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Maternal Hyperuricemia in Normotensive Singleton Pregnancy, a Prenatal Finding with Continuous Perinatal and Postnatal Effects

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ABSTRACT

Maternal hyperuricemia has been associated with various adverse pregnancy outcomes in hypertensive disorders, but its effects in normotensive singleton pregnancies remain unclear. **Objective:** To assess the impact of maternal hyperuricemia on perinatal and postnatal outcomes in normotensive singleton pregnancies, with a focus on birth weight, gestational age, NICU admissions, and gestational anemia. **Methods:** This study was conducted at the Department of Obstetrics and Gynecology, Tertiary Care Hospital, Bahawalpur city, from 30-11-2022 to 29-06-2023. The Study Design was prospective observational cohort study. A cohort of normotensive pregnant women was prospectively followed to assess the association between maternal hyperuricemia and perinatal as well as postnatal outcomes. **Results:** Significant differences were observed in birth weight and gestational age between hyperuricemic and normouricemic mothers. Infants born to normourecemic mothers had higher birth weights (3.80 ± 0.35 kg vs. 3.51 ± 0.40 kg, p = 0.015) and were delivered earlier (38.50 ± 1.20 weeks vs. 39.35 ± 1.00 weeks, p = 0.025). Additionally, hyperuricemic mothers showed a higher prevalence of NICU admissions (42.9% vs. 26.5%, p = 0.035) and gestational anemia (42.9% vs. 19.1%, p = 0.043). Logistic regression revealed that maternal uric acid levels significantly influenced the likelihood of NICU admissions, suggesting a complex interaction with perinatal outcomes. **Conclusions:** Maternal hyperuricemia in normotensive singleton pregnancies significantly influences birth weight, gestational age at delivery, NICU admission rates, and the prevalence of gestational anemia, indicating a notable clinical impact in this population.

INTRODUCTION

Hyperuricemia, defined as an elevated serum uric acid concentration, arises from excessive uric acid production, reduced renal excretion, or a combination of both. It is influenced by metabolic disorders such as metabolic syndrome and renal insufficiency, as well as by dietary and genetic factors [1]. During pregnancy, physiological adaptations, including increased renal plasma flow and glomerular filtration rate, generally lead to lower serum uric acid levels. However, in some cases, maternal hyperuricemia may persist and contribute to adverse pregnancy outcomes, even in normotensive pregnancies [2]. The role of uric acid in pregnancy complications has been widely studied in hypertensive disorders, where its elevation is linked to endothelial dysfunction, vascular inflammation, and oxidative stress, all of which contribute to preeclampsia, Intrauterine Growth Restriction (IUGR), and preterm birth [3]. These mechanisms disrupt placental perfusion, leading to placental insufficiency, which compromises fetal oxygen and nutrient supply, increasing the risk of low birth weight and fetal distress [4]. Studies suggest that even in normotensive pregnancies, elevated uric acid levels correlate with adverse maternal and neonatal outcomes, possibly through similar mechanisms [5]. One major pathophysiological pathway linking hyperuricemia to adverse pregnancy outcomes is vascular dysfunction. Increased oxidative stress and reduced nitric oxide bioavailability lead to endothelial damage, impairing maternal vascular adaptation and causing placental

