Maternal Hyperuricemia and Birth Outcome in Normotensive Singleton Pregnancy: A Prospective Cohort Study

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Abstract

Introduction: Hyperuricemia is a common finding in preeclamptic pregnancies evident from early pregnancy.

Objective: In this study our main goal is to evaluate the effect of maternal hyperuricemia and birth outcome in normotensive singleton pregnancy.

Method: This prospective study was conducted at the department of Obstetrics and Gynecology, Institute of Child and Mother Health, Dhaka from January 2016 to January 2017 where total 102 normotensive singleton pregnant women examined. Two patients were excluded from the study due to lack of data. Data were analyzed using SPSS -21 windows version statistical package. Categorical variables were presented by frequency and percentage, and continuous variable by mean (sd) in case of normally distributed data and median (min-Max) in case of asymmetric data.

Results: During the study SBP mean level was 35.66 higher than DBP and for pregnant women found that gestational age 38 weeks and over then the serum uric acid level was higher. Also, LBWB was 36.7% lower than hyperuricemia.

Conclusion: we can conclude that Hyperuricemia is a risk factor for adverse pregnancy outcome for normotensive mother and LBWB is a concern in this regard. More studies and examinations are needed to confirm these results, as genetic, socioeconomic and dietary factors play key roles in uric acid concentrations.

Keywords: Hyperuricemia, Normotensive, Low birth weight baby (LBWB).

Introduction

Hyperuricemia is an excess of uric acid in the blood. Uric acid passes through the liver, and enters the bloodstream. Most of it is excreted in urine, or passes through intestines to regulate "normal" levels. Normal Uric acid levels are 2.4-6.0 mg/dL (female) and 3.4-7.0 mg/dL (male). Uric acid formation may occur when the blood uric acid level rises above 7 mg/dL and because of that many problems may arise such as such as
kidney stones, and gout (collection of uric acid crystals in the joints, especially in your toes and fingers), may occur. Causes of high uric acid levels (hyperuricemia) can be primary (increased uric acid levels due to purine), and secondary (high uric acid levels due to another disease or condition). Sometimes, the body produces more uric acid than it is able to excrete. Asymptomatic hyperuricemia is a common problem, affecting up to 20% of the general population. In pregnancy, hyperuricemia remains a prevalent problem despite the increase in the glomerular filtration rate (GFR). Elevated plasma uric acid has been connected with many adverse pregnancy consequences. Elevated plasma uric acid is an independent risk factor for preterm birth, low birth weight (LBW) delivery and low 1- and 5-minute Apgar scores.

Fig 1a and 1b: shows x-ray report of pregnant women with Hyperuricemia and its deposition in kidney. [3]

However, despite hyperuricemia antedating other clinical findings of preeclampsia, it has historically been ascribed to impaired renal function. Outside of pregnancy, hyperuricemia is considered a risk factor for hypertension, cardiovascular and renal disease. In pregnancy uric acid concentrations initially fall 25-35% due to the effects of estrogen, expanded blood volume and increased glomerular filtration rate. However, concentrations slowly rise to those observed in non-pregnant women by term gestation (4-6 mg/dL) In women who go on to develop preeclampsia, uric acid concentration is elevated as early as 10 weeks of gestation, a time much earlier than the clinical presentation of the disorder. Increased uric acid often precedes clinical manifestations of the disease, including reduced glomerular filtration rate. In this study our main goal is to evaluate the effect of maternal hyperuricemia and birth outcome in normotensive singleton pregnancy.

Objective
General objective
- To assess the effect of maternal hyperuricemia and birth outcome in normotensive singleton pregnancy.

Specific objective
- To detect SBP and DBP admission level of study population.
- To identify prevalence of different factors in patients.

Methodology
Study type
- This study was a prospective cohort study

Place and period of the study
- This prospective study was conducted at the department of Obstetrics and Gynaecology, Institute of Child and Mother Health, Dhaka from January 2016 to January 2017.

Method
- The study was carried out on total 102 normotensive singleton pregnant women who were admitted for delivery in hospital where two patients were excluded from the study due to lack of data and finally 100 patients were selected for analysis. Upon enrollment physical examinations were done and recorded in a pretested data
collection sheet, and maternal blood were obtained for determining uric acid levels.

Statistical method
- Data were analyzed using SPSS -21 windows version statistical package. Categorical variables were presented by frequency and percentage, and continuous variable by mean (sd) in case of normally distributed data and median (min-Max) in case of asymmetric data. Normality assumption was done by Shapiro Wilk test considering p value below 5% as normal distribution. Chi square test was done to measure the level of association. Mantel Haenszel Odd ratio was done to measure the risk. All tests were two sided and a p value less than 5% was considered as level of significance.

