RESEARCH ARTICLE

A retrospective study of the relationship between weight management and gestational diabetes mellitus concurrent with hypertensive disorders of pregnancy and its clinical characteristics

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Received: November 16, 2022; **accepted:** January 3, 2023.

Gestational diabetes mellitus (GDM) is one of the most common pregnancy complications. Obesity contributes to the occurrence of GDM and can result in complications such as hypertensive disorders of pregnancy (HDP). This study was to examine the clinical characteristics of GDM concurrent with HDP and their correlation with weight management. Total 180 pregnant women with GDM admitted to the Maternal and Child Health Care Hospital of Shandong province between June 2020 and June 2021 were included in this study. Patients were divided into GDM group (120 cases) and GDM complicated with HDP group (60 cases). Additional 100 cases of normal pregnancy were included at random base as the normal control group. The clinical characteristics of pregnant women in each group were analyzed. According to their pre-pregnancy BMI (pBMI), all the enrolled pregnant women were divided into the wasting group, the normal group, the overweight group, and the obese group. In addition, according to weight gain during pregnancy (GWG), the patients were divided into underweight gain, moderate gain, and excessive gain groups. The relationships between weight management and GDM as well as GDM concurrent with HDP were investigated. The results showed that, in the GDM concurrent with HDP group, the risk of perinatal complications was greater than that in the normal pregnancy group and the GDM group. With increased pBMI and GWG, the risks of the occurrence of GDM and GDM concurrent with HDP were raised gradually. The pBMI was an independent risk factor for the development of GDM and GDM concurrent with HDP, and GWG was an independent risk factor for GDM concurrent with HDP. The results of this study confirmed that GDM and HDP were associated with an increased risk of perinatal complications. High pre-pregnancy BMI and excessive weight gain during pregnancy were the risk factors for the occurrence of GDM as well as GDM concurrent with HDP, and good weight management could reduce the incidence of complications during pregnancy.

Keywords: weight management; gestational diabetes mellitus; hypertensive diseases during pregnancy.

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Introduction

Gestational diabetes mellitus (GDM) refers to abnormal glucose tolerance in pregnancy after normal pre-pregnancy blood glucose, excluding T1DM and T2DM that exist prior to pregnancy, and is one of the most common pregnancy complications. GDM is classified as A1 and A2 according to the Guidelines for Diagnosis and Treatment of Hyperglycemia in Pregnancy (2022) [1]. Those with type A1 can optimally control their blood glucose through diet and exercise, while those with type A2 require medication. Hypertensive disorders of pregnancy (HDP) refers

to the rise in blood pressure that occurs during pregnancy, regardless of whether organ function is impaired. A study by Vinturache, *et al*. confirmed that obesity contributes to the occurrence of GDM and can result in complications such as HDP [2]. In accordance with the survey statistics, approximately 25%-32% of pregnant women with GDM have hypertensive disorder of pregnancy (HDP), which is three to five times higher than that of normal pregnant women [3]. The study of Zhu, *et al*. confirmed the mutual influence between hyperglycemia and hypertension [4]. The insulin resistance and obesity may be important factors for GDM to be complicated with hypertension during pregnancy [5]. There are four categories of HDP including hypertension in pregnancy, pre-eclampsia-eclampsia, chronic hypertension in pregnancy, and chronic hypertension with pre-eclampsia condition. Hou, *et al*. pointed out that compared with the control group, pregnant women with GDM had an increased risk of pregnancy-induced hypertension, premature rupture of membranes, fetal distress, abnormal amniotic fluid, *etc*., and the cesarean section rate was increased [6]. The coexistence of hyperglycemia and hypertension during pregnancy can further impair organ function of pregnant women and increase the risk of miscarriage, premature delivery, neonatal asphyxia, and other adverse outcomes [7]. Early detection and screening of risk factors, as well as early prevention and warning, are crucial elements in preventing pregnancy complications. Numerous studies suggest that pre-pregnancy body mass index (pBMI) and pregnancy weight gain (GWG) may increase the risk of adverse pregnancy outcomes by influencing blood glucose and blood pressure levels [8]. To realize the importance of weight management, improve pregnant women's awareness of rational weight management, and take effective measures to do a good job of weight management, are the problems that clinicians need to pay attention to. Therefore, in this retrospective study, the relevant medical records were collected to investigate the correlation between pBMI, GWG and the occurrence of GDM and GDM concurrent with HDP. The results of this study may assist pregnant women in managing their weight more effectively.

