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DETERMINATION THE ROLE OF HYPERURICEMIA IN PERINATAL CONSEQUENCES OF PREGNANCY INDUCED HYPERTENSION

[1]*Dr. Fidaa Najim Abdullah and [2]Dr. Bushra Farhan Awadh

[1]M. B. Ch. B, D.G.O, College of Medicine Baghdad, College of Medicine Baghdad.
[2]M. B. Ch. B, D. G.O, College of Medicine Baghdad, College of Medicine Tikrit.
Department of Gynecology -AlFalluja Teaching Hospital for Gynecology and Pediatrics Falluja-Anbar /Iraq.

***Corresponding Author: Dr. Fidaa Najim Abdullah**
M. B. Ch. B, D.G.O, College of Medicine Baghdad, College of Medicine Baghdad.

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ABSTRACT

This prospective and observational study was carried out in the Department of Obstetrics & Gynecology of Al-Falluja Teaching Hospital in Iraq. The study included (100) primigravida female patients in the third trimester (after 32 weeks gestation) with pregnancy induced hypertension. Serum uric acid assay was done then the patients were classified into three groups according to uric acid level; Group I (low hyperuricemia) uric acid below 25th percentile (5.8 mg/dl). Follow up of maternal outcome as (eclampsia, HELLP, acute renal failure and accidental hemorrhage) and fetal outcomes (stillbirth, prematurity, IUGR and IUFD). Other obstetric complications that can affect pregnancy. Other medical diseases and severe pre-eclampsia that need urgent termination were excluded. This study aimed to determine the relationship between hyperuricemia and perinatal results in pregnancy induced hypertension. Results showed a significant increase in serum uric acid, urea and creatinine in the high group compared to the middle and low ones. Bad fetal outcome and pregnancy complications were directly proportionate to the serum uric acid levels. It can be concluded from the current study that these data reinforce the general agreement about the utility of hyperuricemia in the prognosis of adverse perinatal outcomes in pregnancy induced hypertension. Serum uric acid level measurements are a useful and inexpensive marker for predicting adverse perinatal outcomes.

KEYWORDS: Serum uric acid; Hyperuricemia; Pre-eclampsia; Pregnancy induced hypertension.

INTRODUCTION

Hypertensive disorder of pregnancy is responsible for significant amount of maternal and perinatal morbidity and mortality. Pregnancy may induce hypertension in women who are normotensive before pregnancy and may aggravate hypertension in those that were hypertensive.[1,2] Despite advances in care, preeclampsia remains a leading cause of maternal and perinatal morbidity and mortality worldwide.[3] Preeclampsia affects multiple organ systems and can lead to severe renal, hepatic, neurological and cardiopulmonary complications. Often the fetus is affected, and adverse prenatal outcomes include preterm birth, intrauterine growth restriction and death. Ultimately, delivery is the only definitive treatment for severe preeclampsia; however, many cases can be managed expectantly with increased maternal and fetal monitoring, maternal blood pressure control and maternal seizure prophylaxis.[3] The challenge in caring for women with preeclampsia is to identify those who are at increased risk for complications so that appropriate and timed delivery can be offered. The preeclampsia integrated estimate of risk research program was conceived to address this critical need in preeclampsia management. Using a combination of maternal demographics, signs, symptoms and laboratory findings, the full PIERS model can successfully identify women at risk for preeclampsia complications so that they can access appropriate care worldwide.[4,5] Hypertensive disorder of pregnancy is still the 2nd most common cause of maternal mortality, accounting for 15.5% direct death. Hypertension in pregnancy is also responsible for 18% of fetal and infant mortality and 46% of infants born small for gestational age.[6-8] Early screening for preeclampsia may allow antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae.[9] Elevated uric acid level in maternal blood, presumably due to decreased renal urate excretion, are frequently found in women with preeclampsia.[9] Various studies of serum uric acid level in normal and hypertensive pregnancy and its relation with the early diagnosis of preeclampsia, severity of preeclampsia and associated perinatal outcome have been done in many parts of the world.[10-12] A frequently reported laboratory finding in women with

preeclampsia is elevated serum uric acid. Most accept that hyperuricemia in women with preeclampsia is primarily a result of a reduction in glomerular filtration rate, although others have suggested a possible role for elevated uric acid levels in the pathogenesis of preeclampsia via endothelial dysfunction.[13-15]