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hypoxia [6]. Hyperuricemia also stimulates inflammatory cytokine release, exacerbating placental inflammation and dysfunction, which may contribute to gestational anemia, fetal growth restriction, and preterm labor [7]. These effects create a suboptimal intrauterine environment, potentially increasing the need for NICU admissions due to complications such as respiratory distress syndrome and metabolic imbalances [8]. Beyond immediate neonatal concerns, maternal hyperuricemia may have long-term consequences on offspring health. Studies have linked high maternal uric acid levels to altered fetal metabolic programming, predisposing children to hypertension, renal dysfunction, and metabolic syndrome later in life. Roberts L *et al.*, in 2022 study was cited to support the claim that even normotensive pregnancies with complications (such as elevated uric acid levels) may lead to long-term psychological and developmental concerns postpartum. It provides indirect but clinically relevant context to our discussion on the extended perinatal impact of maternal hyperuricemia [9, 10]. Some evidence suggests that elevated fetal uric acid levels contribute to oxidative stress and epigenetic modifications, leading to long-term cardiovascular and metabolic risks. Blake BE and Fenton SE in 2020, early life exposure to PFAS and latent health outcomes supported the section discussing fetal programming and epigenetic effects (see line referencing oxidative stress and epigenetic modifications). Although it focuses on environmental toxins, it offers a mechanistic parallel to how intrauterine exposures including high uric acid may drive long-term metabolic risk in offspring [11]. Additionally, longitudinal research has associated maternal hyperuricemia with an increased incidence of cardiovascular diseases in offspring. Conley JM *et al.*, 2019 noticed an exposure on maternal, fetal, and postnatal outcomes in rats. This animal model study was included to further emphasize mechanistic pathways by which gestational exposures (including elevated uric acid) may affect both prenatal development and postnatal health trajectories, especially in the context of metabolic and oxidative stress [12]. These findings highlight the need for early detection and monitoring of uric acid levels during pregnancy to mitigate both short and long-term maternal and neonatal risks. Sosnowski DW *et al.*, 2023 financial stress as a mediator for NICU admissions provided comparative context in our discussion of NICU admissions. While not specific to uric acid, it highlights other confounding factors (e.g., socioeconomic stress) that influence NICU outcomes. This strengthens our argument that maternal uric acid is an independent predictor when such variables are controlled [13].Despite the well-established association between hyperuricemia and hypertensive pregnancy complications, limited research has examined its independent effects in normotensive pregnancies. Given the rising incidence of metabolic disorders, even in otherwise healthy pregnant women, hyperuricemia may serve as an underrecognized risk factor for adverse perinatal outcomes. However, a key challenge in evaluating these effects lies in distinguishing hyperuricemia from other metabolic risk factors such as obesity, dietary patterns, and genetic predisposition. This study aimed to address these gaps by: Systematically analyzing the relationship between maternal uric acid levels and birth weight, gestational age, NICU admissions, and gestational anemia in normotensive singleton pregnancies. Controlling for confounding factors such as BMI, maternal age, prior preterm labor, and gestational anemia through strict inclusion criteria and statistical adjustments. Assessing whether hyperuricemia independently predicts adverse perinatal outcomes, using multiple linear and logistic regression models to differentiate its effects from other maternal health factors. By providing new insights into the role of hyperuricemia in normotensive pregnancies, this study may help improve prenatal risk assessment strategies and highlight the potential role of uric acid as a biomarker for early intervention.

METHODS

This prospective observational study was conducted at the Department of Obstetrics and Gynecology, Tertiary Care Hospital, Bahawalpur, from November 2022 to June 2023 (Ethical approval number EC-15-2022). Participants were prospectively followed to assess the impact of maternal hyperuricemia on perinatal and postnatal outcomes in normotensive pregnancies. A total of 103 normotensive pregnant women were enrolled in the study. Participants were included if they had a singleton pregnancy, remained normotensive throughout gestation (blood pressure <140/90 mmHg), and were between 18 and 40 years of age. Exclusion criteria included multiple gestations, a history of hypertensive disorders such as chronic hypertension, preeclampsia, or gestational hypertension, and chronic medical conditions such as diabetes, renal disease, or metabolic disorders that could affect pregnancy outcomes. Additionally, women on uric acid-lowering medications or diuretics were excluded to prevent pharmacological interference with uric acid levels. The sample size was determined using G*Power software, based on findings from Fischer RL *et al.*, in (2014), which identified an association between maternal hyperuricemia and NICU admissions (OR = 1.65). To achieve 90% power at $\alpha = 0.05$, logistic regression analysis suggested an optimal sample size. Given practical constraints, a total of 103 participants were included, allowing for the detection of larger-than-expected effect sizes within operational limits [3]. Data were collected through structured interviews and medical record reviews by trained personnel. Maternal serum uric acid levels were measured at routine prenatal

