CORRELATION BETWEEN SERUM SEX HORMONE LEVEL, ISLET FUNCTION LEVEL AND GLUCOSE AND LIPID METABOLISM IN PATIENTS WITH GESTATIONAL DIABETES MELLITUS

Maohua Ren[1,*], Linxiao Fan[1], Xiaoling Meng[2]
[1]Department of Obstetrics, Shanxi People's Hospital, Taiyuan, PR China - [2]Department of Pediatrics, Shanxi Children's Hospital, Taiyuan, PR China

ABSTRACT

Objective: *To investigate the correlation between serum sex hormone level, islet function level and glycolipid metabolism in patients with gestational diabetes mellitus.*

Methods: *From August 2018 to October, 2019, 56 cases of gestational diabetes mellitus were randomly selected in the obstetrics and gynecology department of our hospital for our experimental group. In addition, another 56 cases of pregnant women with clean bills of health during the same period were selected as our control group. Next, we compared the basic clinical data of patients in each group. The levels of estrogen and progesterone in the two groups of pregnant women were determined through an enzyme-linked immunosorbent assay. Fasting insulin (FINS) levels in the two groups were determined by a double anti-centering method. The fluctuations in the insulin resistance index (IRI), insulin sensitivity index (ISI) and islet β cell secretion function (HOMA-β) were determined according to the formula. The changes of fasting blood glucose (FBG) and glycosylated hemoglobin (HbA1c) levels in the two groups of pregnant women were determined by the chemiluminescence method. The serum lipid index (total cholesterol [TC], triglyceride [TG], low-density lipoprotein [LDL], and high-density lipoprotein [HDL]) levels were measured in these women using an automatic biochemical analyzer. Following this, the Pearson correlation test was used to analyze the correlation between serum sex hormone level, islet function level, and glycolipid metabolism in patients with gestational diabetes mellitus.*

Results: *Compared with the normal group, the levels of estrogen, progesterone, FINS, IRI, FBG, HbA1c, TC, TG, and LDL in the study group were significantly increased, and the ISI, HOMA-β, and HDL levels were significantly decreased. The Pearson correlation analysis showed that estrogen and progesterone were positively correlated with serum FINS, IRI, FBG, HbA1c, TC, TG, and LDL levels and negatively correlated with ISI, HOMA-β, and HDL levels (P<0.05).*

Conclusion: *The serum sex hormone, islet function, and metabolic levels of soup juice in patients with gestational diabetes mellitus were obviously abnormal compared with those in the control group of pregnant women. The former patients' levels displayed obvious correlation, which could be used as an important index by which to judge the severity of gestational diabetes mellitus patients.*

Keywords: *Gestational diabetes mellitus, sex hormone level, islet function level, glucose and lipid metabolism, correlation.*

DOI: 10.19193/0393-6384_2021_5_453

Received *March 15, 2020;* ***Accepted*** *October 20, 2020*

Introduction

Gestational diabetes mellitus refers to the first occurrence or discovery of abnormal glucose metabolism during pregnancy, which is one of the most common complications for women during pregnancy. With the development of social science and technology, medical diagnosis technology and standards of living are constantly improving, but the incidence of gestational diabetes mellitus has also been increasing every year[(1)]. According to statistics, the incidence of gestational diabetes in China is about 1-4%[(2)]. At present, the pathogenesis of gestational diabetes mellitus is unclear, though it is considered to be closely related to many factors, such as insulin resistance, insulin secretion deficiency, chronic

inflammatory reaction, abnormal immune function, and so forth[3]. Pregnant women with gestational diabetes mellitus are prone to complications such as gestational hypertension syndrome, amniotic fluid excess, infection, and ketoacidosis. In addition, the possibility of diabetes mellitus or metabolic syndrome after delivery is significantly higher than for nondiabetic pregnant women[4].

If a pregnant woman's blood sugar remains uncontrolled for a long time, this will lead to chronic intrauterine hypoxia, abnormal growth and development, and malformation. Moreover, after leaving this high-sugar environment, a newborn will often have hypoglycemia, which seriously threatens the health and even the lives of the pregnant woman and the fetus[5]. Therefore, early diagnosis, early intervention, and timely control of maternal blood glucose levels to reduce complications during delivery promote fetal and infant growth and development are crucial. In this study, the serum levels of sex hormones, islet function, and glycolipid metabolism were monitored, and their correlation was analyzed.

