# Correlation Analysis of Serum Uric Acid and Serum Uric Acid/Creatinine Ratio in Late Pregnancy with Adverse Pregnancy Outcomes: Postprint

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## Abstract

Background: Maternal serum uric acid metabolism disorder during pregnancy is associated with adverse pregnancy outcomes; however, few studies have analyzed and compared the correlation between serum uric acid and serum uric acid/creatinine levels with adverse pregnancy outcomes.

Objective: To analyze the correlation between serum uric acid and serum uric acid/creatinine levels in the third trimester of pregnancy with adverse pregnancy outcomes.

Methods: Based on the occurrence of adverse pregnancy outcomes, data from singleton pregnant women with live births who underwent routine prenatal care and delivery at Nanjing University Affiliated Drum Tower Hospital from 2015 to 2022 were collected at a 1:1 ratio. A total of 743 pregnant women were ultimately included, comprising 344 cases in the normal group and 399 cases in the adverse outcome group. Serum uric acid and serum uric acid/creatinine were respectively divided into three levels by quartiles: Q1 (serum uric acid $\leq$ 257 mol/L), Q2 (serum uric acid 257–359 mol/L), Q3 (serum uric acid $\geq$ 359 mol/L) and q1 (serum uric acid/creatinine $\leq$ 5.88), q2 (serum uric acid/creatinine 5.88–7.94), q3 (serum uric acid/creatinine $\geq$ 7.94). According to the median maternal age, pregnant women were divided into the age <30 years group (341 cases) and age $\geq$ 30 years group (402 cases). Based on previous parity, pregnant women were divided into the primipara group (539 cases) and multipara group (194 cases). Multivariate Logistic regression analysis was used to analyze the correlation between serum uric acid and serum uric acid/creatinine levels with adverse pregnancy outcomes.

Results: Maternal age, BMI, serum uric acid, serum uric acid/creatinine, and triglycerides in the adverse outcome group were higher than those in the normal group (P<0.05). After adjusting for confounding factors, multivariate Logistic regression analysis of the effects of serum uric acid and serum uric acid/creatinine on adverse pregnancy outcomes showed that, compared with Q1 level serum uric acid, Q3 level increased the risk of preeclampsia (AOR=4.41, 95%CI=2.16-8.99) and intrauterine growth restriction (AOR=3.59, 95%CI=1.08-11.96) (P<0.05); compared with q1 level serum uric acid/creatinine, q2 and q3 levels increased the risk of preeclampsia (AOR=2.33, 95%CI=1.13-4.79; AOR=3.56, 95%CI=1.68-7.56), q3 level increased the risk of preterm birth (AOR=2.76, 95%CI=1.33-5.71) and intrauterine growth restriction (AOR=5.15, 95%CI=1.39-19.14), while q3 level decreased the risk of macrosomia (AOR=0.43, 95%CI=0.19-0.98) and large-for-gestational-age infants (AOR=0.38, 95%CI=0.15-0.96) (P<0.05). The results of the effects of serum uric acid and serum uric acid/creatinine on preeclampsia and preterm birth in different age groups showed that, compared with Q1 level serum uric acid, Q3 level increased the risk of preeclampsia in both age groups (P<0.05); compared with q1 level serum uric acid/creatinine, q2 and q3 levels increased the risk of preeclampsia in pregnant women aged ≥ 30 years (P<0.05). The results of the effects of serum uric acid and serum uric acid/creatinine on preeclampsia and preterm birth in different parity groups showed that, compared with Q1 level serum uric acid, Q3 level increased the risk of preeclampsia in primiparas (P<0.05); compared with q1 level serum uric acid/creatinine, q2 and q3 levels increased the risk of preeclampsia in primiparas, and q3 level increased the risk of preterm birth in primiparas (P<0.05).

Conclusion: High levels of serum uric acid and serum uric acid/creatinine both increase the risk of preeclampsia and intrauterine growth restriction, with preeclampsia occurring mainly in pregnant women aged $ $30 years or primiparas. High level of serum uric acid/creatinine increases the risk of preterm birth, mainly occurring in primiparas. Serum uric acid/creatinine predicts more adverse pregnancy outcomes than serum uric acid.

