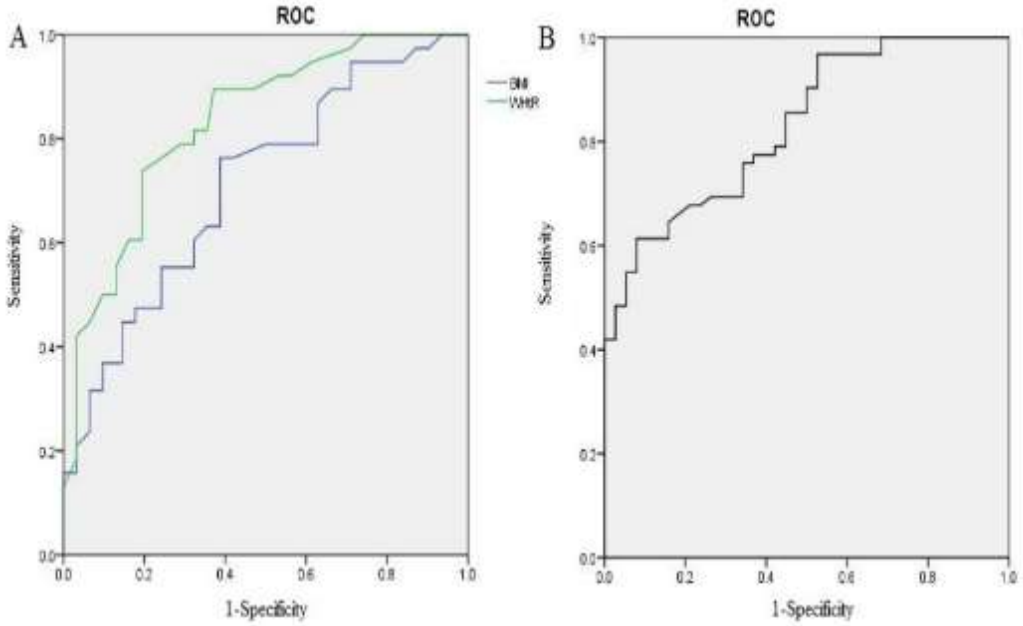

Figure 2: ROC for predicting the c0-existence of HDCP and GDM. (A) BMI and WHtR; (B) AP

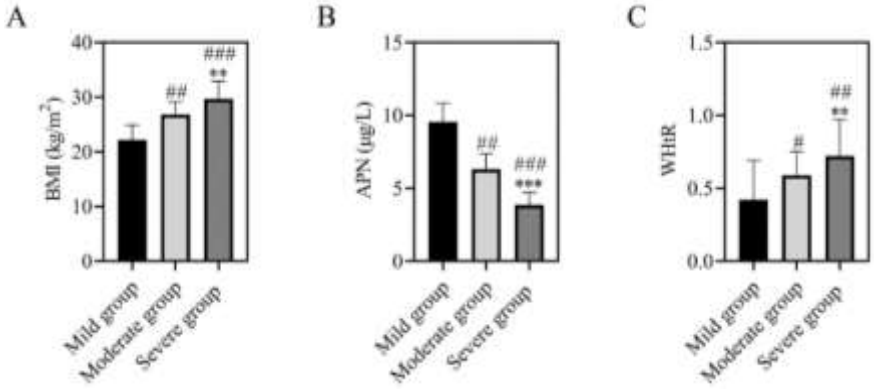

Figure 3: Comparison of BMI, APN, and WHtR in patients with co-existing GDM and HDCP of varying severity. (A) BMI in severe subgroup > moderate subgroup > mild subgroup; (B) APN in severe subgroup < moderate subgroup < mild subgroup; (C) WHtR in the severe subgroup > moderate subgroup > mild subgroup. #*P* < 0.05, ##*p* < 0.01, ###*p* < 0.001; compared with moderate group, **$p < 0.01$

BMI, APN, and WHtR in patients with co-existing GDM and HDCP

The severe group had the highest BMI and WHtR, followed by the moderate group, and the mild group had the lowest BMI and WHtR; the severe group had the lowest APN, followed by the moderate group, and the mild group had the highest APN ($p < 0.05$), indicating that BMI, APN, and WHtR had a close association with the severity of the co-existing GDM and HDCP (Figure 3).

Correlation between BMI, APN, WHtR and their severity in patients with coexisting GDM and HDCP

Pearson correlation showed that BMI and WHtR were positively correlated with their severity in patients with coexisting GDM and HDCP ($r > 0$, $p < 0.05$), while APN had negative correlation with the severity of the disease in patients with coexisting GDM and HDCP ($r < 0$, $p < 0.05$), as shown in Table 5.

