The effect of natural antioxidant levels in pregnancy on birth weight

Ahmet Ziya Sahin\textsuperscript{a,*}, Cagdas Demiroglu\textsuperscript{b}

\textsuperscript{a}Gaziantep University, Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Gaziantep, Türkiye
\textsuperscript{b}SANKO University, Faculty of Medicine, Department of Gynecology and Obstetrics, Gaziantep, Türkiye

ARTICLE INFO

Keywords:
Birth weight
Pregnancy
Oxidative stress
Natural antioxidant

Abstract

Aim: We aimed to investigate the relationship between uric acid, bilirubin, and albumin levels all of which are natural antioxidants and Gamma glutamyl transferase (GGT) one of the components that contribute to maternal oxidative stress and birth weight of newborns.

Materials and Methods: One hundred twenty-six pregnant women aged between 18-40 years and their babies were included in this retrospective cohort study. Uric acid, GGT, bilirubin levels, age, body mass index (BMI), gravida and parity, number of living children, gestational week, and fetal birth weight were reviewed.

Results: The mean age of women was 30.62\pm5.62. There was a positive correlation between birth weight and albumin (r:0.222, p<0.01), serum uric acid levels (r: 0.292, p<0.01), total bilirubin levels (r:0.261, p<0.01) and a negative correlation between birth weight and GGT (r:-0.311, p<0.01).

Conclusion: Natural antioxidants are positively associated with the birth weight of infants, while natural oxidant is negatively related. Oxidative stress should also be considered in pregnant women who are expected to give birth at healthy and normal weight.

Introduction

Fetal development during pregnancy is affected by maternal, placental and environmental factors. The control of these factors in terms of maternal and newborn health still has an important place in the world. While maternal complications may occur in the expectant mother due to these factors, birth weight is one of the most frequently affected parameters in the newborn [1]. It has been reported that newborns with low birth weight have a higher risk of developing metabolic diseases such as cardiovascular diseases, hypertension and diabetes mellitus in the future [2]. Oxidative stress occurs when the balance between the rate of formation and the rate of elimination of free radicals is disturbed in favor of the rate of formation. These oxidants are eliminated by both intracellular and extracellular defense mechanisms. While free radical collecting enzymes are involved in the intracellular defense mechanism, molecules such as albumin, bilirubin, and ceruloplasmin constitute the extracellular defense mechanisms. In addition, molecules such as scavenging antioxidants such as ascorbic acid, carotene, vitamin E, uric acid (UA) and co-enzyme Q help to eliminate extracellular oxidative stress [3, 4].

Gamma-glutamyl transferase (GGT) can be used as a marker of oxidative stress. High GGT levels have been associated with oxidative stress. Uric acid, one of the natural antioxidants and a powerful free radical scavenger, accounts for more than half of the total antioxidant capacity of the blood. Bilirubin is a powerful natural antioxidant that creates a chain-breaking effect by affecting peroxyl radicals. Playing a key role in the distribution of fluid between different parts of the body and the regulation of osmotic pressure, albumin is one of the most important and most effective natural antioxidants in plasma. Bilirubin is a superoxide and hydroxyl radical scavenger [5].

Birth weight is one of the most important factors affecting perinatal mortality and morbidity. In some studies, it has been determined that the presence of fetal oxidative stress effects birth weight [6]. The fetal effects of maternal oxidative factors and whether these effects affect birth weight are still controversial. In this study, we aimed to investigate the effects of GGT, which is one of the maternal oxidative stress factors, and uric acid, bilirubin,
and albumin levels, which are natural antioxidants, on newborn birth weight.

**Materials and Methods**

In the study, the minimum number of people required for the large effect size to be significant was determined as 107 (α=0.05, 1-β=0.80 d=0.80). Analysis was done in G power 3.1 version. Pregnant women who applied to SANKO University Sani Konukoglu Training and Research Hospital Gynecology and Obstetrics Clinic between January 1, 2022 and April 1, 2022 for delivery were included in this study. The data of our study were obtained by routine blood tests taken from the patients during hospitalization and by retrospectively scanning their sociodemographic data.

**Participants**

One hundred twenty-six pregnant women aged between 18-40 years (37 weeks to 40 weeks) who applied for delivery were included in our study. Exclusion criteria; These were the pregnant women with risky pregnancy, chronic inflammatory disease, presenting with premature rupture of membranes, vaginal bleeding, hypertension, diabetes, hypo-hyperthyroidism, smoking or alcohol use history. All pregnant women, which are done regularly during prenatal hospitalization. In other words, they are the results of possible natural antioxidants, and birth weight. A negative correlation was found between the levels of albumin, bilirubin and uric acid, which are known as endogenous natural antioxidants, and birth weight.

**Statistical analysis**

IBM SPSS (Version 23) program was used for demographic distribution and statistical comparison of the data obtained in our study. The data we obtained are independent and because it did not fit the normal distribution according to the Shapiro Wilk test, the Spearmen correlation test was applied. P<0.05 was considered significant.

