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Study on the Correlation between the Expression of Serum Ferritin and Gestational Diabetes Mellitus

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Abstract

Objective: To explore the relationship between serum ferritin (SF) and gestational diabetes mellitus (GDM), for providing new ideas to the prevention and treatment of GDM. ***Methods***: All the pregnant women were selected in Yinan Maternal and Child Health-Care Hospital from December, 2015 to March, 2018 when they were having routine prenatal examination, According to the diagnostic criteria of GDM, 72 patients with GDM were selected as the case group and 72 normal pregnant women were randomly selected as the control group. Fasting venous blood was drawn from all subjects during the first trimester of pregnancy (11 - 13 weeks) and the second trimester of pregnancy (24 - 28 weeks). Fasting plasma glucose was measured by glucose oxidase assay and the expression level of SF was determined by electrochemical method. The application value of SF in GDM diagnosis was evaluated by ROC curve. ***Results***: The levels of SF in the case group at early and middle stages are 49.6 ± 18.8 (μg/ml) and 39.8 ± 21.5 (μg/ml), which re 39.4 ± 15.2 (μg/ml) and 32.2 ± 17.6 (μg/ml) in the control group. The levels of SF in the case group were higher than those in the control group ($p < 0.05$) at early and middle stages. The curve (AUC) of SF level in the diagnosis of GDM was 0.895, $p < 0.001$; the Youden index was 0.651 and the optimum threshold was 38.6 ng/ml, with a sensitivity of 97.8% and a specificity of 67.3%. ***Conclusion***: The expression level of SF in early pregnancy is correlated with the occurrence of GDM, which may be an important indicator for the prevention and monitoring of GDM.

Keywords

Serum Ferritin, Gestational Diabetes Mellitus, Correlation

1. Introduction

The gestational diabetes mellitus (GDM) refers to different degrees of hyperglycemia resulting from abnormal glucose tolerance and diabetes during the gestation period, but the glycometabolism is normal before gestation. According to the report, the morbidity of GDM in China has reached 18.9% in 2014, and tends to have a significant growth due to the influences of many factors such as age of the pregnant woman [1]. We shall pay high attention to pregnant women with GDM because the glycometabolism may result in many adverse outcomes such as infection, premature birth, and dystocia due to its complex process and high risk [2] [3]. Many researchers have indicated that increase of iron element level in serum can result in changes in the blood glucose and have a correlation with insulin resistance [4] [5]. Serum ferritin (SF) is one of the proteins with the highest iron content in the body. It can directly reflect the iron reserves in the body and is a sensitive indicator for evaluating iron deficiency or overload. In recent years, studies have found that abnormal iron metabolism is closely related to the occurrence and development of T2DM. Related, high SF level is an independent risk factor for T2DM. The serum ferritin (SF) is an important index that reflects the content of iron element in body, while high levels of serum iron significantly increase the risk of GDM [6]. At present, there are few researches about correlation between SF and GDM; therefore, we have measured SF expression level at early and middle pregnancy and discussed its correlation with GDM in this research, laying theoretical foundation for early prevention and clinical treatment for GDM.

2. Data and Methods

2.1. General Data

We have selected 72 pregnant women with GDM who have made routine examination in obstetrical department of Hospital from December 2015 to March 2018 as a case group, and randomly selected 72 normal pregnant women as a control group. These pregnant women with GDM must be diagnosed strictly in accordance with Standards for GDM Diagnosis issued by the American Diabetes Association (ADA) in 2013 [7] and selected as GDM group during the second trimester (24^{th} to 28^{th} week). Besides, all objects must sign the Informed Consent Form. The exclusion standards include definite diagnosis of GDM during progestational period, anemia during gestation, ferro-therapy, and trauma, etc.

2.2. SF Measurement

We have drawn venous blood of all pregnant women with an empty stomach during the first trimester (11^{th} to 13^{th} week) and the second trimester (24^{th} to 28^{th} week) to measure SF and blood glucose concentration respectively with DXI800 automatic immune diagnosis device (Beckman, USA). All operations have been made strictly in accordance with general SOPs.

2.3. Statistical Treatment

We have used the software SPSS20.0 for statistical analysis; denoted measurements by "mean + standard deviation" ($\bar{x} \pm s$) and enumeration data by utilization ratio; conducted t-test for mean comparison and χ^2 test for comparison between above two groups; and evaluated value of SF in diagnosing early GDM by ROC (receiver operating characteristic curves). $P < 0.05$ indicates statistical difference.

3. Results

3.1. General Data Comparison

See Table 1. The comparison between the case group and the control group in age, number of pregnancies, gestational weeks, and BMI of pregnant women indicates no statistical difference ($P > 0.05$).

3.2. Comparison between the Case Group and the Control Group in SF (μg/ml) Level in Different Periods of Pregnancy

See Table 2. According to the comparison between the case group and the control group in SF expression level of peripheral blood (PB) in different periods of pregnancy, SF of the case group is higher than the control group, indicating statistical difference ($p < 0.05$).

3.3. Analysis for ROC between SF and GDM in Different Periods of Pregnancy

We have used ROC for analyzing values of clinical diagnosis for GDM, as shown in Figure 1. The AUC in diagram of ROC between SF and GDM at the first

Table 1. Comparison between the case group and the control group in general data ($\bar{x} \pm s$).