Table 5: Correlation between BMI, APN, WHtR and severity of disease in patients with GDM + HDCP

Coefficient	BMI	APN	WHtR
R	0.623	-0.652	0.539
P-value	0.000	0.000	0.000

DISCUSSION

HDCP patients have significant insulin resistance, lipid metabolism disorders, endothelial dysfunction and atherosclerosis, but its pathogenesis has not been fully elucidated [12,13]. Existing evidence confirmed that obesity is a high-risk factor for the progression of HDCP, but the specific mechanism still needs further investigation [3]. In this study, combination had higher BMI than GDM group, and BMI predicted the occurrence of GDM combined with HDCP with an AUC of 0.712, indicating that BMI may be involved in the pathogenesis of coexisting GDM and HDCP, and can effectively predict the occurrence of coexisting GDM and HDCP.

The severe group exhibited higher BMI and WHtR than the moderate and mild groups, and the BMI was positively correlated with the severity of the GDM combined with HDCP. Its mechanism may be related to the following points: (1) abnormal BMI indicates that there may be obesity or excessive weight gain, and the body's energy metabolism level is low, which, together with the long-term accumulation of metabolic substances, is likely to cause a decrease in blood flow velocity and an increase in blood flow viscosity, further damaging the tissue structure of the blood vessel wall, increasing intravascular pressure, and inducing HDCP [14,15]. Overweight and obese patients often experienced reduced parasympathetic activity, increased sympathetic activity, increased peripheral vascular resistance, and increased blood volume, which tend to decrease baroreflex sensitivity and affect vascular endothelial function, thereby increasing vasoconstriction reactivity and increasing the risk of HDCP. Sangrós *et al* [16] found that an abnormal increase in WHtR increased the risk of hypertension and dyslipidemia, which correlated with TG and VLDL-C levels; Lam *et al* [17] suggested in a cross-sectional study that abnormal WHtR is a risk factor for hypertension.

It was observed in this research that WHtR in the combination group was higher than in the GDM group, and it was positively correlated with the severity of GDM coexisting with HDCP, which is similar to the results of the reports mentioned above. This is probably due to the likelihood that the abdominal rise of WHtR may be associated with abdominal obesity, in which most of the fat is accumulated in the abdominal organs, subcutaneous tissues and greater omentum. The body produces more free fatty acids to redistribute and catabolize fat throughout the body. Some of these free fatty acids are substrates for various synthetic functions in the liver, leading to changes in the activity of various TG lipases and lipoprotein lipases, thus causing abnormalities in blood lipids and blood pressure [18]. The remaining fatty acids are transferred and deposited in the liver, insulin cells, muscle and other tissue cells, inhibiting skeletal muscle glucose metabolism, reducing hepatic insulin clearance, thereby inducing hyperinsulinemia. In contrast, insulin resistance and hyperinsulinemia directly contributes to the development of HDCP by increasing sympathetic nervous tension and sodium reabsorption.

Vascular endothelial cell damage and functional changes are particularly critical in the pathogenesis of HDCP. APN reduces the degree of vascular endothelial damage by anti-atherosclerosis, inhibiting inflammatory factors, regulating glucose metabolism and insulin [19]. A trial revealed that APN can stimulate endothelial cells through the PI-3K pathway, which produces nitric oxide and promotes vasodilation [20]. Liu *et al* reported that APN reduced the degree of early inflammatory response and attenuated the impairment of endothelial function through cytokines such as TNF-α and IL-6 by attenuating the activity of mature macrophages [21]. In this study, the combination group had a lower APN level than the GDM group, and the APN level was negatively correlated with the condition of patients with GDM and HDCP. The reason may be that APN inhibits sympathetic nerve activity by inhibiting inflammatory response, improving vascular endothelial function, reducing free fatty acids levels, and inhibiting the proliferation of vascular smooth muscle cells, thus inhibiting the occurrence and development of hypertension.

Limitations of the study

However, there were some limitations in this study. As a cross-sectional research, only the relationships of BMI, WHtR, and APN with HDCP in patients with GDM were determined, and so no causal inference should be made. Furthermore, data collection was susceptible to several factors, resulting in some bias. Moreover, the inclusion factors were not comprehensive.

CONCLUSION

BMI, WHtR and APN are closely correlated to the risk of coexisting HDCP and GDM, and therefore,

these indicators may be used to predict, evaluate and diagnose the disease. Correlation among the three indicators has not been analyzed, and hence further studies are needed.

DECLARATIONS

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Ethical approval

Approval for this work was obtained from Ethics Committee of Ningbo Beilun District People's Hospital, China (approval no. 2023LP006).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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