Materials and methods

Study subject selection

A total of 180 pregnant women with GDM who delivered at Maternal and Child Health Care Hospital of Shandong province (Jinan, Shandong, China) from June 2020 to June 2021, aged 20-44 years old, and with one to three pregnancies were admitted to this study. The mid-pregnancy Oral Glucose Tolerance Test (OGTT) results were used for GDM diagnosis. According to whether the pregnant women with diabetes had concurrent hypertension, the subjects were divided into the diabetes only and the diabetes concurrent with hypertension groups. Since the purpose of this study was to investigate the relationship between GDM and secondary gestational hypertension, only gestational hypertension and preeclampsia-eclampsia were included in the study. Patients with known diabetes and hypertension before pregnancy, as well as those with chronic diseases, infectious diseases, and other systemic diseases were excluded.

(1) Oral Glucose Tolerance Test (OGTT)

OGTT screening was conducted between 24 and 28 weeks of pregnancy. The patient kept eating as usual in 3 days prior to the test day and fasted 8-10 hours right before the test. The test was down by drinking 300 mL of liquid containing 75 grams of anhydrous dextrose within 5 min. The venous blood samples were collected at the time points of before test, 1 hour after, and 2 hours after test to measure the plasma glucose levels. The blood glucose thresholds for above time points were set as 5.1 mmol/L, 10.0 mmol/L, and 8.5 mmol/L, respectively. Wherever those thresholds were reached or exceeded at any time point, the GDM diagnosis was achieved. It was recommended that the venous blood sample was drawn prior to 9:00 a.m. for the OGTT test because the test results might be affected if the blood was drawn later in the day.

(2) Determination of HDP

The GDM associated with hypertension during pregnancy was determined when a pregnant woman who had a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg, with or without urine protein/creatinine ≥0.3, or random urine protein positivity, or abnormalities in the heart, lungs, liver, kidneys, blood system, digestive system, as well as an abnormality of the nervous system or involvement of the placenta.

Data collecting and processing

The retrospective collected clinical data from all enrolled cases included age, height, weight, weight gain value, pregnancy number, delivery number, family history, gestational week of delivery, systolic blood pressure, and diastolic blood pressure. The following maternal and infant outcomes were tallied including excess/low amniotic fluid, premature membrane rupture, placental abruption, postpartum hemorrhage, gestational week of delivery, newborn birth weight, and neonatal Apgar score. The blood levels of triglyceride (TG), low-density lipoprotein (LDL), small dense LDL (sdLDL), urea nitrogen (BUN), creatinine (SCr), and uric acid (SUA) were measured after 8-12 h of fasting. Depending on their conditions, the patients were divided into the normal group, the GDM group, and the GDM concurrent with HDP group. The statistical analysis was performed to check the differences in basic conditions and maternal and infant outcomes between the groups.

Based on the pre-pregnancy height and weight of each subject, the pBMI was calculated using the formulation of BMI = weight (kg) / (height (m))^2. The subjects with BMI < 18.5 were considered wasting, while those BMIs as 18.5 ≤ BMI < 25 were considered normal, 25 ≤ BMI < 30 were considered overweight, and BMI ≥ 30 were considered obese. In accordance with the recommendations of 2009 Institute of Medicine of the National Academy of Sciences (IOM) for weight gain during pregnancy, when the BMIs were < 18.5, 18.5 ≤ BMI < 25, 25 ≤ BMI < 30, and ≥ 30, the recommended weight gains were 12.5-18.0 kg, 11.5-16.0 kg, 7.0-11.5 kg, and 5-9 kg, respectively [9]. According to the pBMI, the subjects were divided into four groups of wasting, normal, overweight, and obese. The patients were also grouped according to GWG into three groups of the underweight gain group, the moderate gain group, and the excessive gain group. The statistical analysis between different groups was conducted on the occurrence of GDM as well as concurrent with HDP in pregnant women with GMD. In addition, the relationship between pBMI, GWG and the occurrence of GDM and HDP was investigated.