PATIENTS AND METHODS

This prospective and observational study was carried out in the Department of Obstetrics & Gynecology of AlFalluja Teaching Hospital on (80) women with pregnancy induced hypertension. Primigravida patients in the third trimester were, presented with pregnancy induced hypertension (PIH) (blood pressure ≥140/90 mmHg), which was measured by mercury sphygmomanometer in reclining position in right brachial artery, and three readings were taken at 10 minutes interval average systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

Exclusion criteria were other obstetric complications that can affect pregnancy (e.g. premature rupture of membrane, preterm labor, placenta previa), other medical diseases (diabetic mellitus) and severe preeclampsia that need urgent termination, systolic blood pressure (SBP) of 160 mm Hg or higher or diastolic blood pressure (DBP) of 110 mm Hg or higher, on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy has previously been initiated), impaired hepatic function as indicated by abnormally elevated blood level of liver enzymes (to double the normal concentration), severe persistent upper quadrant or epigastric pain that does not respond to pharmacotherapy and is not accounted for by alternative diagnoses, or both, progressive renal insufficiency (serum creatinine concentration >1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease) , new onset cerebral or visual disturbances, pulmonary edema and thrombocytopenia (platelet count <100,000/cm^3, all were excluded.

All cases were subjected to a detailed history to detect medical diseases such as chronic hypertension, diabetes, pulmonary diseases, renal disorders or other diseases affecting fetal growth. Also, family history of congenital malformation or chromosomal abnormalities was taken in consideration, obstetric history was taken to detect previous growth restricted baby, malformed or stillbirth. Physical examination was performed to detect hypertension, heart diseases, chest diseases or other medical disorders. Transabdominal ultrasound for assessment of fetal well-being was done. Laboratory investigations were done including; complete blood picture, fasting and postprandial blood sugar, liver function tests, renal function test and serum uric acid assay.

All patients enrolled in the study were classified into three groups according to uric acid level; Group I (low hyperuricemia; 25 cases) uric acid below 25th percentile (<3.7 mg/dL), group II (middle hyperuricemia; 25 cases) uric acid from 25th to 75th percentile (3.8 to 5.7 mg/dL) and group III (high hyperuricemia; 30 cases) uric acid above 75th percentile (>5.8 mg/dL).

RESULTS

Demographic data of the three studied groups showed no significant difference between age and gestational age. There were statistically significant increase in serum uric acid, urea and creatinine in the high group compared to the middle and low ones as shown in table (1).

Table (1): Biochemical parameters of the three studied groups.

	Group	Range	Mean±S. D	F. test	p Value		
Uric acid	Low	2.2 – 3.4	3.05±0.29	2636.7	0.005*	P1	0.001*
	Middle	3.2 – 4.3	4.15±0.10			P2	0.001*
	High	6.1 - 9.0	7.35±0.25			P3	0.001*
Urea	Low	21 – 34	25.95±4.15	75.93	0.005*	P1	0.135
	Middle	25 – 36	29.01±3.50			P2	0.001*
	High	26 – 68	46.92±9.87			P3	0.001*
Creatinine	Low	0.5 – 0.75	0.67±0.10	31.92	0.005*	P1	0.644
	Middle	0.5 – 0.88	0.65±0.15			P2	0.001*
	High	0.5 – 1.29	0.91±0.18			P3	0.001*
The serum uric acid, urea and creatinine are significantly elevated in the high group compared to the middle and low groups.P1: Low & Middle P2: Low & High P3: Middle & High							

The study outcome showed that there were (61) fetuses with good outcome (76.3%), (22 fetuses from the low group, 21 from the middle group and 18 from the high group), and 19 fetuses with bad outcome (intrauterine growth restriction IUGR, Stillbirth, neonatal intensive care unit NICU and preterm baby) (23.7%), (3 fetuses from the low group, 4 fetuses from the middle group and 12 fetuses from the high group) as shown in table (2) and figure (1).

Table (2): Fetal outcomes in the three studied groups.

Feta outcome		Low	Middle	High	Total
Good	N	22	21	18	61
	%	88.0%	84.0%	60.0%	76.3%
Bad	N	3	4	12	19
	%	12.0%	16.0%	40.0%	23.7%
Total	N	25	25	30	80
	%	100.0%	100.0%	100.0%	100.0%
Chi-square	X^2	7.11			
	P value	0.029*			
This table demonstrates good outcome fetuses (full-term, no need for NICU and no IUGR), bad outcome fetuses (IUGR, stillbirth, NICU and preterm baby) that more in high group.					