Results
In Table-1 shows Characteristics of the study subjects where mean (sd) age of the mother was 22.73 years. The following table is given below:

Table-1: Characteristics of the study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of the mother</td>
<td>22.73 years.</td>
</tr>
<tr>
<td>Birth weight of baby</td>
<td>2.86 kg</td>
</tr>
<tr>
<td>Maternal serum uric acid level</td>
<td>4.91 mg/dL</td>
</tr>
</tbody>
</table>

In figure-2 shows SBP (systolic blood pressure) and DBP (diastolic blood pressure) admission level of study population where SBP mean level was 35.66 higher than DBP. The following figure is given below:

![Figure: SBP and DBP admission level of study population](image)

In table-2 shows uric acid values that are considered elevated in pregnancy based on gestational age where in 38 weeks and over then the serum uric acid level was higher among others. The following table is given below:

Table-2: Uric acid values elevation in pregnancy

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Serum uric acid (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 – 32 W</td>
<td>≥ 4.50</td>
</tr>
<tr>
<td>32 W + 1 D - 33 W</td>
<td>≥ 4.70</td>
</tr>
<tr>
<td>33 W + 1 D - 34 W</td>
<td>≥ 4.93</td>
</tr>
<tr>
<td>34 W + 1 D - 35 W</td>
<td>≥ 4.98</td>
</tr>
<tr>
<td>35 W + 1 D - 36 W</td>
<td>≥ 5.04</td>
</tr>
<tr>
<td>36 W + 1 D - 37 W</td>
<td>≥ 5.40</td>
</tr>
<tr>
<td>≥ 38 W</td>
<td>≥ 5.58</td>
</tr>
</tbody>
</table>

In figure-3 shows prevalence of different factors in patients where prevalence of hyperuricemia was 2% less than low birth weight in baby. The following figure is given below:

![Figure-3: Prevalence of different factors in patients](image)

In table-3 shows multivariate logistic regression analysis of factors associated with preterm birth where maternal hyperuricemia B value was 1.15 which was higher than other factors. The following table is given below in detail:

**Table-3: Multivariate logistic regression analysis of factors associated with preterm birth**

<table>
<thead>
<tr>
<th>Factor</th>
<th>B value</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>Adjusted P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age &lt; 26 years</td>
<td>0.2</td>
<td>1.64 (1.1 – 2.44)</td>
<td>1.22 (0.77 – 1.92)</td>
<td>0.38</td>
</tr>
<tr>
<td>History of preterm birth</td>
<td>1.4</td>
<td>3.54 (1.61 – 7.77)</td>
<td>4.05 (1.71 – 9.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Primigravidity</td>
<td>0.59</td>
<td>2.05 (1.09 – 3.9)</td>
<td>1.8 (1.15 – 2.82)</td>
<td>0.009</td>
</tr>
<tr>
<td>Maternal hyperuricemia</td>
<td>1.15</td>
<td>3.68 (2.46 – 5.49)</td>
<td>3.17 (2.1 – 4.79)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Source by: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/1471-2393-14-104[6]*

In figure-4 shows association between maternal hyperuricemia and LBWB in study populations where LBWB was 36.7% lower than hyperuricemia. The following figure is given below in detail:

![Figure-4: Association between maternal hyperuricemia and LBWB](image)
Discussion
Maternal hyperuricemia in normotensive singleton pregnant women constitutes a risk factor for adverse pregnancy outcomes and the development of neonatal hypoglycemia and IVH. In newborns, increased serum uric acid is also associated with neonatal complications and poor prognosis. [4] One article reported that elevated uric acid concentrations in the first postnatal day are associated with the subsequent development of severe intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). In other studies, neonatal hyperuricemia was associated with asphyxia and infant respiratory distress syndrome (RDS). Maternal factors that were associated with increased maternal serum uric acid were as follows: primigravidity, younger maternal age, excessive weight gain and impaired renal function during pregnancy. [6] These associations have also been identified by other studies. [7][8] The association of excessive weight gain and impaired renal function with hyperuricemia can be explained by the overproduction and reduced renal excretion of uric acid, respectively. In this study we found that where LBWB was 36.7% lower than hyperuricemia. The mechanisms by which primigravity can increase maternal uric acid levels remain obscure. The relationship could be due to the immune maladaptation experienced in the first pregnancy; primiparity represents an immune challenge to the mother because of the semi-allogenic nature of the fetus. Other article reported that hyperuricemia during the second trimester or pregnancy was associated with a lower birth weight. [9] Another studies demonstrated that the free transfer of uric acid through the placenta, and suggest that the real etiology for these poor neonatal outcomes might be the elevated uric acid in maternal sera; neonatal hyperuricemia may be only a reflection of maternal and umbilical hyperuricemia. [10]

Limitation
- Sample size was small and study period was short.

Conclusion
After many examinations we can conclude that Hyperuricemia is a risk factor for adverse pregnancy outcome for normotensive mother and LBWB is a concern in this regard. More studies and examinations are needed to confirm these results, as genetic, socioeconomic and dietary factors play key roles in uric acid concentrations. Further, cohort studies are needed to measure serum uric acid before pregnancy and throughout gestation and estimate the effect of uric acid on pregnancy and neonatal outcomes to determine the practical usefulness of measuring and lowering serum uric acid levels before and throughout pregnancy.

Reference
3. https://www.google.com/search?q=hyperuricemia&tbm=isch&tbs=rimg:CSGHmlGx3f wNIjh6f-lZ6rAylgfUmEamIYGpwlyHSLSXVXeBPI kZ9vmxxEFv4iwvD7mMFoYv1DbkbV6_1B yhRgdawvyoSCXp_l6VnqsDKWET9ufOJ LaBvVKhIJB9SYRqYhagkRUt0wWqRX9y AqEgnCXIdItdVdxFrARCN8sXH9yoSCY E8iRn3-bFEQfvdovLytmCkhIj8RXILc8PuYwRdh N3oJC7UZlqEgkWhi_1UnuRtxHvQ2bgI hkBSoScb8HkFGB1rC_1EQ7ia2zi4Hb &tbo=u&sa=X&ved=2ahUKEwiNmJGR8_ rdAhVMuI8KHzHwAIUQ9C96BAgBEBg &biw=1366&bih=662&drp=1#imgrc=vwco UYHWsL-nPM:


