Original Article

Mid-gestational serum uric acid concentration effect on neonate birth weight and insulin resistance in pregnant women

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Abstract

Objective: To investigate the relationship between mid-gestational serum uric acid and birth weight in diabetic pregnant women with or without insulin resistance.

Methods: In a prospective cohort study, fasting uric acid, blood glucose, and serum insulin were measured in 247 pregnant women between 20-22 weeks of gestational period. Insulin resistance was estimated using the homeostasis model assessment-insulin resistance (HOMA-IR). Stratification analysis and independent t-test was used to assess the association between uric acid and birth weights regarding to insulin resistance.

Results: The means of the mid-gestational serum uric acid concentrations were not significantly different in women with and without insulin resistance. But stratification analysis showed that there was a significant difference between uric acid concentration and macrosomic birth in diabetic women without insulin resistance.

Conclusions: Higher mid – gestation serum uric acid concentrations were not significantly different in women with and without insulin resistance. But stratification analysis showed that there was a significant difference between uric acid concentration and macrosomic birth in diabetic women without insulin resistance.

Key Words: Second trimester, hyperuricemia, homeostasis model assessment-insulin resistance , Metabolic syndrome

INTRODUCTION

In human, uric acid is the final product of the metabolism of purine and can cause various disorders if it is accumulated in the serum.[1] Studies carried out in non – pregnant women have shown that hyperuricemia is an important risk factor in the development of coronary heart diseases, hypertension, glucose intolerance, dislipidemia, obesity, and the metabolic syndrome.[2-6] Also it is well established that high fasting blood sugar or affecting to diabetes in pregnancy has a causality effect on birth weight and macrosomic birth.[7-9]

Serum uric acid has also been associated with gestational hypertension, gestational diabetes, and insulin resistance during pregnancy.[10-12] In vitro studies indicate that hyperuricemia affects the amino acid transfer system through the placenta and also damages the endothelium of the blood vessels in the placenta.[13,14] This can cause gestational hypertension.[15] In women suffering from hypertension, an increase in the serum uric acid has been accompanied by undesirable prenatal consequences including preterm labor and small for gestational age (SGA).[16] Moreover, in normotensive pregnant women with SGA newborns, it was found that a high level of uric acid in the last trimester of pregnancy was effective in reducing birth weight.[17] On the other hand, insulin resistance, as a component of the metabolic syndrome, can also be a risk factor to gestational diabetes that may be accompanied by an increase in the fetal growth.[18,19] Therefore, uric acid and insulin resistance may affect the mother and the fetus in the same or opposite ways, despite the fact that they are both constituting elements of the metabolic syndrome. Herein,
we aim to evaluate relation between mid-gestational serum uric acid and birth weight in pregnant women with or without insulin resistance.

**METHODS**

Pregnant women at 20-22 weeks of gestation at prenatal department of Taleghani Hospital (Arak, Iran) were recruited in this study from May 2010 to July 2012. Two hundred and seventy one nulliparous and singleton pregnancies, who agreed to the informed consent form provided, were included. This prospective study was approved for ethical issues by the review committee of Arak University of Medical Sciences. Their gestational age was reconfirmed with last menstrual period and ultrasound. The inclusion criteria were: Women with normal blood pressure, no previous history of hypertension, diabetes mellitus or thyroid disorders, not smoking or consuming alcohol and not taking any medicines except iron. They were excluded if they developed: Preeclampsia, gestational diabetes, thyroid disorder, or delivery earlier than the 38th week of pregnancy. Finally, 247 women were enrolled in the study.

Blood samples were collected and stored in -70°C. Glucose and uric acid were measured colorimetrically using the glucose oxidase method with a coefficient variance of 13 percent and the uric acid was measured by using the uricase method with a coefficient variance of seven percent. Using Mono bind kits (CA, United States), the ELISA sandwich method was employed to assay the concentration of serum insulin. These kits contained rat monoclonal antibodies placed against human insulin which covered plate surfaces, and another biotinylated monoclonal antibody that attached itself to insulin with an interassay variation of 12.4 percent. The HOMA formula described by Mathews et al. (HOMA-IR = Glucose(mg/dl) × Insulin (mu/l)/(405)) was used to calculate insulin resistance. The optimal HOMA-IR cut-off for the diagnosis of Adult Treatment Panel III-defined Metabolic syndrome in non-diabetic Iranian individuals, was 1.775 (sensitivity: 57.3%, specificity: 65.3%). The birth weight was measured using a standard scale.

All data were prepared and analyzed with SPSS 17 for windows (SPSS Inc. Chicago, IL, USA). The quantitative values were represented as means or standard deviations, and the Student’s T – test and the Logistic Regression statistical tests were utilized to investigate the relationships between the data. P ≤ 0.05 were considered statistically significant.

**RESULTS**

By the HOMA formula, 68 of the women were insulin resistant while the other 179 were not. General characteristics and variables of population study are outlined in Table 1. There were no significant differences in maternal age, the proportion of primigravids, height, weight and BMI between two groups. The mean birth weight (3237 ± 438 g vs 3163 ± 517 g; P = 0.2) were not significantly different in the two groups.

As expected, the mean serum insulin concentration and the value of HOMA were substantially higher in insulin resistant mothers, although the means of fasting blood sugar of the women in the two groups were not significantly different. The means of mid gestational serum uric acid concentrations in the two groups were not significantly different, but after adjusting by the resistance to insulin in stratification analysis, it found that there was a significant difference between macrosomic and normal groups in uric acid concentration [Table 2]. Also, using the Pearson correlation test, revealed that only in not insulin resistant group, higher uric acid concentrations was associated with lower birth weight (P = 0.05, r = - 0.2).

**DISCUSSION**

In this research, we studied the relationship between mid-gestational serum uric acid concentration and birth weight in normotensive pregnant women with and without the insulin resistance. Our study showed that, while the means of mid-gestational serum uric acid concentrations in the groups with and without insulin resistance were not significantly different, there was a negative correlation between midgestation uric acid concentration and birth weight only in women without insulin resistance.

The relationship between hyperuricemia with preeclampsia and small for gestational age,[16] and hyperuricemia with fetus death and low birth weight have previously been reported.[22] There is also evidence that hyperuricemia is
related to increased insulin resistance and to decreased birth weight in newborns of normotensive pregnant women.[23] Although changes in the level of uric acid concentration in pregnant women with or without insulin resistance may be very small,[24] our study shows that same small fluctuations in mid-gestational uric acid concentration have a negative effect on the fetal growth of mothers without insulin resistance.

Studies indicate that hyperuricemia can directly inhibit amino acid transfer to the fetus and affect fetal growth[13], and hyperuricemia causes placental blood vessels endothelium proliferation, increase the production of thromboxane A2 and vasoconstrictor substances, and decrease the production of nitric oxide.[25] and, hence, causes small for gestational age. Hyperuricemia can damage the endothelium of maternal blood vessels and, thus, causes hypertension and preeclampsia[14]

In our study, there was no relationship between the mid-gestational uric acid concentration and birth weight in insulin resistant pregnant women. Since, insulin resistance is accompanied by a decline in the glucose consumption in mother, the placenta provides more sugar for the fetus, so; birth weight is expected to be less affected by uric acid.[17] In other words, it can be concluded that insulin resistance somehow restricts the effects of uric acid on the birth weight.

The kidneys are responsible to regulating the level of blood uric acid during pregnancy. In the first trimester, the level of serum uric acid declines by about 30 percent due to the increase in the filtration of glomeruli and because of a reduction in the reabsorption of uric acid from proximal tubules. However, by the time the delivery, blood uric acid concentration increases to about its prepregnancy level due to a reduction in uric acid clearance by the kidneys.[26]

In our study, in those pregnant women who were in the upper quartile of uric acid and in the lower quartile of HOMA, birth weight was 181 grams less than birth weight in those who were in the upper quartile of uric acid and in the lower quartile of HOMA. In a similar study conducted by Langhonsk et al., the difference in birth weight was 435.6 grams.[17] This difference could be due to the different ranges of uric acid in the two studies, or it could be because of racial differences between those who had participated in the two studies.

Although this evidence that insulin resistance can prevent the negative effects of uric acid on the fetal growth, we do not have any evidence suggesting this process is an adaptation for fetal growth, and more research is needed to clarify this hypothesis.

REFERENCES


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