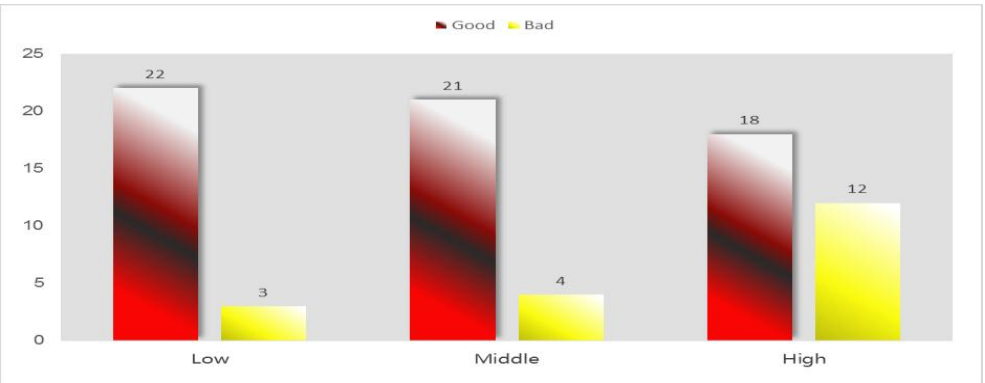

Figure (1): Fetal outcome in the three studied groups.

Bad fetal outcome is directly proportionate to the serum uric acid level. The percentage in the high group was 13 (43.4%) cases from all fetuses of this group compared to the low group 0 (0%) and 1 (4.0%) case in the middle group. There was no complication in low-level uric acid mothers.

Eclamptic cases were (4.0%) in the middle group and (16.6%) in the high group. Accidental hemorrhage presented in only (6.7%) of the high group, HELLP syndrome was in (6.7%) of the high group, acute renal failure in (6.7%) of the high group and intensive care unit admission (ICRU) was (6.7%) in the high group. More complications were observed in the high uric acid serum level associated with pregnancy induced hypertension with a significant variation (P value=0.011) as illustrated in table (3).

Table (3): Maternal outcomes in the studied groups.

Maternal outcome		Low	Middle	High	Total
No complications	N	25	24	17	66
	%	100%	96.0%	56.6%	82.5%
Eclampsia	N	0	1	5	6
	%	0%	4.0%	16.6%	7.5%
Accidental hemorrhage	N	0	0	2	2
	%	0%	0%	6.7%	2.5%
HELLP	N	0	0	2	2
	%	0%	0%	6.7%	2.5%
ICRU	N	0	0	2	2
	%	0%	%0	6.7%	2.5%
ARF	N	0	0	2	2
	%	0%	0%	6.7%	2.5%
Total	N	25	25	30	80
	%	100.0%	100.0%	100.0%	100.0%
Chi-square	X^2	22.88			
	P value	0.011			
This table shows no complication in low level uric acid mothers, more complications were observed in high uric acid serum level associated with pregnancy induced hypertension.					

DISCUSSION

Gestational hypertension is a medical disorder worldwide that complicates approximately 12-22% of the pregnancies.[16] Women with gestational hypertension and hyperuricemia have evidence of endothelial dysfunction and deliver growthretarded babies.[17]

Aneela Khaleeq et al.[18] agreed with our results regarding age as there was no significant difference between the studied groups.

Our study showed that there was significant differences in systolic and diastolic blood pressure between the 3 groups, which agreed with Kaur P et al.[19] who showed that systolic as well as diastolic blood pressure levels in preeclamptic women are much higher than that of normal pregnant women, and this difference is found to be very highly significant. It is also observed that uric acid level is within moderate increase range in patients of the study group (preeclamptic group) and patients of control group, whereas it is above the upper limit of normal range in patients of study group and patients in control group, the mean value of serum uric acid level in study group was quite higher than that of control group and this difference is statistically significant (p=0.0001).

In our study, urea and creatinine were significantly elevated in the high group compared to the middle and low group, and urea and creatinine were significantly different between the different groups (P<0.05). Our results were similar to Apeksha et al,[20] who found that serum uric acid was significantly higher in the PIH group compared to the control group. On the other hand, serum creatinine and urea were approximately similar in between the groups.

Escudero et al,[21] agreed with us, as women with high uric acid levels showed a longer-hospitalization period (1.2 days more), less platelet count and high creatinine plasma levels compared to women with low-levels.