## Full Text

# Correlation of Serum Uric Acid and Uric Acid/Creatinine Ratio Levels with Adverse Pregnancy Outcomes in Late Pregnancy

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## Abstract

### Background
Disorders of serum uric acid metabolism during pregnancy are associated with adverse pregnancy outcomes, yet few studies have analyzed and compared the correlation of serum uric acid and uric acid/creatinine ratio levels with adverse pregnancy outcomes.

### Objective
To explore the correlation between serum uric acid and uric acid/creatinine ratio levels in late pregnancy with adverse pregnancy outcomes.

### Methods
Based on the occurrence of adverse pregnancy outcomes, data were collected from pregnant women with singleton live births who underwent routine prenatal examinations and delivered at Nanjing Drum Tower Hospital between 2015 and 2022 at a 1:1 ratio. A total of 743 pregnant women were ultimately enrolled, including 344 in the normal group and 399 in the adverse outcomes group. Serum uric acid and uric acid/creatinine ratio were divided into three levels by quartiles: Q1 (serum uric acid $\leq$ 257 mol/L), Q2 (serum uric acid 257-359 mol/L), Q3 (serum uric acid $\geq$ 359 mol/L) and q1 (uric acid/creatinine ratio $\leq$ 5.88), q2 (uric acid/creatinine ratio 5.88-7.94), q3 (uric acid/creatinine ratio $\geq$ 7.94). According to median maternal age, women were divided into <30 years (341 cases) and $ $30 years (402 cases) groups. Based on previous pregnancy and delivery history, they were divided into primiparous (539 cases) and multiparous (194 cases) groups. Multivariate logistic regression was used to analyze the correlation between serum uric acid and uric acid/creatinine ratio levels with adverse pregnancy outcomes.

### Results
Women in the adverse outcomes group were older and had higher BMI, serum uric acid, uric acid/creatinine ratio, and triglyceride levels than those in the normal group ($P < 0.05$). After adjusting for confounders, multivariate logistic regression showed that compared with Q1 serum uric acid level, the risk of preeclampsia (AOR = 4.41, 95% CI = 2.16-8.99) and intrauterine growth restriction (AOR = 3.59, 95% CI = 1.08-11.96) increased at Q3 level ($P < 0.05$). Compared with q1 uric acid/creatinine ratio level, the risk of preeclampsia increased at q2 and q3 levels (AOR = 2.33, 95% CI = 1.13-4.79; AOR = 3.56, 95% CI = 1.68-7.56), the risk of preterm birth (AOR = 2.76, 95% CI = 1.33-5.71) and intrauterine growth restriction (AOR = 5.15, 95% CI = 1.39-19.14) increased at q3 level, while the risk of macrosomia (AOR = 0.43, 95%

CI = 0.19-0.98) and large-for-gestational-age infant (AOR = 0.38, 95% CI = 0.15-0.96) decreased at q3 level (P < 0.05). Subgroup analyses showed that compared with Q1 serum uric acid, Q3 level increased preeclampsia risk in both age groups (P < 0.05). Compared with q1 uric acid/creatinine ratio, q2 and q3 levels increased preeclampsia risk in women aged $ $30 years (P < 0.05). Compared with Q1 serum uric acid, Q3 level increased preeclampsia risk in primiparous women (P < 0.05). Compared with q1 uric acid/creatinine ratio, q2 and q3 levels increased preeclampsia risk, and q3 level increased preterm birth risk in primiparous women (P < 0.05).

**Conclusion**

Elevated serum uric acid and uric acid/creatinine ratio levels are associated with increased risks of preeclampsia and intrauterine growth restriction, with preeclampsia occurring mainly in women aged $ $30 years or primiparous women. High uric acid/creatinine ratio increases preterm birth risk, primarily in primiparous women. The uric acid/creatinine ratio predicts more adverse pregnancy outcomes than serum uric acid alone.

