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Research Article

### STUDY OF RELATIONSHIP OF URIC ACID WITH PROGRESSION TO PRE-ECLAMPSIA AND DEVELOPMENT OF ADVERSE CONDITIONS IN PREGNANCIES HAVING GESTATIONAL HYPERTENSION

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**Abstract:**

**Background-** One of the serious complication during pregnancy is Pre-eclampsia whose most common clinical presentation is gestational hypertension (GH). However, the research available on the clinical risk factors related with development of pre-eclampsia from gestational hypertension is not enough. This study aimed to evaluate the levels of serum uric acid as a risk factors with development of pre-eclampsia from gestational hypertension and progression of severe infant condition.

**Methods-** It was a retrospective cohort study conducted in Fatima Memorial Hospital Lahore from March 2018 to Jan 2020 in which total 249 pregnant women with Gestational Hypertension were selected. Serum Uric Acid levels were obtained at the time of presentation in All these selected subjects. All selected patients were kept in observation for examining the development of pre-eclampsia from gestational hypertension and progression of severe infant condition.

**Results-** The subjects who had initial symptoms of gestational hypertension had high level of serum uric acid as compared to normal pregnant women (5.06 vs. 4.59 mg/dl,  $P < 0.01$ ). At initial appearance of gestational hypertension, higher level of uric acid, lower gestational age and need of antihypertensive drug for Blood Pressure (B.P) management were associated with progression of severe infant or maternal conditions and development of pre-eclampsia. It was observed that if level of uric acid increase by one standard dev. the risk of pre-eclampsia progression increased by 2.3-folds and the risk of development of severe conditions in infant or mother increased by 1.5-folds.

**Conclusion-** It was concluded that if in gestational hypertension the level of uric acid increases, it may indicate the high risk of development of severe infant or maternal condition and progression to pre-eclampsia.

**Keywords:** Uric acid, progression, preeclampsia, hypertension, gestational hypertension, blood pressure, adverse conditions.

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**INTRODUCTION:**

The gestational hypertension with proteinuria occurring after 20 weeks of Pregnancy is called as pre-eclampsia and this may be a reason behind major number of adverse conditions in neonate and mothers.<sup>1</sup> One of a serious complication during pregnancy is Preeclampsia whose most common clinical presentation is gestational hypertension. However, the research available on the clinical risk factors related with development of preeclampsia from gestational hypertension is not enough. In many cases before the commencement of proteinuria, preeclampsia's first common clinical presentation is hypertension.<sup>2,3</sup> To treat each patient of gestational hypertension as an emerging case of preeclampsia is very common practice by doctors. However, it is still unknown that why only certain pregnant women have the progression of preeclampsia after the appearance of gestational hypertension. The research is very limited on this with inconsistent findings. However, much research gave evidence that there is a consistent relation between gestational hypertension and progression of preeclampsia.<sup>4,5</sup> In some studies, it was observed that during gestational hypertension higher level of uric acid may be an indicator of progression to preeclampsia, but it is unknown that, is there any association of uric acid with development of adverse infant or maternal conditions.<sup>7,8,9</sup> This study aimed to examine the associated risk factors with development of preeclampsia from gestational hypertension and progression of severe infant condition.

**METHODS:**

It was a retrospective cohort study in which total 249 pregnant women with gestational hypertension were selected. All those women were excluded who had renal disease, or kidney disease during first trimester of pregnancy or with chronic hypertension, chronic or acute hypertension or abnormally high level of Serum creatinine or preeclampsia which was not due to the progression of gestational hypertension. All these selected subjects were kept in observation for examining the associated risk factors with development of preeclampsia from gestational hypertension and progression of severe infant condition. A written consent paper was signed by all the patients. After 20 weeks of pregnancy the appearance of hypertension with proteinuria or without proteinuria (diastolic and systolic BP  $\geq 90$  and  $\geq 140$  mm Hg respectively in two 4 hours apart measurements). Preeclampsia can be defined as the hypertension during gestation with proteinuria ( $\geq 1+$  on dipstick urinalysis or in 24-hour urine collection  $\geq 300$  mg). Moreover, those women also excluded who were diagnosed with the pre-eclampsia in 1<sup>st</sup> week of

diagnosis as these were considered as the primary pre-eclampsia patients who was not suffering in preeclampsia due to the progression of gestational hypertension.