Groups	N	Age (years)	Week	Times	BMI (Kg/m^2)
Case Group	72	29.86 ± 3.68	12.56 ± 1.18	1.95 + 0.50	23.15 ± 7.28
Control Group	72	29.01 ± 4.12	12.21 ± 1.25	2.0 + 0.75	21.18 ± 5.21
t		1.382	0.862	0.49	0.156
p		0.151*	0.560*	0.624*	0.916*

Notes: *: $p > 0.05$ indicates no statistical difference compared to the control group.

Table 2. Comparison between the case group and the control group in SF (μg/ml) level in different periods of pregnancy.

Groups	N	11 - 13 Week	24 - 28 Week
Case Group	72	49.6 ± 18.8	39.8 ± 21.5
Control Group	72	39.4 ± 15.2	32.2 ± 17.6
t		8.260	2.366
p		0.010*	0.025*

Notes: *: $p < 0.05$ indicates statistical difference compared to the control group.

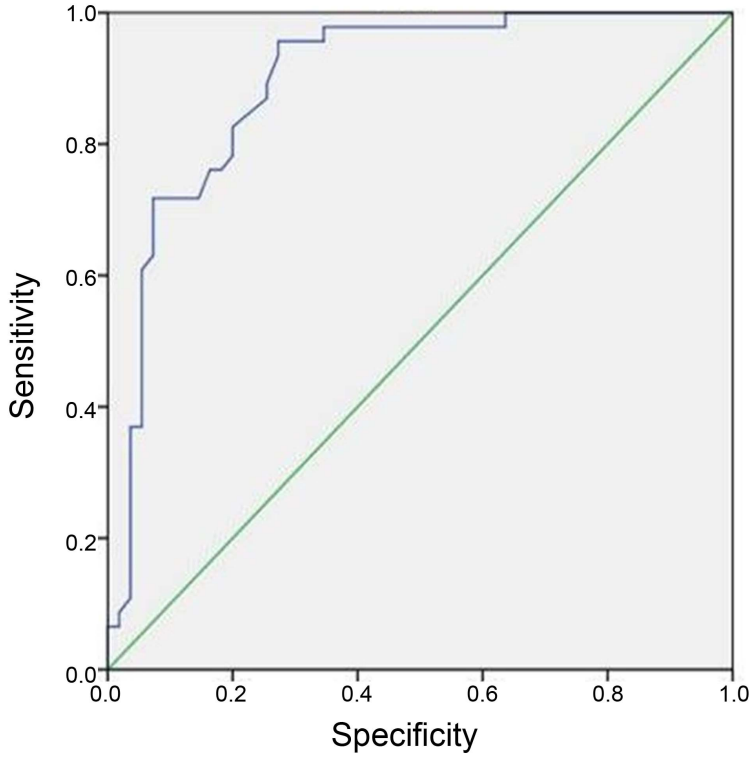

Figure 1. Analysis for ROC between SF and GDM in different periods of pregnancy.

trimester is 0.895 ($p < 0.001$). In ROC, Youden index is 0.651 and SF critical value is 38.6 ng/ml; meanwhile, values of sensitivity and specificity are 97.8% and 67.3% respectively.

4. Discussion

GDM is one of frequent complications in obstetrics department, of which pathogenesis has not been explained completely. Many researches indicate that pathogeny of GDM is influenced by numerous factors, including familial inheritance, insulin resistance, metabolic and autoimmune disorders, and some risk factors such as age, weight, and obesity of pregnant women [8] [9] [10]. There is no significant difference between GDM case group and control group in age, the number of pregnancies, gestational weeks, and BMI of pregnant women, but significant difference in SF expression level, indicating possibly high correlation between SF and pathogeny of GDM.

With complex structure, SF is large-scale colloid ferrous globulin which is not only a major ferrous storage globulin in body, but also an important means of transport for Fe. At present, pathogenesis has not been explained completely, but many researchers have indicated that SF plays an important role in the pathogenic process of GDM. According to the research, as Fe level in the body of a pregnant women increases, morbidity of GDM also increases, which may be based on the inflammatory reaction. Besides, there is a significant correlation between SF and inflammatory factor in expression level [11] [12]. Expressions

between SF and inflammatory factor are mutually stimulated, where inflammatory factor induces synthesis of SF, while SF with high expression acts on islet cells to generate insulin resistance, resulting in rise of blood glucose concentration. However, blood glucose with high concentration also results in a large number of inflammatory substances by cells in the body, which aggravates GDM's damage on the body [13].

ROS is a series of reactive oxygen species generated by aerobic cells in the metabolic process, which can induce cell apoptosis or tissue damage through oxidative stress reaction of cells. The mitochondria and lysosome of organelle in the islet cells have rich ROS of which generation and elimination under physiological conditions are dynamically balanced. When SF storage in the body has reached a high level, redundant ferric ions can catalyze excessive ROS in the body, resulting in insulin resistance, damage on islet cells and restriction for insulin synthesis and secretion through oxidative stress reaction. As a result, this has further accelerated the occurrence and evolution of GDM [14] [15]. The results from ROC indicate that AUC in diagram of ROC between SF and GDM in the first trimester is 0.895 ($p < 0.001$). In ROC, Youden index is 0.651 and SF critical value is 38.6 ng/ml; meanwhile, values of sensitivity and specificity are 97.8% and 67.3% respectively, indicating important values of SF measurement for early GDM screening.

There are some shortcomings to this study. We only detected the index of serum ferritin, and the specificity is not high. If we can add some indicators and make the ROS curve together, it will greatly improve the detection rate of early gestational diabetes.

5. Conclusion

There is a certain correlation between GDM and expression level of SF. Therefore, detecting the expression levels of SF at early pregnancy and middle pregnancy will be of great value for the prevention and treatment of gestational diabetes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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