

Original Article

Blood glucose related to pregnancy induced hypertension syndrome

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Abstract: Background: To investigate the incidence of hyperglycemia caused by abnormal glucose metabolism during pregnancy and the relationship between abnormal glucose metabolism and pregnancy induced hypertension (PIH). Methods: 734 pregnant females were assigned into the PIH group (n=284) and the normal group (n=304). We examined fasting blood glucose (FBG), 1 hour postprandial blood glucose, 2-hour postprandial blood glucose, fasting insulin (FINS), 1 hour postprandial insulin, 2 hour postprandial insulin, triglyceride (TG), total cholesterol (TC), Hemoglobin A1c (HbA1c) and Insulin sensitivity index (ISI), at the same time, we recorded the SBP, DBP, BMI of each pregnant women. Results: The fasting blood glucose, 1 hour postprandial blood glucose and 2 hours postprandial blood glucose in the PIH group were higher than those in the normal group ($P<0.05$). And insulin sensitivity index and hemoglobin A1c (HbA1c) in the PIH group was statistically significant compared with the normal group during 24-28 weeks of gestation. Conclusions: Our results demonstrated that abnormal glucose metabolism in second trimester may be related to higher risk of PIH, and hyperglycemia may be one of the important factors of pregnancy induced hypertension.

Keywords: Blood glucose, pregnancy induced hypertension, relationship

Introduction

Pregnancy induced hypertension syndrome (PIH) is one of the common clinical symptoms in pregnant females. It is often accompanied by obstetric hemorrhage, infection and convulsion, which is a serious threat to the health of pregnant women and fetus [1, 2]. The main physiological changes of PIH were systemic vasospasm and decreased perfusion of various organs. The main clinical symptoms were hypertension, edema and proteinuria [3]. PIH is one of the common obstetric complications which seriously threaten the health of mother and infant [4]. Unfortunately, the etiology of PIH has not been fully elucidated. Recently, a research demonstrated that in a non-diabetic people, blood pressure was higher in the high insulin group compared with that in the normal group, which indicated that blood pressure is associated with abnormal glucose metabolism [5]. Hyperglycemia can be caused by abnormal insulin secretion or dysfunction and/or tissue resistance to insulin. During pregnancy, the placenta secretes various kinds of insulin-resis-

tant hormones, which easily lead to abnormal glucose metabolism and hyperglycemia [6]. It has been found that some patients with gestational hypertension have abnormal gestational glucose tolerance or gestational diabetes mellitus [7]. However, it is unclear whether impaired gestational glucose tolerance or gestational diabetes mellitus is associated with pregnancy induced hypertension syndrome.

This study measured maternal peripheral blood glucose, insulin, glycosylated hemoglobin, and insulin sensitivity index levels to explore the relationship between hyperglycemia and pregnancy-induced hypertension (PIH), and the significance of hyperglycemia in the occurrence and development of PIH. Understanding the pathogenesis may provide theoretical basis to find new ways of prevention and treatment of PIH.

Materials and methods

Study design

The study was an observational research. This study was conducted at Jiaozhou Central

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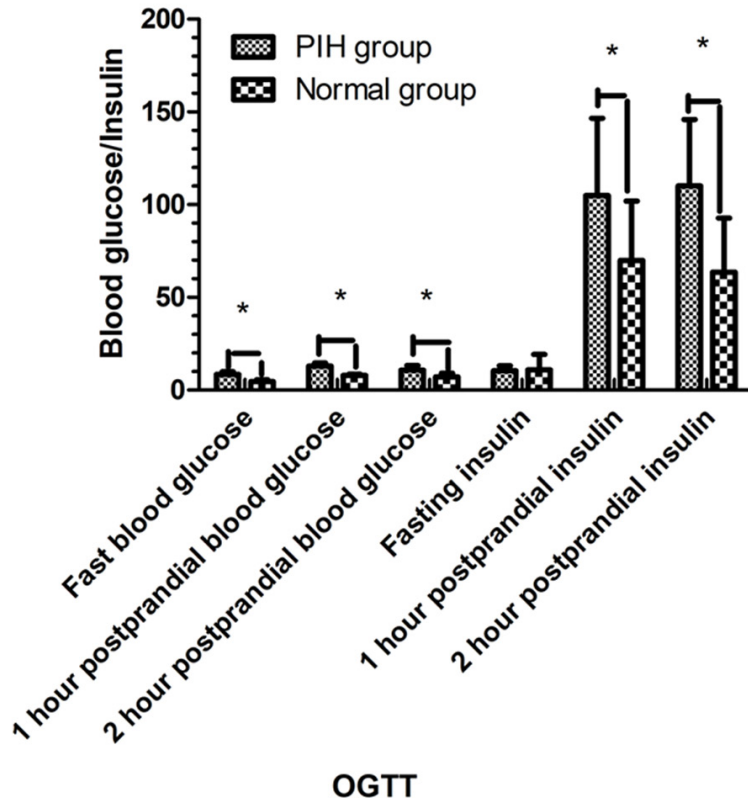