Materials and methods

Basic information

Fifty-six patients with gestational diabetes treated in the department of obstetrics and gynecology of our hospital from August 2018 to October 2019 were randomly selected.

The following were inclusion criteria:

• All patients met the diagnostic and treatment criteria for gestational diabetes[6], confirmed by positive oral glucose tolerance tests;

• Patients had fasting blood glucose over 7.0mmol/L;

• The research of this group was approved by the ethics committee of the hospital and conformed to medical ethics;

• The patients and their family members signed informed consent forms;

• Patients had complete medical records and were able to cooperate with prescribed treatments.

On the other hand, the following were exclusion criteria:

• Patients had preexisting diabetes symptoms, such as polyphagia, polyuria, and weight loss;

• Diabetes was accompanied by mental illness, so patients were unable to cooperate with treatment;

• Patients presented with hepatitis B, AIDS, or other infectious diseases;

• Diabetes was combined with incomplete cardiac, liver, and/or kidney function.

In addition, fifty-six healthy pregnant women who underwent physical examination in our hospital at the same time were selected as the control ("normal") group.

Experimental instruments

The following instruments were employed: a -80 °C ultralow-temperature refrigerator (Beijing Elisa Biotechnology Co., LTD., specification: DW-86L626); a low-temperature, high-speed centrifuge (Shanghai Luxiangyi Centrifuge Instrument Co., LTD., model no.: TGL-17M); a full automatic biochemical analyzer (Neusoft Wittman Biological Technology (Nanjing) Co., LTD., model no. NT480); an Omron glucose meter (Daltai [Tianjin] Industrial Co., LTD., model: HEA-230); an estrogen Elisa kit (Shanghai Jingkang Biological Engineering Co., LTD.); and a progesterone enzyme-linked immunoassay kit (Shanghai Fusheng Industrial Co., LTD.).

Observation indicators

All subjects were forbidden to drink and fasted for more than eight hours before and after admission, and 5mL of venous blood was extracted from each patient at the middle of the hollow of the elbow on the morning on the following day. A cryogenic high-speed centrifuge was used to centrifuge blood samples at the speed of 1500r/min after standing. After this, the supernatant was taken and stored in the refrigerator at -80 °C for subsequent studies.

The basic clinical data from each group were compared, including age, gestational age (at the time of initial diagnosis and the time of delivery), body mass index (before and during pregnancy), blood pressure (systolic and diastolic), number of pregnancies, number of births, and neonatal weight.

Serum sex hormone levels were taken, and the levels of estrogen and progesterone were determined by enzyme-linked immunosorbent assay.

Determination of islet function

This study adopted the double clamp method to determine each woman's fasting insulin resistance (FINS) level. This method determined each woman's insulin resistance index (IRI)—IRI = Fasting blood glucose (FBG) × FINS/22.5); insulin sensitive index (ISI)—ISI = In(22.5/[FBG×FINS]); and the function of islet β cells (HOMA-β)—HOMA-β = 20×FINS/(FBG-3.5).

Determination of glucose and lipid metabolism

FBG and Glycosylated hemoglobin A1c (HbA1c) levels in pregnant women in the two groups were determined by chemiluminescence. Serum lipid levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were measured with an automatic biochemical analyzer.

Correlation analysis

The Pearson correlation test was used to analyze the correlation between serum sex hormone level, pancreatic islet function level, and glucose and lipid metabolism in patients with gestational diabetes.

Statistical methods

All of the count data in this study were compared with an χ^2 test, and a t test was used to compare the measurement data of sex hormone levels, pancreatic islet function levels, and glucose and lipid metabolism levels.

The levels of estrogen and progesterone were determined through an enzyme-linked immunosorbent assay. The FINS levels of the two groups of pregnant women were determined by a double anti-clamping method.

The levels of FBG and HbA1c were determined by chemiluminescence.

The serum lipid levels of TC, TG, LDL, and HDL were measured with an automatic biochemical analyzer. The Pearson correlation test was used to analyze the correlation between serum sex hormone level, islet function level, and glycolipid metabolism in patients with gestational diabetes.

In this study, SPSS20.0 software was used for statistical data analysis, and the statistical results for P<0.05 were considered to be statistically significant.