**Results**

The mean age of the participants was 30.62±5.62. The mean body mass index (BMI) was 30.17±5.05. The median and 25, 75 quartile numbers of gravidas, parites, and live births were 2 (1/3), 1 (0/2), and 1(1/2), respectively. The mean birth weight of babies was 3317±373 grams. The average week of pregnancy was 38.04±1.02. The mean serum albumin levels of the women were measured as 34.48±0.43 mg/dl. A statistically significant relationship was found between birth weight and albumin (r: 0.222, p<0.01). Serum uric acid levels were determined as 5.46±0.43 mg/dl, and a statistically significant correlation was observed between this value and birth weight (r: 0.292, p<0.01). Total bilirubin levels average 0.47±0.25 mg/dl. The relationship between birth weight and total bilirubin was significant (r: 0.261, p<0.01). The mean serum GGT levels of the patients were 14.78±1.15 mg/dl. A statistically significant negative correlation was found between birth weight and total bilirubin (r: -0.311, p<0.01). The correlation of natural antioxidants parameters with birth weight year is shown in Table 1.

**Discussion**

In our study, the relationship between oxidative stress, endogenous antioxidants, which can be measured by simple biochemical tests, and birth weight was investigated. A positive correlation was found between the levels of albumin, bilirubin and uric acid, which are known as endogenous natural antioxidants, and birth weight. A negative correlation was found between the level of GGT, a measurable natural oxidant in serum, and birth weight.

In cases where the production of reactive oxygen species exceeds the cellular defense mechanisms, these unstable reactive molecules interacts with biological macromolecules such as lipids, proteins and DNA, resulting in structural changes [7, 8]. Many disorders such as atherosclerosis, emphysema/bronchitis, Alzheimer, pregnancy preeclampsia, cervical cancer, alcoholic liver disease, chronic obstructive pulmonary disease, hemodialysis patients, major depression, diabetes mellitus, acute renal failure, aging, cerebrovascular disorders, ischemia involve cell damage caused by free oxygen radicals [3, 8-11]. Similarly, it was shown in this study that oxidative stress was associated with another negative outcome, low birth weight.

Studies have reported that oxidative stress in humans has pathogenic effects on maternal and fetal health and is an important factor in the development of various maternal-fetal diseases [12]. Oxidative stress plays a key role in the pathophysiology of placental-related disorders, particularly preeclampsia and intrauterine growth retardation (IUGR). In a meta-analysis, there was a statistically significant decrease in total antioxidant capacity and antioxidants such as nitric oxide (NO), superoxide dismutase (SOD), glutathione (GSH), and vitamins E and C in patients with preeclampsia; An increase was observed in malondialdehyde (MDA), protein carbonyl and total peroxide.

**Table 1. Correlations between assessment tools.**

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Uric Acid</th>
<th>GGT</th>
<th>Bilirubin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
<td>.222**</td>
<td>.292**</td>
<td>-.311**</td>
</tr>
<tr>
<td>Albumin</td>
<td>.579**</td>
<td>-.556**</td>
<td>.292**</td>
</tr>
<tr>
<td>Uric acid</td>
<td>-.522**</td>
<td>.344**</td>
<td></td>
</tr>
<tr>
<td>GGT</td>
<td>-.332**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Correlation is significant at the 0.01 level (2-tailed).**

* Correlation is significant at the 0.05 level (2-tailed).
levels, which are peroxidation products [11]. In studies examining the relationship between intrauterine growth retardation and consumption of antioxidant components during pregnancy, it was found that the levels of natural antioxidants vitamin A, C and E were low [13, 14]. Of course, none of our participants had low birth weight baby. In addition, we showed the relationship between birth weight with natural oxidants and antioxidants in babies with normal birth weight limits.

The sample size and the retrospective cohort design are one of the limitations of our study. There is a need for meticulous, routine monitoring from the beginning of pregnancy and prospective investigation with close follow-up during the birth of babies. The lack of regular follow-up of oxidant and antioxidant parameters throughout pregnancy is another limitation. Oxidant levels may have fluctuated throughout pregnancy. However, it is a very important finding that prenatal oxidative stress is associated with lower birth weight. It is also a limitation that the parameters that can determine the oxidative stress more precisely are not checked. However, the results are important in terms of giving an idea of the parameters that can be monitored routinely. If the infant weights in the study are 2500 g and above, the relationship between infant weights and antioxidative agents may not be adequately examined.

Conclusion

The birth weight of babies with normal birth weight and the levels of albumin, bilirubin and uric acid, which are known as endogenous natural antioxidants, are positively related. The relationship between birth weights and the level of GGT, which is a natural oxidant, is negative. Oxidative stress maintains its importance in pregnant women who are expected to have a healthy delivery. Precautions should be taken to reduce oxidative stress in pregnant women.

Authorship contributions

A.Z.Ş: Conception, design, analysis and interpretation, literature review, writing, critical review.

ÇD: Supervision, materials, data collection and processing.

Ethical approval

Ethics committee approval of this study was received from SANKO University Ethics Committee with the date 12.10.2022 and issue 2022/10.

Conflict of interest

No conflict of interest was declared by the authors.

Financial disclosure

The authors declared that this study received no financial support.

References