The primary finding was progression to pre-eclampsia which was seen in 158 patients and in 89 patients the secondary outcome of this was seen in the form of development of adverse infants outcome or maternal conditions such as:

- i. Perinatal death (infant death during 7 days or fatal death  $\geq 20$  weeks)
- ii. Apgar low 5-min score
- iii. Low weight of infant at the time of birth ( $< 3$  percentile for gestation)
- iv. Abruptio placenta
- v. Eclampsia (development of fits)
- vi. pulmonary edema
- vii. oliguria (urine output  $< 300$ ml/24hrs)
- viii. severe proteinuria
- ix. shortness of breath
- x. chest pain
- xi. visual disturbances
- xii. Vomiting and severe nausea
- xiii. Thrombocytopenia (platelet count  $< 150,000$ )
- xiv. elevated liver enzymes
- xv. hemolytic anemia

During initial diagnosis of gestational hypertension, the routine-based urine protein test were observed of patients. Those patients who had gestation hypertension with diastolic and systolic BP  $\geq 95$  and  $\geq 150$ mm Hg respectively were treated with an antihypertensive agent with target to lessen the systolic and diastolic BP  $\leq 140$  and  $\leq 90$  mm Hg respectively.

In this study  $\chi^2$ -tests, and Wilcoxon rank were used to analyze the clinical characteristics differences. To adjust odd ratios and estimate crude with confidence interval 95% of the development of severe infant or maternal conditions and progression to preeclampsia, logistic regression models were used. For statistical analysis SAS ver. 9 was used.

**RESULTS:**

Out of 249 patients 89 were observed to have adverse maternal or infants' conditions and 158 had progression to pre-eclampsia. The clinical appearance of gestational hypertension in four patients had diastolic BP 110mm Hg and out of these four patients three were found to have progression of pre-eclampsia later. There was no impact of miscarriages, alcohol

use, smoking, maternal age on gestational hypertension.

Table 1 | Patients Characteristics of initial presentation of gestational hypertension (gh) with vs. without the progression to preeclampsia (Pe)

Characteristic	All subjects (N = 249)	GH-PE (N = 158)	GH only (N=91)
<i>Maternal age (years)</i>	30.3 ± 5.8	30.6 ± 6.0	29.7 ± 5.4
Age ≥35	59 (23.7)	41 (26.0)	18 (19.8)
Primiparity	162 (65.1)	101 (63.9)	61 (67.0)
Smoking	28 (11.2)	17 (10.8)	11 (12.1)
<i>Prepregnancy BMI (kg/m<sup>2</sup>)</i>	25.7 ± 5.8	26.3 ± 6.3	23.9 ± 3.7
BMI ≥30	27 (10.8)	25 (15.8)	2 (2.2)
<i>History of miscarriage</i>	97 (39.0)	65 (41.1)	32 (35.2)
Preeclampsia	26 (10.4)	21 (13.3)	5 (5.5)
Gestational hypertension	42 (16.9)	30 (19.0)	12 (13.2)
<i>Prenatal visits, total number</i>	8.4 ± 2	8.4 ± 2	8.5 ± 2
Visits per month	1.0 ± 0.2	1.0 ± 0.2	1.0 ± 0.3
<i>Gestational age (weeks)</i>	33.5 ± 4.8	31.1 ± 4.2	37.6 ± 2.2
<37 weeks	158 (63.5)	146 (92.4)	22 (24.2)
Systolic BP (mm Hg)	146 ± 8	145 ± 7*	147 ± 9
Diastolic BP (mm Hg)	86 ± 9	85 ± 9*	87 ± 8
Hemoglobin (g/dl)	121.4 ± 11.3	121 ± 10	122 ± 12
Hematocrit (%)	0.36 ± 0.03	0.36 ± 0.03	0.36 ± 0.03
Platelet (×10 <sup>9</sup> /ml)	214 ± 57	213 ± 50	215 ± 69
Serum AST(U/l)	24.1 ± 6.0	24.5 ± 5.7	23.5 ± 6.4
ALT (U/l)	17.2 ± 6.0	17.7 ± 6.4	16.3 ± 5.0
LDH (U/l)	150.8 ± 23.9	150.2 ± 24.6	151.9 ± 22.8
Creatinine (mg/dl)	0.67 ± 0.13	0.67 ± 0.12	0.65 ± 0.13
Uric acid (mg/dl)	4.89 ± 0.90	5.06 ± 0.78	4.59 ± 1.01
GH onset to PE	3.0 ± 2.7	3.0 ± 2.7	—
GH onset to delivery	2.3 ± 2.5	3.0 ± 2.7	1.1 ± 1.3
Antihypertensive drug treatment	106 (42.6)	101 (63.9)	5 (5.5)
Caesarean section	88 (35.3)	69 (43.7)	19 (20.9)
Labor induction	137 (55.0)	84 (53.2)	53 (58.2)
<i>Gestational age (weeks)</i>	36.4 ± 3.5	35.1 ± 3.6	38.7 ± 1.8
Birth weight <3rd percentile	20 (8.0)	15 (9.5)	5 (5.0)
Adverse maternal or infant conditions <sup>a</sup>	89 (38.2)	82 (51.9)	7 (7.7)