Results

Comparison of basic data of pregnant women in the two groups

There was no statistically significant difference in the age, gestational weeks, or other basic clinical data between the two groups (P>0.05) (see Table 1).

Comparison of serum sex hormone levels between the two groups

Compared with the normal group, the levels of estrogen and progesterone in the study group were significantly increased (P<0.01). The results are shown in Table 2.).

Group	Study (n=56)	Normal (n=56)	χ^2/t	*P*
Age (year)	30.14±1.96	29.48±2.43	1.582	0.117
Gestational (week)				
Initial diagnosis	26.45±1.22	26.57±1.42	0.480	0.632
Delivery	38.99±1.12	39.21±0.98	1.106	0.271
Body mass index (kg/m^2)				
Pregnancy	22.63±1.32	22.33±1.22	1.249	0.214
Late pregnancy	30.21±1.62	29.55±2.32	1.746	0.084
Blood pressure (mmHg)				
Systolic blood pressure	117.96±13.31	119.11±14.21	0.442	0.659
Diastolic blood pressure	73.16±10.86	74.51±9.42	0.703	0.484
Pregnancy (times)	1.58±0.75	1.63±0.82	0.337	0.737
Parity (times)	1.02±0.39	1.07±0.35	0.714	0.477
Newborn weight (kg)	3.69±1.11	3.18±1.78	1.819	0.072

Table 1: Comparison of basic data of pregnant women in the two groups.

Group	Case (n)	Estrogen (pg/mL)	Progesterone (pg/mL)
Study	56	6514.83±2101.59	108.74±33.47
Normal	56	2271.66±733.48	2.06±0.67
t		14.265	23.847
P		<0.001	<0.001

Table 2: Comparison of serum sex hormone levels between two groups of pregnant women ($\bar{x}\pm s$).

Comparison of islet function between the two groups

Compared with the normal group, the levels of FINS and IRI in the study group were significantly increased, and the levels of ISI and HOMA-β were significantly decreased (P<0.01) (see Table 3).

Group	Case (n)	FINS (mU/L)	IRI	ISI	HOMA-β
Study	56	16.14±0.57	3.99±0.66	-1.44±0.45	179.17±49.33
Normal	56	11.99±0.67	2.38±0.29	-0.81±0.26	488.36±146.85
T		35.304	16.712	9.071	14.936
P		<0.001	<0.001	<0.001	<0.001

Table 3: Comparison of islet function between the two groups ($\bar{x}\pm s$).

Comparison of glucose and lipid metabolism between the two groups

Compared with the normal group, FBG, HbA1c, TC, TG, and LDL levels in the study group were significantly higher, while HDL levels were significantly lower (P<0.01) (see Table 4).

Group	Case (n)	FBG (mmol/L)	HbA1c (%)	TC (mmol/L)	TG (mmol/L)	LDL (mmol/L)	HDL (mmol/L)
Study	56	5.19±0.63	5.53±0.52	4.64±0.49	6.69±0.76	3.42±0.39	1.53±0.18
Normal	56	4.33±0.52	5.02±0.42	3.29±0.43	5.31±0.67	2.71±0.32	1.69±0.22
T		7.878	5.710	15.497	10.193	10.532	4.212
P		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 4: Comparison of glucose and lipid metabolism between the two groups ($\bar{x}\pm s$).

Correlation analysis between serum sex hormone level, pancreatic islet function level, and glucose and lipid metabolism in patients with gestational diabetes

According to the Pearson correlation analysis, estrogen and progesterone were significantly positively correlated with serum FINS, IRI, FBG, HbA1c, TC, TG, and LDL levels and negatively correlated with ISI, HOMA-β and HDL levels ($P<0.05$), as shown in Table 5.

Indicator	Progesterone		Estrogen	
	r	*P*	*R*	*P*
FINS	0.641	<0.05	0.665	<0.05
IRI	0.729	<0.05	0.746	<0.05
ISI	-0.717	<0.05	-0.733	<0.05
HOMA-β	-0.753	<0.05	-0.784	<0.05
FBG	0.630	<0.05	0.656	<0.05
HbA1c	0.538	<0.05	0.587	<0.05
TC	0.689	<0.05	0.231	<0.05
TG	0.706	<0.05	0.196	<0.05
HDL	-0.584	<0.05	-168	<0.05
LDL	0.714	<0.05	0.113	<0.05

Table 5: Correlation between serum sex hormone levels, pancreatic islet function levels, and glucose and lipid metabolism in patients with gestational diabetes mellitus.