Figure 1. Comparison of OGTT between the two groups. PIH group: Pregnant induced hypertension. * $P < 0.05$.

Hospital from January 2017 and January 2020. Inclusion criteria: 1) Pregnant women who underwent antenatal examination at 24-28 weeks of gestation; 2) Pregnant women was no history of hypertension before pregnancy; 3) All pregnant females had a single fetus; 4) The subjects were willing to cooperate and implement the experiment. Exclusion criteria: 1) Had a history of mental illness; 2) Had a history of blood system diseases; 3) Had a history of chronic diseases such as diabetes, nephropathy or coronary heart disease before pregnancy; 4) Had a history of malignant tumor; 5) had not suffer from gestational diabetes before our trial. The procedures of this clinical trial are presented **Figure 1**. The researchers systematically explained the role, purpose and process of the study to the patients and their families. The patients and their families voluntarily signed the informed consent form to participate in this study. This study was approved and recognized by the ethics committee of our hospital.

Participants and subgroup

987 pregnant females were admitted to the outpatient department of Jiaozhou Central Hospital, including 734 patients meeting the inclusion and exclusion criteria. The 734 eligible patients enrolled in this study were allocated into two group: the PIH group (suffered from regnant induced hypertension) (n=284) or the normal group (healthy pregnant females) (n=304).

Interventions

Pregnant females underwent prenatal examination were screened for 75 g glucose at 24-28 weeks of gestation, that is, 75 g glucose was dissolved in 300 ml of water and drank within 5 min. before taking the glucose, no restriction was imposed on diet before taking sugar. 2 ml blood was collected from elbow vein at 1 hour after taking sugar. The glucose

value of plasma was measured by glucose oxidase method. Fasting (fasting for 8-12 h) 2 ml blood was drawn from elbow vein. The plasma glucose value was measured by serum glucose oxidase method, and the blood insulin and glycosylated hemoglobin were measured by radioimmunoassay. Meanwhile, the blood pressure of each pregnant woman was measured, and the difference of blood glucose level, insulin level and glycosylated hemoglobin level between the PIH group and the normal group without PIH was compared to explore whether the blood glucose was related to the pathogenesis of PIH. The diagnose of PIH [8]: Pregnant women were no history of hypertension before pregnancy, blood pressure $>130/90$ mmHg (1 kPa = 7.5 mmHg) after 20 weeks of gestation, or the mean arterial pressure increased more than 20 mmHg compared with baseline blood pressure, and no or accompanied with proteinuria. If there is a history of chronic hypertension before pregnancy, the mean arterial pressure after 20 weeks of gestation is more than 20

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Table 1. Comparison of clinical characteristics of pregnant females between two groups

	PIH group (n=284)	Normal group (n=304)	t/ χ^2	P
Age (years)	30±1.51	29±2.44	3.12	0.20
BMI				
BMI before pregnancy	21.1±0.83	20.65±1.19	4.28	0.19
BMI during pregnancy	22.6±1.11	21.6±1.12	7.43	0.009
Average gestational weeks	26.35±1.56	25.95±1.63	8.29	0.44
SBP (mmHg)	162.3±5.21	113.3±5.68	18.72	0.000
DBP (mmHg)	106.85±4.66	73.85±3.31	23.48	0.000
TG (mmol/L)	3.28±1.35	2.55±1.23	13.78	0.000
TC (mmol/L)	5.93±1.32	5.92±0.76	2.49	0.986
LDL (mmol/L)	3.13±1.36	3.17±0.87	3.21	0.233
HDL (mmol/L)	1.94±0.58	2.07±0.47	12.46	0.351

Note: Significant difference as $P < 0.05$. PIH group: Pregnant induced hypertension; TG, triglyceride; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density; lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Differences in OGTT between normal and PIH groups

	PIH group (n=284)	Normal group (n=304)	t/ χ^2	P
Blood glucose (mmol/L)				
Fast blood glucose	8.35±1.49	4.65±0.85	3.76	0.000
1 hour postprandial blood glucose	12.85±1.71	7.9±0.76	6.25	0.000
2-hour postprandial blood glucose	10.8±2.4	7.1±1.9	6.23	0.000
Insulin (mU/L)				
Fasting insulin	10.36±2.69	10.86±8.44	1.69	0.76
1 hour postprandial insulin	104.89±41.63	69.92±31.99	17.73	0.000
2 hour postprandial insulin	110.11±35.84	63.52±29.23	27.21	0.000

Note: Significant difference as $P < 0.05$. PIH group: Pregnant induced hypertension.

mmHg higher than that of the basic blood pressure.

Primary outcome measure

The primary outcome measure was fasting blood glucose (FBG), 1 hour postprandial blood glucose, 2 hour postprandial blood glucose, fasting insulin (FINS), 1 hour postprandial insulin, 2 hour postprandial insulin, triglyceride (TG), total cholesterol (TC), Hemoglobin A1c (HbA1c) and Insulin sensitivity index (ISI) ($= (\text{FBG} \times \text{FINS}) / 25$). At the same time, we recorded SBP, DBP, BMI of each pregnant women.

Statistical analysis

All data were analyzed by SPSS 22.0. The statistical results are expressed by mean \pm standard deviation ($\bar{x} \pm \text{SD}$), the data comparison is conducted by t-test and the correlation analysis is conducted by person linear phase, $P < 0.05$ was the difference with statistical significance.

Result

Clinical characteristics

Table 1 shown characteristics of the participants. The research included 284 pregnant females in the PIH group, a mean age (30±1.51) years old, while 304 pregnant females in the normal group, a mean age (29±2.44) years old. The BMI before pregnancy in the PIH group was (21.1±0.83) kg/m², and in the normal group was (20.65±1.19) kg/m², there was no statistical significance between two group ($P = 0.19$, > 0.05), however, the BMI during pregnancy (24-28 weeks of gestation) in the PIH group was (22.6±1.11) kg/m², and in the normal group was (21.6±1.12) kg/m², and there was statistical significance between two group ($P = 0.009$, < 0.05). The average gestational weeks in the PIH group was (26.35±1.56) weeks, and in the normal group was (25.95±1.63) weeks, there was no statistical significance between two

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Table 3. Hemoglobin A1c(HbA1c) between normal and PIH groups

Group	Number of cases	Before pregnancy	24-28 weeks of gestation
PIH group	284	5.75±1.22	8.8±1.6
Normal group	304	5.61±1.1	6.3±1.4
t	-	4.218	5.514
P	-	0.17	0.000

Note: Significant difference as $P < 0.05$. PIH group: Pregnant induced hypertension.

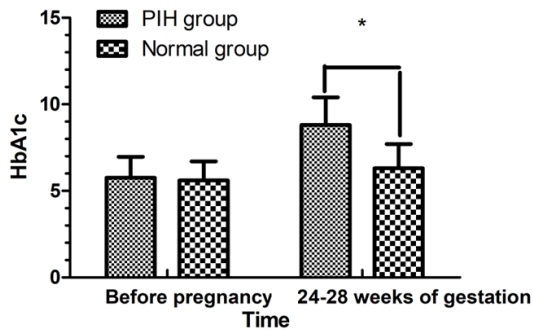


Figure 2. Comparison of HbA1c between the two groups. PIH group: Pregnant induced hypertension. * $P < 0.05$.

group ($P = 0.44$, > 0.05). The systolic blood pressure (SBP) in the PIH group was (162.3±5.21) mmHg, while in the normal group was (113.3±5.68) mmHg, and the diastolic blood pressure (DBP) in the PIH group was (106.85±4.66) mmHg, in the normal group was (73.85±3.31) mmHg, there was statistical significance of SBP and DBP between two group ($P < 0.05$). The triglyceride level (TG) in the PIH group was (3.28±1.35) mmol/L, while in the normal group was (2.55±1.23) mmol/L, and there was statistical significance between the two group ($P < 0.05$). The total cholesterol level (TC), the low-density lipoprotein (LDH) and the high-density lipoprotein (HDL) in the two groups were similar, and there were no statistical significance between two group ($P > 0.05$).

Differences in OGTT between the normal and the PIH groups

As shown in **Table 2** and **Figure 1**, the fasting blood glucose in the PIH group was (8.35±1.49) mmol/L, while that in the normal group was (4.65±0.85) mmol/L; 1 hour postprandial blood glucose and 2 hours postprandial blood glucose in the PIH group respectively were

(12.85±1.71) mmol/L and (10.8±2.4) mmol/L, and that in the normal group respectively were (7.9±0.76) mmol/L and (7.1±1.9) mmol/L, and there had statistically difference between two groups in fasting blood glucose, 1 hour postprandial blood glucose and 2 hours postprandial blood glucose ($P < 0.05$). The fasting insulin in the PIH group was (10.36±2.69) mU/L, and that in the normal group was (10.86±8.44) mU/L, there was no statistically significant between two groups (10.36±2.69) VS. (10.86±8.44), $P = 0.76 > 0.05$). While the 1 hour postprandial insulin and 2 hour postprandial insulin in the PIH group were (104.89±41.63) mU/L and (110.11±35.84) mU/L, and that in the normal group were (69.92±31.99) mU/L and (63.52±29.23) mU/L respectively. There had statistical difference between two groups in 1 hour postprandial insulin and 2 hour postprandial insulin ($P < 0.05$).

Hemoglobin A1c (HbA1c) in the normal and PIH groups

The HbA1c in the PIH group before pregnancy was (5.75±1.22), and that in the normal group was (5.61±1.1), there had no statistical difference between two groups ((5.75±1.22) VS. (5.61±1.1), $P = 0.17$). While the HbA1c in the PIH group during 24-28 weeks of gestation was (8.8±1.6), and that in the normal group was (6.3±1.4), there was statistical significantly between two group ((8.8±1.6) VS. (6.3±1.4), $P < 0.05$) (**Table 3** and **Figure 2**).

Insulin sensitivity index (ISI) in the two groups

Insulin sensitivity index in the PIH group during 24-28 weeks of gestation was (0.75±0.17), and that in the normal group was (0.62±0.37). There was statistical significance between two groups during 24-28 weeks of gestation ((0.75±0.17) VS. (0.62±0.37), $P < 0.05$) (**Table 4**).

Discussion

In our research, we indicated that fasting blood glucose (FBG), 1 hour postprandial blood glucose, 2 hour postprandial blood glucose, 1 hour postprandial insulin, 2-hour postprandial insulin, triglyceride (TG), Hemoglobin A1c (HbA1c) and Insulin sensitivity index (ISI) were higher in the PIH group compared with the normal group, and there was a statistical significance

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Table 4. Insulin sensitivity index (ISI) between normal and PIH groups

Group	Number of cases	24-28 weeks of gestation
PIH group	284	0.75±0.17
Normal group	304	0.62±0.37
t	-	6.742
P	-	0.000

Note: Significant difference as $P < 0.05$. PIH group: Pregnant induced hypertension.

between two group ($P < 0.05$). Furthermore, incidence of PIH in gestational impaired glucose tolerance or gestational diabetes was higher than that of the normal group.