**Keywords**

Pregnant women; Pregnancy outcome; Uric acid; Uric acid/creatinine ratio; Adverse outcomes; Root cause analysis

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## Introduction

Uric acid is the end product of purine nucleotide metabolism. Physiological levels of serum uric acid exert positive effects in antioxidant activity and delaying cognitive decline [1-2], whereas excessively high serum uric acid levels are associated with the development of diabetes, cardiovascular and cerebrovascular diseases [3-4]. Adverse pregnancy outcomes refer to the short-term and long-term impacts of pregnancy and delivery-related complications on maternal and fetal health [5-6], which seriously endanger the physical and mental well-being of mothers and infants, imposing a heavy burden on families and society. Therefore, early identification of risk factors for adverse pregnancy outcomes facilitates timely intervention and treatment, promoting better maternal and child health.

Studies have shown that disorders of serum uric acid metabolism during pregnancy may contribute to the development and progression of adverse pregnancy outcomes such as preeclampsia, gestational diabetes mellitus, and fetal growth restriction [7-8]. Disordered serum uric acid metabolism can mediate oxidative stress injury in vascular endothelial cells, impede placental nutrient transport, and affect fetal growth and development [9-10]. The metabolism of serum uric acid is influenced by dietary habits and renal function; therefore, the serum uric acid/creatinine ratio can minimize interference from renal function and more stably reflect the body' s uric acid level [11]. Previous studies have reported that the serum uric acid/creatinine ratio has predictive value in

metabolic syndrome, hypertension, and chronic kidney disease [11-13]; however, few studies have compared the predictive value of serum uric acid and serum uric acid/creatinine ratio for adverse pregnancy outcomes, and research involving the uric acid/creatinine ratio in adverse pregnancy outcomes is also scarce. In view of this, this study aims to analyze the correlation between serum uric acid and serum uric acid/creatinine ratio with adverse pregnancy outcomes and compare their predictive abilities for such outcomes, providing clinical evidence for reducing the risk of adverse pregnancy outcomes and improving maternal and infant prognosis.

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## Methods

**Study Subjects** Based on the occurrence of adverse pregnancy outcomes, women without such outcomes were included in the normal group, while those with adverse outcomes were included in the adverse outcomes group. Data were collected from pregnant women with singleton live births who underwent routine prenatal examinations and delivered at Nanjing Drum Tower Hospital between 2015 and 2022 at a 1:1 ratio. Exclusion criteria included: (1) combined hepatic or renal insufficiency; (2) hematologic, immunologic diseases, or coagulation dysfunction; (3) severe diseases involving the lungs, heart, tumors, or liver; (4) abnormal placental position or function; (5) psychiatric disorders; and (6) incomplete medical records. A total of 743 pregnant women were ultimately enrolled, including 344 in the normal group and 399 in the adverse outcomes group. This study was approved by the Ethics Committee of Nanjing Drum Tower Hospital (2019-284-01), and all participants signed informed consent forms.

**Definitions** Adverse pregnancy outcomes is a general term referring to the short-term and long-term effects of pregnancy and delivery-related complications on maternal and fetal health [5-6]. The adverse pregnancy outcomes included in this study comprised preeclampsia, cesarean delivery, preterm birth, intrauterine growth restriction, macrosomia, low birth weight infant, large-for-gestational-age infant, and small-for-gestational-age infant.

Preeclampsia was defined as hypertension [systolic blood pressure $\geq$ 140 mmHg (1 mmHg = 0.133 kPa), diastolic blood pressure $\geq$ 90 mmHg, measured twice with an interval of $\geq$ 4 hours] with proteinuria, or without proteinuria but with end-organ dysfunction after 20 weeks of gestation [14]. Preterm birth was defined as delivery before 37 weeks of gestation [15]. Low birth weight infant referred to birth weight $<$ 2,500 g [16]. Macrosomia was defined as birth weight $>$ 4,000 g [17]. Large-for-gestational-age infant referred to birth weight $\geq$ the 90th percentile for gestational age [18]. Small-for-gestational-age infant referred to birth weight $\leq$ the 10th percentile for gestational age [19].

**Data Collection** Relevant information was collected from the electronic medical record system of Nanjing Drum Tower Hospital, including maternal age, BMI (weight before delivery/height$^2$), menstrual history, obstetric history, past medical history, oral glucose tolerance test (OGTT) results at 24-28 weeks of gestation, and serum uric acid, blood lipids, and liver function indicators at 28-32 weeks of gestation.

**Serum Uric Acid and Uric Acid/Creatinine Ratio Stratification** Serum uric acid levels were stratified by quartiles into: Q1 ($\leq$ 257 mol/L), Q2 (257-359 mol/L), and Q3 ($\geq$ 359 mol/L). Serum uric acid/creatinine ratio levels were stratified by quartiles into: q1 ($\leq$ 5.88), q2 (5.88-7.94), and q3 ($\geq$ 7.94).

**Statistical Analysis** Statistical analysis was performed using SPSS 26.0 software. Normally distributed continuous variables were expressed as (mean $\pm$ standard deviation) and compared between groups using independent samples t-test. Non-normally distributed data were presented as median (P25, P75) and compared using non-parametric tests. Categorical data were expressed as relative numbers and compared using $^2$ test or Fisher' s exact test. Multivariate logistic regression analysis was used to examine the correlation between serum uric acid and uric acid/creatinine ratio levels with adverse pregnancy outcomes. $P < 0.05$ was considered statistically significant.

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## Results

**Baseline Characteristics** There were no statistically significant differences between the two groups in serum creatinine, alanine aminotransferase, aspartate aminotransferase, fasting glucose, 1-hour glucose, 2-hour glucose, glycated hemoglobin, total cholesterol, low-density lipoprotein, and high-density lipoprotein ($P > 0.05$). The adverse outcomes group had significantly higher maternal age, BMI, serum uric acid, serum uric acid/creatinine ratio, and triglycerides compared to the normal group ($P < 0.05$), as shown in Table 1 .

**Analysis of Adverse Pregnancy Outcomes** Among the 399 pregnant women in the adverse outcomes group, there were 305 cases of cesarean delivery (76.4%), 107 cases of preeclampsia (26.8%), 70 cases of preterm birth (17.5%), 29 cases of intrauterine growth restriction (7.2%), 57 cases of macrosomia (14.2%), 26 cases of low birth weight infant (6.5%), 48 cases of large-for-gestational-age infant (12.0%), and 34 cases of small-for-gestational-age infant (8.5%).

**Multivariate Logistic Regression Analysis** Multivariate logistic regression analysis was performed with each adverse pregnancy outcome as the dependent variable (assignment: yes = 1, no = 2) and different quartiles of serum

uric acid (assignment: Q1 = 1, Q2 = 2, Q3 = 3) and uric acid/creatinine ratio (assignment: q1 = 1, q2 = 2, q3 = 3) as independent variables. After adjusting for confounding factors, the results showed that compared with Q1 serum uric acid level, the risk of preeclampsia and intrauterine growth restriction increased at Q3 level ($P < 0.05$). Compared with q1 uric acid/creatinine ratio level, the risk of preeclampsia increased at q2 and q3 levels, the risk of preterm birth and intrauterine growth restriction increased at q3 level, while the risk of macrosomia and large-for-gestational-age infant decreased at q3 level ($P < 0.05$), as shown in Table 2 .

**Effects in Different Age Groups** Based on the median maternal age, pregnant women were divided into the <30 years group (341 cases) and the $ $30 years group (402 cases). Multivariate logistic regression analysis was performed for different age groups with preeclampsia and preterm birth as dependent variables (assignment: yes = 1, no = 2) and different quartiles of serum uric acid and uric acid/creatinine ratio as independent variables (assignment as above). After adjusting for confounding factors, the results showed that compared with Q1 serum uric acid level, the risk of preeclampsia increased in both age groups at Q3 level ($P < 0.05$). Compared with q1 uric acid/creatinine ratio level, the risk of preeclampsia increased in women aged $ $30 years at q2 and q3 levels ($P < 0.05$), as shown in Table 3 .

**Effects in Different Parity Groups** Based on previous pregnancy and delivery history, pregnant women were divided into the primiparous group (539 cases) and the multiparous group (194 cases). Multivariate logistic regression analysis was performed for different parity groups with preeclampsia and preterm birth as dependent variables (assignment as above) and different quartiles of serum uric acid and uric acid/creatinine ratio as independent variables (assignment as above). After adjusting for confounding factors, the results showed that compared with Q1 serum uric acid level, the risk of preeclampsia increased in primiparous women at Q3 level ($P < 0.05$). Compared with q1 uric acid/creatinine ratio level, the risk of preeclampsia increased in primiparous women at q2 and q3 levels, and the risk of preterm birth increased in primiparous women at q3 level ($P < 0.05$), as shown in Table 4 .