Discussion

Gestational diabetes mellitus is a common pathology with abnormal endocrine levels during pregnancy, threatening the health of both the pregnant woman and the fetus. It can lead to energy function disorder, which can cause spontaneous abortion, fetal malformation, neonatal hypoglycemia, or ketoacidosis, in which insulin resistance is a key issue[7]. Some studies have found[8] that offspring of patients with gestational diabetes are more likely to suffer from obesity, abnormal glucose tolerance, and even diabetes in adolescence. With poor blood glucose control, the incidence of complications during delivery or fetal or infant complications significantly increases. Obviously, when the pregnant woman's blood sugar control is good, the newborn's birth weight and chance of developing hypoglycemia or macrosomia are lower than those of pregnant women with poor blood sugar control.

Therefore, early diagnosis, early screening, and early intervention are crucial for improving the prognoses of patients with gestational diabetes mellitus, effectively reducing the obstetric complications of parturient women, and promoting the growth and development of fetuses and newborns. For these reasons, this study aimed to investigate the correlation between serum sex hormone levels, islet function levels, and glycolipid metabolism in patients with gestational diabetes mellitus. Sex hormones are essential components to the female reproductive system, and they include estrogen and progesterone, which together play an important role in the maintenance of early pregnancy. For instance, progesterone can reduce the excitability of uterine fibers and the sensitivity of a pregnant[9] uterus to oxytocin, reduce uterine contraction, and inhibit maternal immune responses, all beneficial to the growth and development of an embryo in the uterus. In addition, the endometrium is then rich in nutrients and conducive to the implantation of fertilized eggs.

Moreover, progestin may be a necessary immunomodulator in early pregnancy, since progestin can inhibit the maternal immune response to fetal antigen and the maternal rejection of trophoblast. At the beginning of pregnancy, estrogen levels can reflect the quality of dominant follicles and the function of the ovarian luteal body. In the human syncytiotrophoblast, estrogen can increase progesterone formation by increasing LDL uptake[10]. In this vein, the results of this study showed that the levels of estrogen and progesterone in the study group were significantly higher than those of the normal group. Therefore, these abnormal estrogen and progesterone levels may be closely related to the occurrence and development of gestational diabetes mellitus.

Insulin resistance refers to the decrease in insulin sensitivity of insulin target tissues (skeletal muscle, adipose tissue, liver, etc.); the decrease of glucose utilization; and the decrease of the effect of inhibiting hepatic glucose output. The latter is mainly manifested in the decrease of the binding of

insulin to the membrane receptors of pawn cells and the decrease of intracellular information conduction disorder after economic and receptor binding[11]. A high concentration of sex hormones can increase insulin resistance and decrease ISI[12].

By affecting the translocation and absorption of glucose carrier 4 in skeletal muscle and adipose tissue, estrogen can protect islet β cells from injury, increase insulin biosynthesis, and increase the sensitivity of islet cells to glucose-stimulating insulin secretion. Furthermore, for insulin receptor-depleted islet cells or pretreatment of islet β cells using estrogen receptor antagonists, insulin secretion was significantly reduced[13]. FINS, IRI, ISI, HOMA-β, and other patients in the study group were involved in the occurrence and development of gestational diabetes mellitus, which was significantly related to sex hormone levels, as was also shown in a study by Tan et al.[14]. Abnormal glucose and lipid metabolism are the most important clinical manifestations in patients with gestational diabetes mellitus. As gestation continues, the average of glycolipid metabolic water in patients may abnormally vary. When a patient in this study developed gestational diabetes mellitus, the insulin sensitivity of that patient would decrease significantly, whereas fasting blood glucose would gradually increase[15].

In addition, the results of this study showed that the FBG, HbA1c, TC, TG, and LDL levels of patients in the study group were significantly higher than those of the normal group, and the former group's HDL levels were significantly lower than those of the normal group. This may be the case for gestational diabetes patients with increased insulin resistance, blood glucose levels, and FINS levels. In such patients in this study the islet β cell function later weakened., and abnormal blood sugar levels were aggravated and insulin secretion function deteriorated, thus exacerbating gestational diabetes mellitus[16].