It was shown that bad fetal outcome is directly proportionate to the serum uric acid level. In the high group it was higher than the low group and the middle group with P value (0.029).

These results are comparable to those of Aneela Khaleeq et al,[18] who shows that serum uric acid level measurement is a useful and inexpensive marker for predicting preeclampsia and fetal growth retardation in women suffering with gestational hypertension.. In group A, newborns were found small-for-gcstational-age (SGA), whereas in Group B, newborns were found to be SGA. The relative risk was calculated for development of SGA in hyperuricemia and was found significant.

Moreover, in pregnancy outcomes overview of Amini et al,[22] 59 women gave birth to a small for gestational age (SGA) neonate (birth weight <10:" percentile for gestational age (11.3%). Seventy nine neonates required NICE admission (19.5%). Forty neonates had low I minute Apgar scores, and 40 neonates had low 5 minute Apgar scores (Apgar score <7) (9.9%). Twenty seven required resuscitation in the delivery room (6.6%). Seven neonates developed IVH (1.7%) and 16 neonates suffered from respiratory distress syndrome (RDS) (3.9%). Maternal hyperuricemia in normotensive singleton pregnant women constitutes a risk factor for adverse pregnancy outcomes and the development of neonatal hypoglycemia and intraventericular hemorrhage.

In addition Kondareddv T et al,[23] revealed 165 fetuses with good outcome (65.50%) in group A (uric acid<6mg/dL)and (34.50%) in group B (uric acid>6mg/dL). While bad outcome IUGR (36) (19.40% in group A and 80.60% in group B). Still birth (7) all in group B. NICE (41) (29.30% in group A and 70.70% in group B), preterm (28.12% in group A and 71.90% in group B.

In the study conducted by J. Dhaka et al,[24] the relationship of high blood uric acid in preeclamptic women with poor fetal outcome (low birth weight (LBW1) fetus and stillbirth) was observed.

Adverse maternal outcome in our study related more to hypertension and hyperurecimia than women with low uric acid level. None of low-level uric acid mothers were complicated.

These results are comparable to those ol Kondareddv T et al,[23]

Hawkins et al,[25] showed that maternal hyperuricaemia. Measured near delivery is associated with adverse maternal and fetal outcomes. Hyperuricaemia is associated with an increased prevalence of small for gestational age (SGA) infants and prematurity. Observations suggest that gestational hypertension in the presence of hyperuricaemia is a disease with increased fetal risk.

REFERENCES

1. Muti M, Tshimanga M, Gombe N, Chonzi P. Prevalence of pregnancy induced hypertension and pregnancy outcomes among women seeking maternity services in Harare, Zimbabwe. BMC Car¬diovascular Disorders, 2015; 15: 111. doi: 10.1186/sl2872-015-0110-5
2. Lin S, Leonard D, Co MA, et al. Pre-cclampsia has an adverse impact on maternal and fetal health. Transl Res., 2015; 165(4): 449-63. doi: 10.1016/j.trsl.2014.10.006
3. Nardozza LMM, Caetano AC, Zamarian ACP, et al. Fetal growth restriction: Current knowledge. Arch Gynecol Obstet, 2017; 295: 1061-1077. doi: 10.1007/s00404-0n-4341-9
4. Von Dadelszen P, Payne B, Li j, et al. Prediction of adverse maternal outcomes in preeclampsia:

Developmentand validation of the full PIERS model, lancet, 2011; 377: 219-22". doi: 10.1016/ S0140-6736(10)61351.
5. Magee LA, Pels A, Helewa M, et al. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. Pregnancy Hjpertens, 2014; 4(2): 105-145. doi: 10.1016/j.preghy.2014.01.003.
6. Goldenberg RL, Jones B, Griffin IB, et al. Reducing maternal mortality from preeclampsia and eclampsia in low-resource coun¬tries - what should work? Ada Obstet Gynecol Scand, 2015; 94(2): 148-155. doi: 10.1111/aogs.l2533.
7. Clavcn T, Djurovic S, Henriksen T. Dvslipidcmia in early 2nd tri¬mester is mainly a leature of women with early onset preeclampsia. BJOG, 2001; 108(10): 1081-1087.
8. Damien S, Patric G, Francies P, et al. Aspirin (1 OOmg) used for prevention of preeclampsiain nulliparous women: The F.ssai Re¬gional Aspirin Mere - Enfant study (Part-1). BJOG, 2003; 110: 475-484.
9. Shaker el Saved Azzaz AM. Antenatal care booking during preg¬nancy and its effect on maternal and fetal outcomes. (Doctoral thesis). Enivcrsidad de Scvilla, Sevilla, 201; 7.
10. von Dadelszen P, Magee LA. Preventing deaths due to the hypertensive disorders of pregnancy. Best Pract Res Clin Obstet Gynae-col, 2016; 36: 83-102. doi: 10.1016/j.bpobgvn.2016.05.005.
11. Livingston JR, Pavnc B, Brown M, et al. Eric Acid as a predic¬tor ot adverse maternal and perinatal outcomes in women hospi¬talized with preeclampsia. / Obstet Gynaecol Can, 2014; 36(10): 870-877. doi: 10.1 ("116/S1 "01-2163(15)30435'"-7.
12. .Zhou G, Holzman C, Luo Z, Margerison C. Maternal serum uric acid levels and blood pressure during pregnancy: A commu-nity-based cohort study. Eur J Ohstet Gynecol Reprod Biol, 2018; 222: 64-69. doi: 10.1016/j.ejogrb.2018.01.008.
13. Kang DH, Finch J, Nakagawa T, et al. Uric acid, endothelial dysfunction and preeclampsia: Searching for a pathogenetic link. J Hjpertens, 2004; 22(2): 229-235.
14. Bainbridge SA, Roberts JM. Uric acid as a pathogenic factor in preeclampsia. Placenta, 2008; 29(Suppl A): S67-S72. doi: 10.1016/j. placenta.2007.11.001.
15. Martin AC, Brown MA. Could uric acid have a pathogenic role in pre-dampsia? Nat Rev Nepbrol, 2010; 6: 744-748. doi: 10.1038/ nrneph.2010.125.
16. Lisonkova S, Sabr Y, Mayer C, et al. Maternal morbidity associ¬ated with early-onset and late-onset preeclampsia. Obstet Gynecol, 2014; 124: "71-781. doi: 10.1097/AOG.0000000000000472.
17. Phad X, Dahlstrom JE, Ellwood D, Kent AL. The effect of pregnancy-induced hypertensive disorders on placental growth along short and long axes and neonatal outcomes. AustX ZJ Obstet Gynaecol, 2015; 55: 239-244. doi: 10.1111/ajo.l2308.
18. Khaleeq A, W'aheed K, Ejaz S, Kamal A. Hyperuricemia as a predictor of poor fetal outcome in pre-eclamptic women. Journal of Rawalpindi Medical College (jRMC), 2015; 171-173.
19. Patel K, Kaur P, Deepak A, et al. Association of serum uric acid and C-reactive protein levels in prediction of preeclamp¬sia. Int J Reprod Contracept Obstet Gynecol, 2016; 5(2): 495-502. doi: 10.18203/2320-1770.ijrcog20160398.
20. Niraula A. Lamsal M, Majhi S, Khan SA, Basnet P. Significance ot serum uric acid in pregnancy induced hypertension. J XatlMed Assoc., 2011; 109(3): 198-202. doi: 10.1016/j.jnma.20n.01.009.
21. Escudero C, Bertoglia P, Acurio], Escudcro A. Hyperuricemia in the prognosis of adverse perinatal outcomes: An International. journal of IIY omen's Cardiovascular Health, 2012; 2: 240-339.
22. Amini E, Sheikh M, Hantoushzadeh S. Maternal hyperuricemia in normotensive singleton pregnancy, a prenatal finding with con¬tinuous perinatal and postnatal effects. BMC Pregnancy Childbirth, 2014; 14: 104. doi: 10.1186/14^1 -2393-14-104.
23. Kondareddy T, Prathap T. Uric acid as an important biomarker in hypertensive disorders in pregnancy. Int J Reprod Contracept Obstet Gynecol, 2016; 5(12): 4382-4384. doi: 10.18203/2320-1770. ijrcog20164348.
24. Hussain SS, Choudhury MBK, Akhter J, et al. Fetal outcome of pre-eclamptic mothers with hyperuricemia. J Dhaka National Med. Coll. Hos, 2011; 17(01): 41-43. doi: 10.3329/jdnmch.v17i1.12192.
25. Hawkins T, Roberts J, Mangos G, et al. Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: A retrospective cohort study. BJOG, 2012; 484-492. doi: 10.1111/j.1471-0528.2011.03232.x.