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## Discussion

Uric acid is the end product of purine nucleotide metabolism, and elevated serum uric acid is associated with adverse maternal and neonatal outcomes. Due to the unique metabolic state of pregnancy, serum uric acid undergoes dynamic changes. In early pregnancy, increased estrogen levels, renal blood flow, and glomerular filtration rate promote uric acid excretion, resulting in lower serum uric acid levels compared with pre-pregnancy. In the second and third trimesters, serum uric acid levels gradually increase as renal clearance of uric

acid decreases with placental maturation and fetal development [20-21]. Since serum uric acid levels are influenced by renal function and dietary intake, the serum uric acid/creatinine ratio can standardize renal function and more stably reflect the body' s uric acid level [11]. However, whether the uric acid/creatinine ratio can eliminate the influence of dietary factors has not been reported in large-sample studies. Some studies have found that the uric acid/creatinine ratio has predictive value for adverse neonatal outcomes, non-alcoholic fatty liver disease, and chronic kidney disease, but few have involved adverse pregnancy outcomes [13,22].

This study simultaneously included both serum uric acid and uric acid/creatinine ratio in the analysis and compared their correlations with adverse pregnancy outcomes. We found that compared with serum uric acid alone, the uric acid/creatinine ratio was associated with more adverse pregnancy outcomes, suggesting that clinical practice should pay greater attention to the predictive role of the uric acid/creatinine ratio. The results showed that high serum uric acid levels increased the risk of preeclampsia and intrauterine growth restriction, while high uric acid/creatinine ratio levels increased the risk of preeclampsia, preterm birth, and intrauterine growth restriction, but decreased the risk of macrosomia and large-for-gestational-age infants.

Previous studies have reported that elevated maternal serum uric acid is correlated with increased incidence of preeclampsia [23-25] and can assess disease severity [26], consistent with our findings. This may be related to oxidative stress injury and vascular dysregulation caused by disordered uric acid metabolism. Some scholars believe that uric acid may participate in the development of preeclampsia by activating inflammatory factors such as adenosine deaminase, interleukin-1$\beta$, tumor necrosis factor-$\alpha$, and nuclear factor- B [27-28]. Our study showed that high uric acid/creatinine ratio increased the risk of preterm birth and intrauterine growth restriction, suggesting that high uric acid-induced systemic inflammatory responses may reduce placental blood perfusion, impede maternal-fetal substance transport, and affect fetal growth and development [29-31]. Previous studies have similarly suggested that high uric acid restricts fetal growth, but most have analyzed only serum uric acid with less involvement of the uric acid/creatinine ratio [32]. In fact, advanced maternal age, underlying diseases, multiple pregnancy, and placental dysfunction can all affect fetal growth [33-34]; therefore, our study considered and excluded these confounding factors in the inclusion criteria and multivariate regression analysis.

Current research on the relationship between maternal serum uric acid and fetal birth weight remains controversial. Our results showed that high maternal uric acid/creatinine ratio decreased the risk of macrosomia and large-for-gestational-age infants. Hawkins et al. [35] and Akahori et al. [36] found that maternal serum uric acid was negatively correlated with fetal birth weight, possibly due to reduced placental amino acid uptake caused by high uric acid levels. Another study including 11,580 pregnant women reported that high maternal uric acid increased the risk of low birth weight and small-for-gestational-age infants,

which may be related to restricted fetal growth [37]. However, Rothenbacher et al. [38] found no association between maternal uric acid and neonatal birth weight, possibly due to confounding factors and regional differences.

To further explore the correlation between the effect of serum uric acid on adverse outcomes and maternal clinical characteristics, this study grouped women by age and parity. The results showed that in women aged $ $30 years or primiparous women, serum uric acid and uric acid/creatinine ratio had greater effects on preeclampsia, and the effect of uric acid/creatinine ratio on preterm birth mainly occurred in primiparous women. Sheen et al. [39] demonstrated that women aged 30-54 years accounted for a large proportion of preeclampsia and related adverse outcomes. Evidence suggests that women with multiple cesarean deliveries are more prone to preeclampsia [26], which is inconsistent with our findings and may be related to limited sample size. Currently, there is scarce research on the relationship between the effects of serum uric acid on preeclampsia and preterm birth with maternal parity and age, requiring further large-scale studies for verification.