In summary, the serum sex hormone, islet function, and soup juice metabolism levels in gestational diabetes mellitus patients were abnormal compared with those of normal pregnant women. These levels displayed obvious correlations, which could be collectively used as an important index to judge the severity of gestational diabetes mellitus.

References

1) Rowan JA, Rush EC, Plank LD, Lu J, Obolonkin V, et al. Metformin in gestational diabetes: The offspring follow-up (MiG TOFU). BMJ Open Diabetes Res Care. 2018; 73: 565-567.
2) Lee KH, Han YJ, Chung JH, Kim MY, Ryu HM, et al. Treatment of gestational diabetes diagnosed by the IADPSG criteria decreases excessive fetal growth. Obstet Gynecol Sci. 2020; 63: 19-26.
3) Falcone V, Stopp T, Feichtinger M, Kiss H, Eppel W, et al. Pregnancy after bariatric surgery: A narrative literature review and discussion of impact on pregnancy management and outcome. BMC Pregnancy Childbirth. 2018; 18: 507.
4) Nahavandi S, Price S, Sumithran P, Ekinci EI. Exploration of the shared pathophysiological mechanisms of gestational diabetes and large for gestational age offspring. World J Diabetes. 2019; 10: 333-340.
5) Silva-Zolezzi I, Samuel TM, Spieldenner J. Maternal nutrition: Opportunities in the prevention of gestational diabetes. Nutr Rev. 2017; 75: 32-50.
6) Floriano JF, Willis G, Catapano F, Lima PR, Reis FVDS, et al. Exosomes could offer new options to combat the long-term complications inflicted by gestational diabetes mellitus. Cells. 2020; 9: 675.
7) Koivusalo SB, Rönö K, Klemetti MM, Roine RP, Lindström J, et al. Gestational diabetes mellitus can be prevented by lifestyle intervention: The Finnish gestational diabetes prevention study (RADIEL). Diabetes Care. 2017; 40: 1133.
8) Kuo CH, Li HY. Diagnostic strategies for gestational diabetes mellitus: Review of current evidence. Curr Diab Rep. 2019; 19: 155.
9) Hu S, Ma S, Li X, Tian Z, Liang H, et al. Relationships of SLC2A4, RBP4, PCK1, and PI3K gene polymorphisms with gestational diabetes mellitus in a Chinese population. Biomed Res Int. 2019; 2019: 7398063.
10) Tsiotra PC, Halvatsiotis P, Patsouras K, Maratou E, Salamalekis G, et al. Circulating adipokines and mRNA expression in adipose tissue and the placenta in women with gestational diabetes mellitus. Peptides. 2018; 101: 157-166.
11) Onalan E, Gozel N, Donder E. Can hematological parameters in type 2 diabetes predict microvascular complication development? Pak J Med Sci. 2019; 35: 1511-1515.
12) Kamon T, Kaneko H, Itoh H, Kiriyama H, Mizuno Y, et al. Gender-specific association between the blood pressure category according to the updated ACC/AHA guidelines for hypertension and cardio-ankle vascular index: A community-based cohort study. J Cardiol. 2020; 75: 578-582.
13) Sun GY. Changes and significances of isletβ-cell function, oxidative stress and adipocyte factor in gestational diabetes mellitus. J Hainan Med Univ. 2016;22:92–94.
14. Tan J, Jiang SL. Changes of serum sex hormone levels in patients with gestational diabetes mellitus and their effects on glucose metabolism and islet function. Guizhou Med. 2019; 43: 1127-1129.
15) Xu L, Xu K, Wu Z, Chen Z, He Y, et al. Pioglitazone attenuates advanced glycation end products-induced

apoptosis and calcification by modulating autophagy in tendon-derived stem cells. J Cell Mol Med. 2020; 24: 2240-2251.

16) Tabrizi R, Moosazadeh M, Lankarani KB, Akbari M, Heydari ST, et al. The effects of symbiotic supplementation on glucose metabolism and lipid profiles in patients with diabetes: A systematic review and meta-analysis of randomized controlled trials. Probiotics Antimicrob Proteins. 2018; 10: 329-342.

Corresponding Author:
Maohua Ren
Email: jj245y@163.com
(China)