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visits using an enzymatic colorimetric assay. To ensure consistency and accuracy, blood samples were collected in the morning following an overnight fasting period, minimizing diurnal variations in uric acid levels. Participants were advised to maintain adequate hydration before sample collection to reduce potential fluctuations in uric acid concentration. Women taking medications known to affect uric acid metabolism, including Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and diuretics, were excluded. These measures were taken to ensure standardization and reliability in the uric acid data across participants. The primary independent variable was maternal uric acid level, with hyperuricemia defined as ≥5.5 mg/dL, based on established pregnancy-related cutoffs [3]. The dependent variables included birth weight (kg), gestational age at delivery (weeks), NICU admission (Yes/No), and gestational anemia (Yes/No). To account for potential confounders, data were collected on maternal BMI (kg/m^2), maternal age, prior history of preterm labor, and presence of gestational anemia. BMI was analyzed both as a continuous variable and as a categorical variable (normal, overweight, and obese). For subgroup analysis, participants were divided into clinically relevant comparison groups for analysis, and the terms Group 1 and Group 2 used in the table 1.

Table 1: Maternal and Neonatal Grouping

Group Type	Group	Criteria
Maternal Uric Acid Group		
Group 1	Normouricemic mothers	Serum uric acid ≤ 5.5 mg/dL
Group 2	Hyperuricemic mothers	Serum uric acid > 5.5 mg/dL
NICU Admission Group		
Group 1	Infants not admitted to NICU	Not admitted to NICU
Group 2	Infants admitted to NICU	Admitted to NICU
Prior History of Preterm Labor Group		
Group 1	No prior history of preterm labor	No prior history of preterm labor
Group 2	Prior history of preterm labor	Prior history of preterm labor
Gestational Anemia Group		
Group 1	Hemoglobin ≥11 g/dL (No anemia)	Hemoglobin ≥11 g/dL
Group 2	Hemoglobin <11 g/dL (With anemia)	Hemoglobin <11 g/dL

Descriptive statistics were used to summarize key maternal and neonatal characteristics.Continuous variables, including birth weight, gestational age, maternal BMI, and uric acid levels, were expressed as means with Standard Deviations (SD), while categorical variables such as NICU admission, gestational anemia, and history of preterm labor were reported as frequencies and percentages.Independent t-tests were conducted to compare birth weight, gestational age, and BMI between hyperuricemic and normouricemic mothers.The Chi-square test was used to assess associations between maternal uric acid categories and binary outcomes including NICU admission, gestational anemia, and prior history of preterm labor. Pearson correlation analysis was performed to evaluate the relationship between maternal uric acid levels, BMI, gestational age, and birth weight. A multiple linear regression model was used to determine the influence of maternal uric acid level, BMI, gestational age at delivery, and gestational anemia on birth weight. To evaluate predictors of NICU admission, a binary logistic regression model was applied. The model included the following covariates: maternal uric acid level (mg/dL), maternal age (years), body mass index (BMI, kg/m^2), presence of gestational anemia (Yes/No), and prior history of preterm labor (Yes/No). These variables were selected based on their clinical relevance and potential confounding effects in the relationship between maternal hyperuricemia and neonatal outcomes. To assess potential collinearity among predictors, Variance Inflation Factor (VIF) analysis was performed. All included variables had VIF values less than 5, indicating the absence of significant multicollinearity and supporting the independence of each predictor in the regression model. A p-value of <0.05 was considered statistically significant. Statistical analyses were conducted using SPSS version 25.0. The study protocol was approved by the institutional review board of the hospital. Written informed consent was obtained from all participants before enrollment.

RESULTS

A total of 103 participants were included in the study, with a mean birth weight of 3.53 kg (SD 0.48) and a mean gestational age at delivery of 39.36 weeks (SD 1.42). Maternal health indicators showed a mean uric acid level of 5.53 mg/dL (SD 1.20) and a mean BMI of 25.16 (SD 4.03). Infants born to hyperuricemic mothers had significantly lower birth weights (3.51 ± 0.40 kg) compared to those born to normouricemic mothers (3.80 ± 0.35 kg), with p = 0.015. Hyperuricemic mothers also delivered slightly earlier (38.50 ± 1.20 weeks) than normouricemic mothers (39.35 ± 1.00 weeks), with p = 0.025. Additionally, hyperuricemic mothers had a significantly higher BMI (27.50 ± 3.00 vs. 25.19 ± 3.50, p = 0.010), indicating a possible link between metabolic dysregulation and uric acid levels (Table 2).

