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Original Article

Biochemistry Section

Relation between Chromium, Iron and Copper with Gestational Diabetes in Zabol, Iran

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ABSTRACT

Introduction: Diabetes is one of the most common chronic diseases. Gestational Diabetes Mellitus (GDM) is a type of diabetes that starts during pregnancy.

Aim: To study the levels of chromium, iron, and copper in women with GDM compared with non-diabetic pregnant women.

Materials and Methods: In this case-control study that was performed in Amir Al Momenin Hospital (Zabol-IRAN) in 2016 (from may to October). Sixty pregnant women with GDM were included in the study group and 60 non-diabetic pregnant women were included in the control group. Seven millilitres of blood was taken from the study participants for serum separation. For measuring the levels of chromium, iron, and copper Atomic Absorption Spectrometry was used. Data analysis was performed by Student's t-test using the Statistical Package for the Social Sciences (SPSS) software version 16.

Results: Serum levels of chromium (7.76±2.83 vs 6.52±2.74 ng/dL), iron (0.60±0.10 vs 0.55±0.14 µg/dL) and copper (0.97±0.22 vs 0.83±0.22 µg/dL) were lower in the case group compared with the control group. Their difference was not statistically significant (p>0.05). The average age of participitants was 34.4±8.01 years. There was no significant difference in age between groups.

Conclusion: The present research showed that levels of Chromium, Iron and Copper in diabetic pregnant women were lower than that of non-diabetic pregnant women; but, these values did not had statistically significant difference.

Keywords: Deficiency, Gestational diabetes mellitus, Pregnancy

INTRODUCTION

Diabetes Mellitus (DM) is a common chronic metabolic disorder caused by complex interactions between genetic and environmental factors that may lead to various complications [1,2]. DM is the third most common cause of death in America [3].

Approximately 6% of the world's population and 7.8% of Iran's population is suffering from this disease [4,5]. GDM is defined as any degree of abnormal glucose tolerance during pregnancy [6]. Prevalence of GDM in Iran is about 1.3-1.9% which indicates its high prevalence in iranian pregnant women [7]. A 30-60% of GDM cases lead to type II diabetes during postpartum phase. Pregnancy is a stressful situation, since many physiological and metabolic functions significantly change during this period [8]. In a healthy person, levels of free radicals and oxidants are in equilibrium normally, but they can be disturbed by stress and the oxidative stress respectively that damage tissue and cause various diseases [9-11].

Oxidative stress is involved in various complications such as preterm delivery, foetal growth restriction, pre-eclampsia, and abortion [12]. Moreover, oxidative stress is increased in pregnant women with diabetes [13]. GDM can stimulate oxidative stress, impaired antioxidant system, and various complications during pregnancy [13,14].

Latest evidence suggests that the metabolism of trace elements is changed in diabetes mellitus, and these metals may contribute to the pathogenesis and progression of the disease, due to various metabolic characteristics and their operations [15].

Chromium (Cr) is a micro-nutrient. It is an essential antioxidant and can be found in high levels in human body [16-18]. The most fundamental biological function of chromium is its effect on insulin and receptors [19]. Chromium deficiency may be involved in the development of diabetes in animals and humans [20]. Chromium could reduce lipid peroxidation through glucose-insulin system and chromium supplementation reduces blood glucose [21].

Copper (Cu) is known as an essential micronutrient, that is a component of many metalloenzymes which are involved in oxidation [22] and reduction processes [2].

In GDM cases, serum Cu level has been seen to be significantly higher, compared to healthy pregnant women [22].

Activating enzyme, Aminolevulinic Acid (ALA) synthase regulates heme synthesis. Copper is essential in the transport of iron from the gut into the plasma. On the other hand, transfer of trace elements in blood is supported by haemoglobin. Moreover, iron (Fe) is the most abundant trace element in metabolism associated with haemoglobin formation. About 75% of haemoglobin molecule contains iron [23].

Altered metabolism of Iron (Fe) has been reported in diabetes [24]. Iron (Fe), as a strong pro-oxidant, catalyses several cellular reactions that result in the production of ROS with a subsequent increase in the level of oxidative stress. Therefore, high concentrations of free iron could be harmful. Increasing evidence now suggests a potential influence of Fe metabolism on type-2 DM [25]. The relationship between Fe and insulin is bidirectional as Fe influences insulin activity by influencing glucose uptake and consumption, while insulin affects Fe uptake and storage by increasing the cell surface transferrin receptors [26].

Serum trace element measurement is a proper way to assess the nutritional status and health of individuals [27].

With regard to the importance of the complications of GDM such as possible role in the antioxidant system disturbance and important roles of trace elements on insulin physiology and

antioxidant system activity [22], the aim of present research was to evaluate the levels of chromium, copper and iron in pregnant women suffering from diabetes and comparing with healthy pregnant controls.

MATERIALS AND METHODS

This cross-sectional study was conducted in 2016 in Zabol (from may to October), on mothers who referred to the clinic of the hospital in the 20th to 40th weeks of pregnancy. During the study period, total of 120 pregnant women completed the consent form, 60 of them were diabetic pregnant women and 60 others were healthy pregnant women.

The sample size was calculated based on Formula ratios comparison in each group.

$$n=\frac{(Z_{1-\alpha/2}+Z_{1-\beta})^2\ p\ q}{d^2}$$

With Confidence level 95%, error possibility in diabetic pregnant women (α) up to 0.05, error possibility in healthy pregnant women (β) up to 0.1, possibility percent of diabetic pregnant women (p) 0.03 up to 0.05 and acceptable errors in ratio estimation in two groups (d) 0.13.

Healthy pregnant women as control group were confirmed with blood measurements. The diagnosis of diabetic pregnant women with high or medium risk was carried out in the second trimester of pregnancy. At first, Fasting Blood Sugar (FBS) was estimated in the diabetic pregnant women and then Glucose Challenge Test (GCT) was carried out after 50g glucose consumption, regardless of the time of the last meal. Blood sugar was 50-140 mg/dL one hour after consumption of glucose. Oral Glucose Tolerance Test (OGTT) was carried out by using 100g glucose. This test spanned three hours and the test results for the second hour showed that diabetic pregnant women had a glucose level above 130 mg/dL. In the present study, a blood glucose level above 130 mg/dL was considered as a criteria for pregnancy diabetes [28].

In this study, case group was compared with the control group in terms of age, Body Mass Index (BMI), problems during pregnancy. None of the participants had a history of smoking, consumption of drugs, immune system disorders, antibiotic use, neurotoxicity induced disease and discordance during the last 3 months. There was no history of hormonal disease and pre-eclampsia.

For blood glucose measurements and measuring chromium, iron, and copper in the pregnant women, 7 mL blood was taken and serum was immediately separated. Levels of FBS, challenge blood sugar (GCT), and GTT were measured using Bionik kit from Biotechnica (Italy) and with BT 3000 Plus Auto analyser.

After collecting all serum samples from the participants, 1 mL serum was diluted with 4mL deionised distilled water in order to measure iron and copper levels in pregnant women. Then, levels of iron and copper were measured in the diluted samples using Atomic Absorption Spectrometry (Rey Leight WFX-210 AA Spectrophotometer, China) and by addition standard method of flame technique [29]. Levels of chromium in serum of pregnant women was also measured using standard addition method by Graphite furnace technique [30].

STATISTICAL ANALYSIS

Statistical analysis was performed by SPSS software version 16. In the present research, we used independent student t-test to compare mean of values in the case and control groups and p-value less than 0.05 was considered as significant difference.

RESULTS

In the present investigation, 60 pregnant women with GDM and 60 healthy pregnant women participated with average age of 34.4±8.01 years (age range=19-47 years). The age difference between the two groups was not statistically significant (p=0.29). Means of BMI in the case and control groups were 29.7±3.53 kg/m^2 and 29.61±3.49 kg/m^2, respectively, which is statistically non-significant [Table/Fig-1].

The Cr, Fe, and Cu plasma levels in the case and control groups were not statistically significant (p>0.05, [Table/Fig-1]).

Parameter	Non-diabetic n=60	Diabetic n=60	p-value
Age (year)	34.90±8.10	33.90±7.96	0.29
BMI (kg/m^2)	29.61±3.49	29.7.0±3.53	0.097
Cr (µg/dL)	7.76±2.83	6.52±2.74	0.3
Fe (µg/dL)	0.60±0.10	0.55±0.14	0.14
Cu (µg/dL)	0.97±0.22	0.83±0.22	0.5

[Table/Fig-1]: Comparing mean age, BMI, and trace elements in diabetic and non-diabetic pregnant women in Zabol in 2016.
*p<0.05 is statistically significant.