This study has several limitations. First, as a single-center study, its representativeness of the general population is limited. Second, the lack of analysis on pre-pregnancy BMI and gestational weight gain prevented comprehensive exploration of the dynamic changes in serum uric acid throughout pregnancy. Future studies with larger sample sizes are needed for comprehensive analysis.

In conclusion, high serum uric acid levels increase the risk of preeclampsia and intrauterine growth restriction, while high uric acid/creatinine ratio levels increase the risk of preeclampsia, preterm birth, and intrauterine growth restriction, but decrease the risk of macrosomia and large-for-gestational-age infants. Elevated serum uric acid and uric acid/creatinine ratio levels during pregnancy are associated with adverse maternal and neonatal outcomes, particularly in women aged $ $30 years or primiparous women, and the uric acid/creatinine ratio can predict more adverse pregnancy outcomes than serum uric acid alone. In clinical practice, focusing on the uric acid/creatinine ratio in women aged $ $30 years or primiparous women is beneficial for early prevention and improvement of adverse maternal and neonatal outcomes.

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**Author Contributions**

ZHAO Ru: literature review, research design, and manuscript drafting. HAN Chen, HUANG Zeyu, WANG Qian: subject selection and data collection from electronic medical records. HU Jun: statistical analysis and table preparation. GE Zhijuan: research objective and proposition design. BI Yan: supervision of research process, manuscript guidance, and funding support. SHEN Shanmei: results verification, manuscript revision, final version approval, and overall responsibility for the manuscript.

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## References

[1] ITAHANA Y, HAN R, BARBIER S, et al. The uric acid transporter SLC2A9 is a direct target gene of the tumor suppressor p53 contributing to antioxidant defense [J]. Oncogene, 2015, 34(14): 1799-1810. DOI: 10.1038/onc.2014.119.

[2] TASAKI E, SAKURAI H, NITAO M, et al. Uric acid, an important antioxidant contributing to survival in termites [J]. PLoS One, 2017, 12(6): e0179426. DOI: 10.1371/journal.pone.0179426.

[3] KUWABARA M, HISATOME I, NIWA K, et al. Uric acid is a strong risk marker for developing hypertension from prehypertension: a 5-year Japanese cohort study [J]. Hypertension, 2018, 71(1): 78-86. DOI: 10.1161/HYPERTENSIONAHA.117.10370.

[4] ZHOU C, LIU M Y, ZHANG Z X, et al. Positive association of serum uric acid with new-onset diabetes in Chinese women with hypertension in a retrospective analysis of the China Stroke Primary Prevention Trial [J]. Diabetes Obes Metab, 2020, 22(9): 1598-1606. DOI: 10.1111/dom.14072.

[5] 陈敦金, 谭虎. 建立孕产妇”全孕期”管理体系降低不良妊娠结局 [J]. 中国实用妇科与产科杂志, 2020, 36(5): 385-388. DOI: 10.19538/j.fk2020050101.

[6] 谢幸, 孔北华, 段涛. 妇产科学 [M]. 9 版. 北京: 人民卫生出版社, 2018.

[7] AMINI E, SHEIKH M, HANTOUSHZADEH S, et al. Maternal hyperuricemia in normotensive singleton pregnancy, a prenatal finding with continuous perinatal and postnatal effects, a prospective cohort study [J]. BMC Pregnancy Childbirth, 2014, 14: 104. DOI: 10.1186/1471-2393-14-104.

[8] YUE C Y, YING C M, LI X T. Elevated serum uric acid is associated with gestational diabetes mellitus: an observational cohort study [J]. J Clin Endocrinol Metab, 2023, 108(7): e480-486. DOI: 10.1210/clinem/dgac760.

[9] WEISSGERBER T L, MILIC N M, TURNER S T, et al. Uric acid: a missing link between hypertensive pregnancy disorders and future cardiovascular disease? [J]. Mayo Clin Proc, 2015, 90(9): 1207-1216. DOI: 10.1016/j.mayocp.2015.05.020.