In 89 patients it was observed to have the development of severe infant of maternal conditions including 20 patients having intrauterine growth restrictions, 2 cases of perinatal death, 2 eclampsia, 12 of HELLP syndrome (low platelet, elevated liver enzyme, and hemolytic anemia).

The subjects who had initial symptoms of gestational hypertension had high level of serum uric acid as compared to normal pregnant women (5.06 vs. 4.59 mg/dl, P < 0.01). At initial appearance of gestational hypertension, higher level of uric acid and lower gestational age and for BP control the need of antihypertensive drug were associated with progression of severe infant or maternal conditions

and development of preeclampsia. It was observed that if level of uric acid increase by one standard dev. then the risk of preeclampsia progression increased by 2.3-

folds and the risk of development of severe conditions in infant or maternal increased by 1.5-folds.

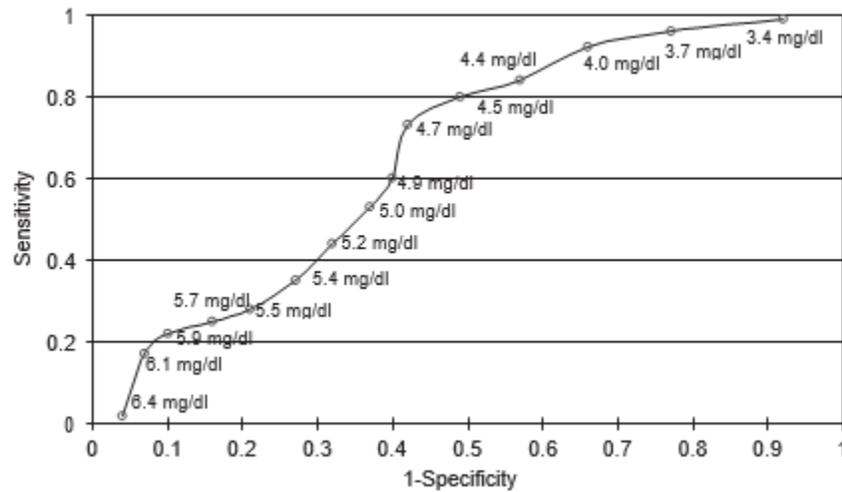


Figure 1. Receiver-operator characteristic curve at the clinical appearance of gestational hypertension for serum uric acid level predicting the progression to preeclampsia.

### DISCUSSION:

In this study it was found that higher level of uric acid can be an indicator of the higher risk of development of severe infant or maternal conditions and progression to preeclampsia in hypertensive patients.<sup>11</sup> Many studies have been done on this but still the research available on the clinical risk factors related with development of preeclampsia from gestational hypertension is not enough.<sup>13,14,15</sup> In many cases before the commencement of proteinuria, preeclampsia's first common clinical presentation is hypertension.<sup>16</sup> To treat each patient of gestational hypertension as an emerging case of preeclampsia is very common practice by doctors. However, it is still unknown that why only certain pregnant women have the progression of preeclampsia after the appearance of gestational hypertension.<sup>18</sup> The research is very limited on this with inconsistent findings. However, much research gave evidence that there is a consistent relation between gestational hypertension and progression of preeclampsia.<sup>19</sup> At initial appearance of gestational hypertension, higher level of uric acid and lower gestational age and for BP control the need of antihypertensive drug were associated with progression of severe infant or maternal conditions and development of preeclampsia. In an Australian study it was observed that miscarriage also have impact on worsening the conditions of gestational hypertension but in this study no impact was found of miscarriages, alcohol use, smoking, maternal age on

gestational hypertension.<sup>20</sup> The reason behind this can be that it was a limited study in which small number of patients were taken for observation so to clarify these assessments cohort study at larger scale is required.

### CONCLUSION:

It was concluded that if in gestational hypertension the level of uric acid increases then it may indicate the high risk of development of severe infant or maternal condition and progression of preeclampsia.

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