Statistical analysis

The collected data was analyzed statistically by using SPSS (version 10.0) (SPSS Inc., Chicago, IL, USA). Measurement data conforming to the normal distribution were represented by mean ± standard deviation. Student t-test and one-way ANOVA were applied to exam the difference between the groups. The measurement data that did not conform to the normal distribution were expressed as percentiles, and a rank sum test was used to determine their significance. Measurement data were expressed as percentages and tested using χ^2. Binary logistic regression was used to analyze pre-pregnancy BMI, as well as correlation of pregnancy weight gain with the occurrence of GDM and GDM concurrent with HDP. The statistically significant difference was defined as $P < 0.05$.

Results

Comparison of general information in normal, GDM, and GDM concurrent with HDP groups

The comparison of general information across three pregnant women groups were shown in Table 1. The average age in normal pregnancy group (n = 100) (30.04 ± 4.136 years old) was younger than that in GDM group (n = 120) (31.63 ± 4.083) and GDM concurrent with HDP group (n = 60) (31.92 ± 5.182). The GDM concurrent with HDP group showed higher pBMI, systolic blood pressure, diastolic blood pressure, fasting, glucose,

Table 1. Comparison of general information in normal, GDM, and GDM concurrent with HDP groups of pregnant women.

	Normal Pregnancy	GDM	GDM concurrent with HDP	F Value	P Value
Age	30.04±4.136[ab]	31.63±4.083	31.92±5.182	4.904	0.008
pBMI	21.16±2.954[ab]	23.25±3.450[b]	25.50±4.476	28.872	0.000
GWG	14.66±4.237[a]	13.17±5.329[b]	15.28±6.490	3.978	0.020
Number of pregnancies	1.93±1.121	2.17±1.192	2.15±1.273	1.289	0.277
Number of deliveries	0.43±0.573	0.49±0.550	0.45±0.565	0.343	0.710
Systolic pressure	116.15±11.270[ab]	119.64±9.925[b]	151.42±13.938	205.806	0.000
Diastolic blood pressure	70.54±8.380[b]	72.18±7.773[b]	93.68±11.210	150.889	0.000
Fasting blood glucose	4.52±0.360[ab]	5.33±0.065[b]	5.84±0.180	52.815	0.000
Triglycerides	3.47±1.713	3.69±1.616	4.13±1.928	2.778	0.064
Total cholesterol	6.50±1.347	6.43±1.348	6.17±1.224	1.211	0.299
Creatinine	47.64±6.851[b]	47.73±8.35[b]	51.80±9.776	5.921	0.003
Uric acid	286.37±55.697[ab]	311.69±73.027[b]	371.15±91.746	26.230	0.000

Note: a: comparison with GDM group ($P < 0.05$). b: comparison with GDM concurrent with HDP group ($P < 0.05$).

Table 2. Comparison of the outcomes of maternal and infant health among three groups of pregnant women.

	Normal Pregnancy	GDM	GDM concurrent with HDP	Chi-square/F Value	P Value
Amniotic fluid abnormality	2 (2%)	1 (0.83%)	3 (5%)	3.327	0.189
Premature rupture of fetal membranes	7 (7%)	18 (15%)	4 (6.67%)	4.880	0.087
Gestational week of delivery	38.669±1.899[b]	38.884±1.462[b]	37.365±2.382	14.307	0.000
Neonatal birth weight	3260.79±419.588[b]	3327.667±484.976[b]	3032.167±768.549	6.138	0.002
Apgar score	9.95±0.261[b]	9.85±0.455[b]	9.65±0.633	8.575	0.000

Note: a: comparison with GDM group ($P < 0.05$). b: comparison with GDM concurrent with HDP group ($P < 0.05$).

creatinine, and uric acid than that in normal pregnancy group and GDM group. The GDM concurrent with HDP group also demonstrated the higher GWG than that in GDM group. All the differences between the groups showed statistically significant ($P < 0.05$).