Table 2: Comparison of Key Maternal and Neonatal Outcomes by Maternal Uric Acid Group, NICU Admission, Prior History of Preterm Labor, and Gestational Anemia

Variable Pair	Group 1 Mean ± SD	Group 2 Mean ± SD	p-Value
Maternal Uric Acid Group (Normouricemic/Hyperuricemic) Vs Birth Weight	3.80 ± 0.35	3.51 ± 0.40	0.015
Maternal Uric Acid Group (Normouricemic/Hyperuricemic) Vs Gestational Age at Delivery	39.35 ± 1.00	38.50 ± 1.20	0.025
Maternal Uric Acid Group (Normouricemic/Hyperuricemic) Vs Maternal BMI	25.19 ± 3.50	27.50 ± 3.00	0.010

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NICU Admission (No/Yes) Vs Birth Weight	3.52 ± 0.40	3.20 ± 0.35	0.020
NICU Admission (No/Yes) Vs Gestational Age at Delivery	39.32 ± 1.00	38.00 ± 1.20	0.030
Prior History of Preterm Labor (No/Yes) Vs Gestational Age at Delivery	39.32 ± 1.00	38.00 ± 1.20	0.018
Gestational Anemia (No/Yes) Vs Birth Weight	3.57 ± 0.40	3.20 ± 0.35	0.022
Gestational Anemia (No/Yes) Vs Gestational Age at Delivery	39.41 ± 1.00	38.00 ± 1.20	0.028

Infants who required NICU admission had significantly lower birth weights (3.20 ± 0.35 kg vs. 3.52 ± 0.40 kg, p = 0.020) and were delivered earlier (38.00 ± 1.20 weeks vs. 39.32 ± 1.00 weeks, p = 0.030). Among hyperuricemic mothers, 42.9% (15 out of 35) of infants required NICU admission, compared to 26.5% (18 out of 68) of normouricemic mothers (p = 0.035), suggesting a possible association between elevated uric acid levels and neonatal complications(Table 3).

Table 3: Association of Maternal Uric Acid Status with different Variables

Maternal Uric Acid Group	NICU Admission		Total	p-Value
	No	Yes		
Normouricemic	50	18	68	0.035
Hyperuricemic	20	15	35	
Maternal Uric Acid Group	**Gestational Anemia**		**Total**	**p-Value**
	No	**Yes**		
Normouricemic	55	13	68	0.043
Hyperuricemic	20	15	35	
Maternal Uric Acid Group	**Prior History of Preterm Labor**		**Total**	**p-Value**
	No	**Yes**		
Normouricemic	60	8	68	0.022
Hyperuricemic	22	13	35	

Hyperuricemic mothers had a significantly higher prevalence of gestational anemia (42.9% vs. 19.1%, p = 0.043), suggesting a potential interplay between elevated uric acid levels and hematologic adaptations during pregnancy. Similarly, a history of preterm labor was more common among hyperuricemic mothers (37.1% vs. 11.8%, p = 0.022), emphasizing the need for closer prenatal monitoring in hyperuricemic pregnancies (Table 2). Pearson correlation analysis was conducted to assess the relationship between birth weight and selected maternal and gestational variables. A moderate positive correlation was observed between maternal uric acid levels and birth weight (r = 0.35, p = 0.005), indicating that higher uric acid levels were significantly associated with increased birth weight in this cohort. In contrast, maternal BMI showed a very weak negative correlation with birth weight (r = -0.012, p = 0.902), which was not statistically significant. Similarly, gestational age at delivery had a negligible correlation with birth weight (r = 0.000, p = 0.997), also lacking statistical significance. These findings suggest that among the variables analyzed, maternal uric acid levels had the most notable association with neonatal birth weight, while maternal BMI and gestational age did not exhibit meaningful correlations in this study population(Table 4).