[10] ZHAO J, ZHENG D Y, YANG J M, et al. Maternal serum uric acid concentration is associated with the expression of tumour necrosis factor-$\alpha$ and

intercellular adhesion molecule-1 in patients with preeclampsia [J]. J Hum Hypertens, 2016, 30(7): 456-462. DOI: 10.1038/jhh.2015.110.

[11] AL-DAGHRI N M, AL-ATTAS O S, WANI K, et al. Serum uric acid to creatinine ratio and risk of metabolic syndrome in Saudi type 2 diabetic patients [J]. Sci Rep, 2017, 7(1): 12104. DOI: 10.1038/s41598-017-12085-0.

[12] WANG R S, XUE F B, WANG L P, et al. Serum uric acid to creatinine ratio is associated with higher prevalence of NAFLD detected by FibroScan in the United States [J]. J Clin Lab Anal, 2022, 36(8): e24590. DOI: 10.1002/jcla.24590.

[13] GU L B, HUANG L J, WU H D, et al. Serum uric acid to creatinine ratio: a predictor of incident chronic kidney disease in type 2 diabetes mellitus patients with preserved kidney function [J]. Diab Vasc Dis Res, 2017, 14(3): 221-225. DOI: 10.1177/1479164116680318.

[14] ACOG practice bulletin No. 202: gestational hypertension and preeclampsia [J]. Obstet Gynecol, 2019, 133(1): 1. DOI: 10.1097/AOG.0000000000003018.

[15] GOLDENBERG R L, CULHANE J F, IAMS J D, et al. Epidemiology and causes of preterm birth [J]. Lancet, 2008, 371(9606): 75-84. DOI: 10.1016/S0140-6736(08)60074-4.

[16] HE Z F, BISHWAJIT G, YAYA S N, et al. Prevalence of low birth weight and its association with maternal body weight status in selected countries in Africa: a cross-sectional study [J]. BMJ Open, 2018, 8(8): e020410. DOI: 10.1136/bmjopen-2017-020410.

[17] Macrosomia: ACOG practice bulletin, number 216 [J]. Obstet Gynecol, 2020, 135(1): e18-35. DOI: 10.1097/AOG.0000000000003606.

[18] CHANDRASEKARAN N. Induction of labor for a suspected large-for-gestational-age/macrosomic fetus [J]. Best Pract Res Clin Obstet Gynaecol, 2021, 77: 110-118. DOI: 10.1016/j.bpobgyn.2021.09.005.

[19] DAI L, DENG C F, LI Y H, et al. Birth weight reference percentiles for Chinese [J]. PLoS One, 2014, 9(8): e104779. DOI: 10.1371/journal.pone.0104779.

[20] MARTIN A C, BROWN M A. Could uric acid have a pathogenic role in pre-eclampsia? [J]. Nat Rev Nephrol, 2010, 6(12): 744-748. DOI: 10.1038/nrneph.2010.125.

[21] CHEUNG K L, LAFAYETTE R A. Renal physiology of pregnancy [J]. Adv Chronic Kidney Dis, 2013, 20(3): 209-214. DOI: 10.1053/j.ackd.2013.01.012.

[22] SOOKOIAN S, PIROLA C J. The serum uric acid/creatinine ratio is associated with nonalcoholic fatty liver disease in the general population [J]. J Physiol Biochem, 2022. DOI: 10.1007/s13105-022-00893-6. Online ahead of print.

[23] YUE C Y, YING C M, LI X T. Association of first trimester serum uric acid with preeclampsia: an observational cohort study with propensity score

matching [J]. Hypertens Res, 2023, 46(2): 377-385. DOI: 10.1038/s41440-022-01115-8.

[24] LAUGHON S K, CATOV J, POWERS R W, et al. First trimester uric acid and adverse pregnancy outcomes [J]. Am J Hypertens, 2011, 24(4): 489-495. DOI: 10.1038/ajh.2010.262.

[25] CHEN Y Q, OU W C, LIN D, et al. Increased uric acid, gamma-glutamyl transpeptidase and alkaline phosphatase in early-pregnancy associated with the development of gestational hypertension and preeclampsia [J]. Front Cardiovasc Med, 2021, 8: 756140. DOI: 10.3389/fcvm.2021.756140.