Abnormal glucose metabolism is a disease caused by many factors. It is often caused by abnormal insulin secretion or islet dysfunction and/or tissue resistance to insulin, which may aggravate or cause various complications during pregnancy. In our study, hyperglycemia is an independent risk factor for PIH. It was previously reported that PIH caused by hyperglycemia may be related to the following factors [9-14]: 1) The placenta secretes various hormones that resist insulin during pregnancy, such as cortisone, progesterone, placental prolactin, prolactin, and estrogen, which cause the surrounding tissues to respond to insulin. The sensitivity of the reaction decreased. 2) Insulin resistance can lead to barriers to the membrane transport system. Through $\text{Na}^+\text{-K}^+\text{-ATPase}$, $\text{Ca}^{2+}\text{-Mg}^{2+}\text{-ATPase}$ activity decreases, and intracellular Ca^{2+} increases through $\text{Na}^+\text{-K}^+$, $\text{Na}^+\text{-Ca}^{2+}$ exchange. At the same time, with the increase of insulin growth factor effect, vascular smooth muscle cell proliferation increases, resulting in vascular stenosis, increased vascular resistance, resulting in increased blood pressure and impaired left ventricular diastolic function. 3) During pregnancy, renal gluconeogenesis increased, glucose was up-taken by muscle and fat decreased, glycogen and gluconeogenesis of liver were inhibited, blood glucose level increased, renal sodium reabsorption increased and blood volume increased. 4) The islet function in vivo is absolutely or relatively insufficient, and the reserve function of insulin is poor. Our research showed that fasting blood glucose (FBG), 1 hour postprandial blood glucose, 2 hour postprandial blood glucose, 1 hour postprandial insulin, and 2-hour

postprandial insulin were higher in the PIH group, and the incidence of PIH increased significantly, which demonstrated that there was a certain relationship between gestational hyperglycemia and pregnancy induced hypertension. We speculate that the blood insulin level of pregnant women with hyperglycemia is higher. The high level of insulin in blood can promote the increase of renal sodium reabsorption and blood volume. Meanwhile, it can also enhance the response of small blood vessels in the whole body to sympathetic nerve excitation, which makes pregnancy induced hypertension more likely. Excessive insulin can also promote the proliferation of vascular smooth muscle cells, resulting in vascular stenosis, increased vascular resistance and increased blood pressure, in addition, hyperinsulinemia can stimulate sympathetic nerve, strengthen its excitability, and thus lead to high blood pressure.

In addition, the patients with high hemoglobin A1c (HbA1c) are also prone to PIH. Our results are consistent with the results reported by combs et al. [15] that the incidence of PIH in patients with increased HbA1c is about during 14-20 weeks of gestation. Some researches believed that the increase of hemoglobin A1c (HbA1c) is related to the occurrence of microvascular disease [16], which may play a certain role in the pathogenesis of pregnancy induced hypertension.

The course of diabetes mellitus and blood glucose control before pregnancy are closely related to the occurrence of preeclampsia. Some studies have shown that the more serious the abnormal degree of glucose metabolism is, the more serious the systemic small vessels are involved, which leads to the increase of preeclampsia [17-19]. It can be seen that the importance of blood glucose control in patients with abnormal glucose metabolism and PIHD during pregnancy. Therefore, it is necessary to screen diabetes in prenatal examination to guide the diet of pregnant women with abnormal glucose metabolism, monitor blood glucose, and if necessary, exercise therapy and insulin therapy should be used to control blood glucose level, improve insulin resistance and reduce the incidence of PID in pregnant women with abnormal glucose metabolism in pregnancy [20]. Because the glucose screening is carried out in the second trimester of pregnancy,

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PID usually occurs in the second trimester of pregnancy. Therefore, pregnant women with abnormal glucose metabolism need more intensive follow-up and more examination. 24-hour ambulatory blood pressure monitoring should be carried out to detect PID earlier.

In summary, this study provides preliminary evidence that hyperglycemia may be one of the important factors of pregnancy induced hypertension. Therefore, effective measures should be taken as early as possible in the second trimester of pregnancy in order to improve the insulin sensitivity of patients and reduce the occurrence of PIH. And further researches are needed to investigate the possible mechanism between hyperglycemia and pregnancy induced hypertension.

Disclosure of conflict of interest

None.

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