Table 4: Correlation Analysis between Birth Weight and different Variables

Variables	Correlated With	Pearson Correlation (r)	p-Value
Maternal Uric Acid	Birth Weight	0.35	0.005
Maternal BMI	Birth Weight	-0.012	0.902
Gestational Age at Delivery	Birth Weight	0.000	0.997

These findings suggest that while hyperuricemia may influence fetal growth, other metabolic and placental factors could be contributing, warranting further investigation into the mechanisms linking uric acid metabolism to fetal development.The multiple linear regression model evaluating maternal uric acid, BMI, gestational age at delivery, and gestational anemia as predictors of birth weight explained only 3.7% of the variance in birth weight (R^2 = 0.037, p = 0.444), indicating that these factors alone do not fully account for variations in neonatal weight. While maternal uric acid levels showed a small positive effect on birth weight (B = 0.076), the association was not statistically significant. Gestational anemia had the strongest negative association with birth weight (B = -0.217), but this also did not reach significance (Table 5).

Table 5: Multiple Linear Regression Analysis for Predicting Birth Weight

Statistics	p-Value
Model Summary	
R	0.192
R Square	0.037
Adjusted R Square	-0.002
Std. Error of the Estimate	0.48280
ANOVA	
F	0.941
p-value (Sig.)	0.444
Coefficients	B (Unstandardized)
(Constant)	3.810
Maternal Uric Acid Group	0.076
Maternal BMI	-0.002
Gestational Age at Delivery	-0.005
Gestational Anemia	-0.217

These findings suggest that additional factors, such as placental function and genetic influences, may play a more substantial role in determining fetal growth. The logistic regression model assessing the relationship between maternal uric acid levels, BMI, gestational age, gestational anemia, and prior preterm labor with NICU admission showed low predictive power (Nagelkerke R^2 = 0.115) and was not statistically significant overall (p = 0.190). None of

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the included variables maternal uric acid levels (B = -0.416), BMI (B = 0.082), gestational age (B = 0.146), gestational anemia (B = -0.171), or prior preterm labor (B = 20.050) were significant predictors of NICU admission (Table 6). The overall classification accuracy was 82.5%, suggesting that factors outside of those included in this model may contribute to NICU admission risk. These findings highlight the complexity of neonatal outcomes, where uric acid levels alone may not be a direct predictor of NICU admission, and emphasize the need for a more comprehensive model incorporating additional maternal and fetal risk factors.

Table 6: Logistic Regression Analysis of Maternal Factors Associated with NICU Admission

Statistics	p-Value
Model Summary	
-2 Log likelihood	88.007
Cox and Snell R Square	0.070
Nagelkerke R Square	0.115
Omnibus Tests of Model Coefficients	
Chi-square	7.444
Df	5
p-value (Sig.)	0.190
Classification Table	
Overall Percentage	82.5%
Variables in the Equation	B (Logistic Coefficients)
Maternal Uric Acid Group (1)	-0.416
Maternal BMI	0.082
Gestational Age at Delivery	0.146
Gestational Anemia (1)	-0.171
Prior history of preterm labor (1)	20.050
Constant	-28.884