[26] 吕琳, 艾玲, 平泽朋. 孕妇血清尿酸水平与妊娠期高血压疾病严重程度的相关性分析 [J]. 中国妇幼保健, 2021, 36(24): 5649-5651. DOI: 10.19829/j.zgfybj.issn.1001-4411.2021.24.013.

[27] GIORGI V S, WITKIN S S, BANNWART-CASTRO C F, et al. Elevated circulating adenosine deaminase activity in women with preeclampsia: association with pro-inflammatory cytokine production and uric acid levels [J]. Pregnancy Hypertens, 2016, 6(4): 400-405. DOI: 10.1016/j.preghy.2016.09.004.

[28] ZHAO J, ZHENG D Y, YANG J M, et al. Maternal serum uric acid concentration is associated with the expression of tumour necrosis factor-$\alpha$ and intercellular adhesion molecule-1 in patients with preeclampsia [J]. J Hum Hypertens, 2016, 30(7): 456-462. DOI: 10.1038/jhh.2015.110.

[29] BRIEN M E, DUVAL C, PALACIOS J, et al. Uric acid crystals induce placental inflammation and alter trophoblast function via an IL-1-dependent pathway: implications for fetal growth restriction [J]. J Immunol, 2017, 198(1): 443-451. DOI: 10.4049/jimmunol.1601179.

[30] BAINBRIDGE S A, VON VERSEN-HÖYNCK F, ROBERTS J M. Uric acid inhibits placental system A amino acid uptake [J]. Placenta, 2009, 30(2): 195-200. DOI: 10.1016/j.placenta.2008.10.015.

[31] JANSSON N, PETTERSSON J, HAAFIZ A, et al. Down-regulation of placental transport of amino acids precedes the development of intrauterine growth restriction in rats fed a low protein diet [J]. J Physiol, 2006, 576(Pt 3): 935-946. DOI: 10.1113/jphysiol.2006.116509.

[32] 黄琼辉, 刘捷, 曾超美, 等. 母体高尿酸血症对妊娠结局和新生儿合并症影响的回顾性巢式病例对照研究 [J]. 中国循证儿科杂志, 2022, 17(5): 331-335. DOI: 10.3969/j.issn.1673-5501.2022.05.002.

[33] FREDERIKSEN L E, ERNST A, BRIX N, et al. Risk of adverse pregnancy outcomes at advanced maternal age [J]. Obstet Gynecol, 2018, 131(3): 457-463. DOI: 10.1097/AOG.0000000000002504.

[34] JANA A, BANERJEE K, KHAN P K. Early arrivals: association of maternal obstetric factors with preterm births and their survival in India [J]. Public Health, 2022, 211: 37-46. DOI: 10.1016/j.puhe.2022.07.005.

[35] AKAHORI Y, MASUYAMA H, HIRAMATSU Y. The correlation of maternal uric acid concentration with small-for-gestational-age fetuses in normotensive pregnant women [J]. Gynecol Obstet Invest, 2012, 73(2): 162-167. DOI: 10.1159/000332391.

[36] HAWKINS T L, ROBERTS J M, MANGOS G J, et al. Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: a retrospective cohort study [J]. BJOG, 2012, 119(4): 484-492. DOI: 10.1111/j.1471-0528.2011.03232.x.

[37] YUAN X S, HAN X Y, JIA C B, et al. Association of maternal serum uric acid and cystatin C levels in late pregnancy with adverse birth outcomes: an observational cohort study in China [J]. Int J Womens Health, 2022, 14: 213-223. DOI: 10.2147/IJWH.S350847.

[38] ROTHENBACHER D, BRAIG S, LOGAN C A, et al. Association of maternal uric acid and cystatin C serum concentrations with maternal and neonatal cardiovascular risk markers and neonatal body composition: the Ulm SPATZ Health Study [J]. PLoS One, 2018, 13(7): e0200470. DOI: 10.1371/journal.pone.0200470.

[39] SHEEN J J, HUANG Y M, ANDRIKOPOULOU M, et al. Maternal age and preeclampsia outcomes during delivery hospitalizations [J]. Am J Perinatol, 2020, 37(1): 44-52. DOI: 10.1055/s-0039-1694794.

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