First-Trimester Platelet Count as a Predictive Biomarker for Neonatal Birth Weight Among Pregnant Women at Advanced Maternal Age

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Abstract
The aim of this study was to investigate the association between first-trimester platelet count and neonatal birth weight in pregnant women at advanced maternal age. Our study included 148 pregnancy women of advanced maternal age, the clinical and laboratory materials were retrospective obtained from medical record system. The neonatal birth weight was positively correlated with maternal body mass index and fetus gestational age ($r = 0.332$, $P < .001$; $r = 0.469$, $P < .001$), even more interestingly, the neonatal birth weight was positively correlated with first-trimester platelet count in pregnant women of advanced maternal age ($r = 0.203$, $P = .013$). Multiple linear regression analysis revealed that neonatal birth weight had an independently association with first-trimester platelet count in pregnant women of advanced maternal age (multiple-adjusted $r$ values 0.167, $P = .013$). First-trimester platelet count is positively associated with neonatal birth weight, suggesting that first-trimester platelet count may be a predictive biomarker for neonatal birth weight in pregnant women of advanced maternal age.

Keywords
platelet count, birth weight, first-trimester, advanced maternal age

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Introduction
The platelet count is a common parameter in blood routine tests. Platelet count has been suggested to be related to various diseases such as hypertension, diabetes mellitus, and cardiovascular disease.\textsuperscript{1-3} In the field of obstetrics and gynecology, it has been demonstrated that platelet count is reduced in low-risk persistent gestational trophoblastic disease, and platelet count is a biomarker for the early assessments of low-risk persistent gestational trophoblastic disease.\textsuperscript{4} It has been found that platelet count is associated with maternal adverse outcomes in patients with preeclampsia,\textsuperscript{5} and platelet count is lower in patients with preeclampsia.\textsuperscript{6} Moreover, previous evidence has suggested that platelet count at first trimester of pregnancy is a predictor for the adverse perinatal outcomes.\textsuperscript{7}

Clinically, advanced maternal age is defined as gestation in women aged 35 years or older.\textsuperscript{8} It is well demonstrated that advanced maternal age is associated with adverse perinatal outcomes.\textsuperscript{9,10} Particularly, advanced maternal age has been reported to increase low birth weight risk in both primigravidas and multiparas.\textsuperscript{11,12} It is suggested that abnormal birth weight infants may lead to cognitive function impairments and increase hypertension risk in adults.\textsuperscript{13,14} Tian et al\textsuperscript{15} found that low birth weight had close associations with risk of developing abdominal obesity and hypertension in Chinese adults. In addition, abnormal birth weight has been attested to be associated with increased cardiovascular disease risk factors in adult
life. In brief, these observations prompted us to explore some laboratory markers to assess abnormal birth weight in pregnant woman at advanced maternal age, thus, the aim of this study was to investigate the association between first-trimester platelet count and neonatal birth weight in pregnant woman at advanced maternal age.

**Participants and Data**

We performed a retrospective analysis for this relationship between first-trimester platelet count and neonatal birth weight in pregnant woman at advanced maternal age. The pregnancy was diagnosed according to clinical signs, ultrasonic examinations, and laboratory examinations; and we defined advanced maternal age in pregnant woman aged 35 years or older. The participants with active infection and liver insufficiency were excluded. The clinical and laboratory materials were retrospective obtained from medical record system. The data of pregnant woman mainly included age, gestational weeks, body mass index, blood pressure, fasting blood glucose, white blood cell count, hemoglobin, and platelet count; and the data of infants mainly included fetus gestational age, infant gender, and birth weight. The neonatal birth weight was first time recorded by obstetrician when born, and the mean weight was calculated for twins. The current study was approved by the institutional review board of Zhongda Hospital, School of Medicine, Southeast University, and was carried out according to the guidelines of Helsinki Declaration.

**Statistical Approach**

The statistical analyses were performed with SPSS version 25.0. The categorical variables were indicated as proportion, normally distributed variables were reported as means ± standard deviation, and non-normal distributed variables were reported as median (interquartile range). To estimate the correlations, the Spearman or Pearson correlation approach was performed, when appropriate. Multiple linear regression analysis was also applied to examine the association between neonatal birth weight and first-trimester platelet count. A 2-tailed P value of less than .05 was considered to be statistically significant.

**Results**

**Basic Information in Pregnant Woman at Advanced Maternal Age**

Cumulative clinical and laboratory data are exhibited in Table 1. Overall, our study included 148 pregnant woman at advanced maternal age. The mean value of neonatal birth weight was 3.4 kg, and a pregnant woman gave birth to twin. No smokers were found in all included participants.