Comparison of maternal and infant health outcomes among normal, GDM, and GDM concurrent with HDP groups

The results of chi-square/one-way ANOVA test were shown in Table 2. The incidence of amniotic fluid abnormalities and premature rupture of membranes showed no significant differences among the three groups. However, the gestational week of delivery, neonatal birth weight, and neonatal Apgar score in GDM concurrent with HDP were lower than that in normal and GDM ($P < 0.05$).

Comparison of incidence rates between groups based on pBMI and GWG grouping

Four groups were divided based on pBMI, which included wasting group (n = 28), normal group (n = 171), overweight group (n = 67), and obese group (n = 14). In addition, three groups were divided according to the GWG, which were under-increased group (n = 68), moderately increased group (n = 106), and over-increased group (n = 106). The Chi-square test was used to examine the prevalence of GDM and GDM concurrent with HDP in various groups. The test results showed that the incidence of GDM and GDM concurrent with HDP increased substantially as pBMI rose (Table 3). In GWG under- and over- increased groups, the incidence

Table 3. Comparison of incidence rates between different groups based on pBMI and GWG grouping.

Groups	Number of cases	GDM			GDM concurrent with HDP		
		Yes	No	Incidence	Yes	No	Incidence
Grouped according to pBMI							
Wasting group	28	10	18	35.71%	1	9	10%
Normal group	171	101	70	59.06%	27	74	26.73%
Overweight group	67	55	12	82.09%	21	34	38.18%
Obese group	14	14	0	100%	11	3	78.57%
Chi-square value		29.014			17.905		
P Value		0.000			0.000		
Grouped by GWG							
Under-increased group	68	52	16	76.47%	16	36	30.77%
Moderately increased group	106	56	50	52.83%	8	48	14.29%
Over-increased group	106	72	34	67.92%	36	36	50%
Chi-square value		11.067			18.297		
P Value		0.004			0.000		

of GDM and GDM concurrent with HDP were higher than that in moderately increased group ($P < 0.05$).

The relationship between pBMI, GWG, and GDM and GDM concurrent with HDP

A binary logistic regression analysis was performed based on pBMI and GWG as independent variables, as well as whether GDM and GDM concurrent with HDP were the dependent variables. The results demonstrated that, in addition to being a risk factor for GDM, pBMI was also associated with GDM concurrent with HDP, while GWG was a risk factor for GDM concurrent with HDP.

Discussion

During the period of pregnancy, GDM and HDP are common complications. Pregnancy itself is a physiological state of relatively high blood sugar tolerance. As gestational weeks increase, the insulin antagonists in pregnant women decrease, which reduces their ability to regulate blood sugar and easily induces diabetes [10]. There is still some uncertainty regarding the pathogenesis of HDP, which is influenced by several factors including genetics, immunity, and oxidative stress. Studies have shown that about 1/3 of patients with hypertension developed GDM during pregnancy, indicating that hyperglycemia and hypertension share a similar pathogenesis and affect each other [11]. Due to the fact that both GDM and HDP involve changes in the metabolic environment, these changes can result in abnormalities of relevant laboratory indicators in the body, which may be detected clinically. Based on the results of this study, the serum creatinine, urea nitrogen, and uric acid levels of the normal, GDM, GDM concurrent with HDP groups differed significantly, as did the body's response under different disease states. In addition, it explained the damage to organ function caused by GDM and HDP, as well as the adverse consequences of such diseases on pregnant women, and how these adverse effects affected a fetus directly or indirectly.