The lowest and highest blood sugar levels in the diabetic pregnant women were 70 mg/dL and 223 mg/dL, respectively; its mean was 122.4 mg/dL. Also, the average of blood suger level in healthy pregnant women was 95.5 mg/dL with the lowest level of it as 65 mg/dL and the highest level 126 mg/dL.

DISCUSSION

Body needs more quantity of trace elements in pregnancy not only due to increased demand, but also increased loss [31]. Women with GDM are exposed to considerable type 2 diabetes risks, even in the coming years after the delivery [1,8]. Moreover, the damage caused to the mother and the embryo cannot be properly elucidated [14,32]. Among the most important factors which are significantly associated with GDM are high age and obesity [5]. In the present study, the age of participants in both group had no significant difference.

In GDM, there is an excessive nutrient loss that may be due to glucosuria [31]. In the present research, according to the results; chromium (Cr), iron (Fe), and copper (Cu) levels in the pregnant women with GDM were lower than those of the healthy pregnant women, but the difference was not statistically significant. Results of this study were similar to those of Woods S et al., [33]. In the study done by Shindea U et al., Cr level in the control group was significantly more than that of the case group [34]. Some studies including that of Babalola O et al., could not find any relationship between serum chromium levels and type 2 diabetes [35]. In the study by Akhlaghi F et al., Fe level in the control group was more than that in the case group. but amount of other elements in the case group was higher than the control group [36]. In the study by Ugwuja EI et al., Cu level in the control group was higher than that in the case group [37].

In the present study, GDM was not associated with low levels of Cr; however its low consumption in pregnant women can behave as a possible underlying factor in inducing GDM. With this assumption, in some studies including that of Balk E et al., chromium supplementation in patients with diabetes led to satisfactory results [38]. In an animal experiment by Shindea U et al., this beneficial effect was observed [34]. In Rajendran K et al., study, chromium levels in type 2 diabetic patients were lower than normal and this deficiency was greater in older patient and their results indicated to essential role of chromium for insulin function [39]. Choi R et al., in a study conducted in 2016 inferred that increased risk of gestational diabetes was associated with

higher levels of ferritin and serum iron and dietary heme iron intakes that warrants further investigation. They also found Cu absorption rises during pregnancy due to the increased need for maternal Cu-containing enzymes such as cytochrome c oxidase and superoxide dismutases [27].

In a study in Bangladesh, 172 pregnant women in the second and third trimester were selected, of which 86 were diabetic. The result showed that serum Cu levels in GDM cases were significantly higher in both trimesters compared to those of non-diabetic women. They suggested that the possible causes of high serum Cu concentration in GDM cases could be due to the hormonal, metabolic and enzymatic changes in pregnancy and also decreased insulin sensitivity in GDM [22].

It is documented in the study by Atari-Hajipirloo S et al., that Fe affects glucose metabolism and it has been shown that free iron concentrations in the patients with T2DM are higher than healthy people, which could contribute to tissue damage that may potentially lead to complications associated with T2DM [26].

Previous studies have also demonstrated that impaired trace element metabolism is an additional risk factor in the development and progress of disease and they contribute to the pathogenesis of T2DM. Trace elements plays an important role in various metabolic processes and are crucial for many physiological processes [15]. Since diabetes is a multi-factorial disease and various factors including race, nutrition, and environment plays a role in it, more research with a higher sample size should be carried out in this field. As confirmed by the findings of this research, it is recommended to pregnant women to use chromium supplement in their diet and avoid the environment with pollutants and consumption of food produced in these polluted areas as far as possible.

LIMITATION

One of the limitations of this study was insufficient funds for conducting experiments on a larger number of samples. It was also difficult to find mothers who had study conditions.

The assessment of mothers with the history of some diseases was done via self-report in the questionnaires; therefore, a misclassification is probable.

CONCLUSION

Reults of this study showed no significant difference in serum levels of chromium, copper and iron between pregnant diabetic and healthy mothers although some studies have shown that deficiency of these trace elements can disturb glucose metabolism.

Also, it is better for the future work, to compare the levels of chromium, iron, copper and other trace elements in diabetic individuals with conditions and different types of diabetes. With regard to the point that pregnancy causes changes in the quantity of elements, it is natural for both groups to experience some changes. In further future research, it is better to compare healthy non-pregnant women and diabetic non-pregnant women.

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