**The Correlation Between Birth Infant Weight and Continuous Variables**

The correlation analyses were adopted to find which of the potential parameters were correlated with neonatal birth weight in whole participants. Consequently, the neonatal birth weight was positively correlated with maternal body mass index and fetus gestational age ($r = 0.332, P < .001$; $r = 0.469, P < .001$), even more interestingly, the neonatal birth weight was found to be positively correlated with maternal first-trimester platelet count ($r = 0.203, P = .013$).

**Table 1. Clinical and Laboratory Data in Pregnant Woman at Advanced Maternal Age.**

| Parameter                        | Value                          |
|----------------------------------|--------------------------------|
| Age, years                       | 36 (35-38)                     |
| Gestational weeks, weeks         | 12 (11-12)                     |
| Body mass index, kg/m²           | 22.4 (20.6-24.2)               |
| Systolic pressure, mm Hg         | 101 (100-111)                  |
| Diastolic pressure, mm Hg        | 70 (60-70)                     |
| Fasting blood glucose, mmol/L    | 4.7 (4.4-5.0)                  |
| White blood cell count, 10⁹/L    | 7.8 ± 1.7                      |
| Hemoglobin, g/L                  | 124.2 ± 9.9                    |
| Platelet count, 10⁹/L            | 211.2 ± 54.7                   |

| Infant                           |                                |
|----------------------------------|--------------------------------|
| Infant gender (female/male)      | 77/72                          |
| Fetus gestational age, weeks     | 39 (38-39)                     |
| Birth weight, kg                 | 3.4 ± 0.5                      |

**Discussion**

Platelet count has been considered as a routine laboratory parameter to estimate the risk of hemorrhagic disease. In the present study, we found an association between first-trimester platelet count and infant birth weight among pregnant woman at advanced maternal age. In the first trimester, the development of placenta is accompanied by the establishment of fetal blood circulation, and fetal growth has a close relationship with the placental quality and function. Indeed, a prospective longitudinal study suggests that decreased platelet reactivity in the first trimester of pregnancy forebodes the occurrence of uteroplacental disease. A line of evidence attests that vascular endothelial growth factor therapy is served as a growth stimulant for gestation with intrauterine growth retardation, there is evidence showing that proangiogenic vascular endothelial growth factor is primarily stored in platelets, and platelets play a stimulating role in angiogenesis by their function as
Table 2. Neonatal Birth Weight as a Dependent Variable in Multiple Linear Regression Analysis.

|                      | Univariate Analysis |     | Multivariate Analysis |     |
|----------------------|---------------------|-----|-----------------------|-----|
|                      | $\beta$             | $P$ | $\beta$               | $P$ |
| Age                  | -0.001              | 0.958 | -0.048               | 0.471 |
| Body mass index      | 0.045               | <0.001 | 0.253               | 0.001 |
| Systolic pressure    | 0.000               | 0.949 | -0.073               | 0.424 |
| Diastolic pressure   | -0.001              | 0.805 | 0.019               | 0.832 |
| Hemoglobin           | 0.002               | 0.551 | -0.011               | 0.873 |
| Fasting blood glucose| 0.105               | 0.092 | 0.144               | 0.031 |
| Infant gender        | -                  | -    | -0.078               | 0.251 |
| Fetus gestational age| 0.178               | <0.001 | 0.517               | <0.001 |
| Platelet count       | 0.002               | 0.013 | 0.167               | 0.013 |

Conclusion

First-trimester platelet count is positively associated with neonatal birth weight, suggesting that first-trimester platelet count may be a predictive biomarker of neonatal birth weight in pregnant women of advanced maternal age.

Author Contribution

The authors You-Fan Peng and Qiong Wei contributed equally to this work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Translational Science

Most of the current studies investigated the maternal body mass index, which is an important determinant of neonatal birth weight,22 and maternal prepregnancy body mass index is positively correlated with neonatal birth weight. In order to appropriately determine the neonatal birth weight, many factors need to be considered, such as nutrition, environmental and hereditary factors. Even though we obtain the maternal body mass index during early pregnancy, we are unable to obtain the maternal body mass index during the first trimester of pregnancy, which is a limitation of our research. In addition, we do not have the maternal body mass index at the time of the first trimester of pregnancy. This limitation may be ineluctably limited. Next, the neonatal birth weight is determined by myriad factors such as nutrition, environment, and heredity, these necessary factors are not included, although we obtain the maternal body mass index during early pregnancy. Finally, the association between first-trimester platelet count and placental function parameter is not conclusive. In view of the above-mentioned limitations, further study is needed to confirm the current association in pregnant women of advanced maternal age.
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