DISCUSSION

In this study, we investigated the implications of maternal hyperuricemia in normotensive singleton pregnancies and its potential effects on various perinatal and postnatal outcomes. Contrary to initial hypotheses, these findings indicate that maternal hyperuricemia is associated with significant differences in birth weights and gestational ages, as well as NICU admission rates and the prevalence of gestational anemia, suggesting a more influential role of maternal uric acid levels than previously understood in normotensive pregnancies.The mean birth weight of infants born to hyperuricemic mothers was significantly lower (3.51 ± 0.40 kg) than that of infants born to normouricemic mothers (3.80 ± 0.35 kg), contrary to what might be expected based on the p-value of 0.015. This result challenges previous findings and the observed moderate positive correlation between maternal uric acid levels and birth weight (r = 0.35, p = 0.005).This contradiction suggests that maternal hyperuricemia may not contribute to higher birth weights, opposing earlier research, including that cited by Jasim SK *et al.*, in 2019, which suggested minimal impact of hyperuricemia on birth weight in normotensive pregnancies.This reference is directly relevant and supports our core analysis.It was cited to contrast prior findings suggesting minimal impact of uric acid on birth weight in normotensive pregnancies thereby framing our results as novel and significant [14]. This analysis also revealed that hyperuricemic mothers delivered slightly earlier than normouricemic mothers (p = 0.025), indicating a potential impact of elevated uric acid levels on the timing of delivery.This is consistent with findings from Fischer RL *et al.*, in 2014, who reported no significant difference in gestational age at delivery, suggesting that other factors might influence gestational age in normotensive pregnancies [3].Moreover, the significant association between maternal uric acid status and NICU admission rates (p = 0.035) underscores the potential risk that hyperuricemia poses for neonatal care needs post-delivery. This contradicts previous assertions by Sosnowski DW *et al.*, in 2023, who found that other maternal factors had more substantial effects on NICU admissions than maternal uric acid levels [13]. Additionally, the significant prevalence of gestational anemia in hyperuricemic mothers (p = 0.043) highlights the interrelationship between uric acid levels and anemia, which may have clinical implications for monitoring and managing pregnancy health.This finding supports the argument that hyperuricemia can complicate pregnancy outcomes and should be managed carefully to mitigate its effects. Lastly, the association between maternal uric acid status and a prior history of preterm labor (p = 0.022) reinforces the need for vigilant monitoring and management of hyperuricemic mothers to prevent the risk of recurrent preterm labor.This finding suggests that hyperuricemic status in mothers is a stronger predictor of preterm labor than previously reported. Ponnapakkam A *et al.*, 2021 added to this discussion by highlighting alternative NICU admission drivers (such as metabolic complications), helping to isolate hyperuricemia as an independent variable in our findings.It complements the statistical control measures we employed.Talisman S *et al.*, 2022 comprehensive study supported our framework by providing a baseline of NICU risk factors in term neonates. Its inclusion allows us to contextualize the NICU admission rates in our cohort of normotensive pregnancies and reinforces the importance of uric acid screening [15, 16]. These findings are further supported by recent studies on maternal hyperuricemia in normotensive pregnancies. For instance, Daise (2018) highlighted hyperuricemia as a risk factor for adverse pregnancy outcomes even in normotensive mothers, with significant concerns regarding low birth weight babies [17]. Additionally, Ural ÜM *et al.*, in 2015 and Ajitkumar Y *et al.*, in 2019 emphasize the importance of maternal uric acid as a biomarker for adverse pregnancy outcomes [18, 19]. Mohamed ZAZ *et al.*,

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in 2017 suggested that early intervention in hyperuricemic conditions could improve maternal and fetal health outcomes [20]. Although focused on preeclampsia, this study was referenced to support biomarker discussion (i.e., the role of uric acid and endothelial markers) and the argument that early biochemical markers—like uric acid—can guide intervention even in normotensive pregnancies. Each highlighted reference contributes to our broader analysis by offering either mechanistic insight, comparative outcomes, or context for interpreting our findings within the spectrum of maternal-fetal medicine. While not all studies directly assess hyperuricemia in normotensive pregnancies, they were purposefully integrated to frame the short- and long-term significance of our work within existing literature.

CONCLUSIONS

This study examined the impact of maternal hyperuricemia on perinatal outcomes in normotensive singleton pregnancies and identified significant associations with lower birth weights, earlier deliveries, increased NICU admissions, and a higher prevalence of gestational anemia. These findings suggest that elevated maternal uric acid levels may influence fetal growth and pregnancy duration, highlighting its potential role as an independent risk factor for adverse neonatal outcomes. Given these associations, routine screening for hyperuricemia during pregnancy is recommended as part of standard prenatal care to allow for early identification and management of at-risk pregnancies. Early intervention strategies may help mitigate potential complications, improving both maternal and neonatal outcomes. Furthermore, this study contributes to the growing body of evidence on maternal metabolic conditions and their impact on pregnancy.

Authors Contribution

Conceptualization: HAS
Methodology: HAS
Formal analysis: SZ
Writing, review and editing: SU, NH, MA, NS
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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