It is known that pregnant women with GDM are at an increased risk of gestational hypertension, oligohydramnios, premature rupture of membranes, fetal distress, and abnormal presentation during pregnancy, which all have serious adverse effects on both mother and child [6]. There is a risk of fetal growth and development disorders in pregnant women with GDM [12]. A common side effect of hyperglycemia is the overgrowth of the fetus, which results in the delivery of a large-for-

gestational-age (LGA) fetus. As LGA progresses in the later stage, obesity, diabetes, and other metabolic diseases are more likely to develop [13]. In pregnant women with HDP, the onset background is complex, including a multitude of factors, mechanisms, and pathways. It typically occurs during the second and third trimesters and within two weeks after delivery. In HDP, the central link is systemic vasoconstrictor spasms. Insufficient placental perfusion adversely affects placental function. As a result, there is fetal ischemia and hypoxia, resulting in fetal distress [14, 15]. Additionally, HDP can cause placental abruption, disseminated intravascular coagulation (DIC), and stillbirth, as well as being an important cause of perinatal maternal and infant mortality during pregnancy [16, 17]. Postpartum blood pressure in women with HDP can return to normal. However, the risk of hypertension increases significantly and may last for more than 20 years or even longer [18]. According to this study, the gestational age, neonatal birth weight, and neonatal Apgar score in GDM concurrent with HDP group were lower than that in normal pregnancy group and GDM group, which confirmed that the adverse effects of GDM and HDP on pregnancy were consistent with other clinical studies.

In the present day, as standards of living continue to improve and people expect more from their offspring, people pay more attention to nutritional supplements before and during pregnancy. Unreasonable energy supplies have led to the increase of obese in the women before pregnancy and gaining excessive weight during pregnancy. It has been reported in some regions of China that the proportion of pregnant women who gained excessive weight during pregnancy was as high as 48.7-50.9% [19]. There are, however, a significant number of pregnant women who are unaware of the seriousness of this issue. The serum of overweight or obese individuals is over expressed with inflammatory factors such as TNF, IL-6, and CRP. There is evidence that these inflammatory markers are associated with cardiovascular and metabolic diseases [20]. In addition, high blood lipid levels can lower the body's ability to compensate for the physiological increase in insulin resistance that occurs during pregnancy [21]. As a result, obesity is associated with an increased risk of diabetes in pregnant women [22], and excessive weight gain can exacerbate diabetes symptoms [23]. It has also been established that excessive weight gain during pregnancy increases the incidence of pregnancy complications such as GDM and HDP, as well as postpartum obesity [24-26]. During pregnancy, excessive weight gain may result in fetal growth restriction, low birth weight, and preterm delivery. According to this study, with an increase in pBMI value, the risk of GDM and GDM concurrent with HDP increased. In contrast, in groups with insufficient GWG and excessive increases, the risks of GDM and GDM concurrent with HDP were higher than that in group with moderate increases. Despite this, the results of the current studies are inconsistent. Based on the study by Wang, *et al*., it was concluded that the incidence of GDM in individuals with insufficient weight gain during pregnancy was higher than that in individuals with moderate weight gain, whereas the incidence of GDM in individuals with excessive weight gain was lower than that in individuals with moderate weight gain [27]. According to Feng, *et al*., individuals with excessive weight gain were more likely to develop GDM than those with moderate weight gain [28], which was consistent with the findings of this study.

According to logistic regression analysis, it was determined that pBMI was a risk factor for GDM, while pBMI and GWG were risk factors for GDM concurrent with HDP, which confirmed that unreasonable pBMIs and weight gains during pregnancy could lead to gestational diabetes and hypertension, and could negatively impact both mothers and their children. During pregnancy, pregnant women suffer serious damage to their organs that may affect their quality of life for the rest of their lives. There will be adverse long-term effects on the baby as a result of macrosomia resulting from GDM pregnancy women and fetal growth restriction resulting from HDP pregnancy women. It has been confirmed by studies that an

appropriate birth weight reduces the risk of chronic diseases later in life and may also have benefits for the individuals' health for the remainder of their lives [29]. Therefore, the suggestions for women of childbearing age to actively prepare for pregnancy, control pre-pregnancy BMI, and maintain moderate weight gains during pregnancy can effectively reduce the risk of gestational diabetes and hypertension, and further, reducing the occurrence of pregnancy complications. Pregnancy weight management has an important positive effect on pregnancy outcomes.

Acknowledgments

This study was supported by the project of “The hospital-level topic of Maternal and Child Health Care Hospital of Shandong province: An investigation of the relationship between RDW, SOD, CysC, and hypertensive disorders during pregnancy.” (Project number: 2021SFF056).

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