https://doi.org/10.37939/jrmc.v27i3.2262

Assessment Of Predictive Value Of Serum Uric Acid Levels For Low Birth Weight In Pre-Eclampsia

Sadaf Asma[1], Sidratul Muntaha[2], Amerzish Liaqat[3], Farhan Hassan[4], Sara Hayat[5], Rafiq Ahmed[6]

Abstract

Objective: To assess the diagnostic accuracy of raised serum uric acid level in females with pre-eclampsia, in predicting low birth weight.

Material and Methods: Cross sectional study carried out at Gynecology Department, FGSH Poly Clinic, Islamabad & duration of study was 6 months from July 21, 2021 to Jan 20, 2022. A total of 225 Preeclampsia pregnant female were clinically examined and included in the study. Blood sample were collected for serum uric acid and followed till the birth of the baby.

Results: The study included age ranged from 18 up to 40 years. Average age was 28.69years±5.01SD. Sensitivity & specificity of uric acid level in Serum in diagnosis of low birth weight are 85.71% and 81.42% respectively while it has positive predictive & negative predictive value of 51.43% & 96.13% respectively. Diagnostic accuracy of uric acid level in serum was 82.22%. CONCLUSION: Uric acid level in serum is of great diagnostic and prognostic importance in women with pre-eclampsia & helps in predicting low birth weight.

Keywords: Preeclampsia, serum uric acid, low birth weight.

[1,5] Medical Officer, Federal Government Polyclinic Hospital, Islamabad; [2] Consultant Paediatrician, Cantt General Hospital, Rawalpindi; [3] Trainee Medical Officer, Federal Government Polyclinic Hospital, Islamabad; [4] Senior Demonstrator, Community Medicine, Rawalpindi Medical University, Rawalpindi; [6] Post Graduate Trainee, Rawalpindi Medical University, Rawalpindi.

Correspondence: Dr. Sidratul Muntaha, Consultant Paediatrician, Cantt General Hospital, Rawalpindi. **Email:** sidratulmuntaha1485@yahoo.com

Cite this Article: Asma, S., Muntaha, S. T., Liaqat, A., Hassan, F., Hayat, S., & Ahmed, R. (2023). Assessment Of Predictive Value Of Serum Uric Acid Levels For Low Birth Weight In Pre-Eclampsia. *Journal of Rawalpindi Medical College*, *27*(3). https://doi.org/10.37939/jrmc.v27i3.2262.

Received March 28, 2023; accepted August 01, 2023; published online September 26, 2023

1. Introduction

Hyperuricemia is a frequent finding in pregnant women with pre-eclampsia and elevation in uric acid in women having pre eclampsia comes before hypertension. Hypertensive during pregnancy affect almost 10% of all pregnancies. Pre eclampsia leads to increase in both maternal and fetal mortality and morbidity.[1] Pre-eclampsia is defined as a syndrome induced in pregnancy with hypertension and proteinuria at or after the 20 weeks of gestation. Severity of Pre eclampsia can be defined as presence of one of following features such as blood pressure ≥160 systolic/110 diastolic mm Hg, impairment in both renal & hepatic function, pulmonary edema, cerebral & visual disturbance and thrombocytopenia. Early diagnosis of pre-eclampsia may decrease both mortality and morbidity in the mother and infant.[2] Uric acid has several sources in women with pre eclampsia; altered kidney function, tissue breakdown, acidosis, and enzyme xanthine oxidase & dehydrogenase activity are sources of Uric acid level in pre eclampsia. Severe pre-eclampsia leads to higher uric acid.[3]A positive relation between higher maternal uric acid and poor both maternal and fetal outcomes exists. Different tests and parameters, including uric acid are being carried out in 2nd or 3rd trimester of pregnancy as a predictor of preeclampsia.[4] One study found that frequency of low birth weight was 36.2% in women having hyperuricemia & hypertension during pregnancy.[5] Study carried by Ryu et al mean uric acid level was 5.8 ranging from (4.7 – 6.6) in pre-eclamptic women compared to 3.9 and ranging from (3.1 – 4.6) in patients with normal blood pressure. Pre-eclampsia was associated significantly with preterm labor, LBW (low birth weight) and SGA (small for Gestational age).[6]

Study carried by Le TM et al. sensitivity and specificity of raised serum uric acid level (>393 μmol/L) were 69.8% and 75.7% for prediction of low birth weight.[7] Study carried by Ryu A et al. showed that elevated uric acid in serum predicted low birth weight as sensitivity = 58% and specificity = 95.0%.[6] While Livingston JR reported that sensitivity and specificity were 78.21% and 29.92% for prediction of adverse perinatal outcome.[8]

Rationale of our study is to find out predictive accuracy of high uric acid in Serum for poor perinatal outcome in patients having pre-eclampsia. Early prediction of preeclampsia with elevated serum uric acid which is a simple investigation can help in

lowering complication to both mother and fetus at delivery. Since Pakistan has a high population growth rate and lower birth gap, the women and child's health remain on risk in pregnancy.

2. Materials & Methods

It was a cross sectional study was carried out at Department of Obs/Gyne, Federal Government Polyclinic Hospital Islamabad from July 2021 to Jan 2022. Total of 225 females were recruited by Consecutive sampling (non-probability based). All women aged between 18-40 years, parity less than 5 and gestational age 28 to 40 weeks with pre eclampsia were included in study. Females with multiple pregnancies and women with history of hypertension (BP≥140/90mmHg before conception), diabetes mellitus (blood sugar>200mg/dl), renal (creatinine>1.2mg/dl) or liver disease (ALT & AST>40IU) were excluded. The baseline characteristics (name, age, gestational age, parity, BMI, BP and proteinuria) were noted. Then blood sample was taken by using 3cc disposable syringe. All samples were sent to the hospital laboratory for assessment of blood uric acid. Uric acid in serum was noted and females were labeled as either positive or negative. Women were then followed till delivery. At time of delivery, birth weight of neonate were noted and low birth weight were labeled if birth weight <2500 grams & patients confirmed as positive or negative. All this data were noted on the Performa. Data entered & analyzed in SPSS version 20.0. The numerical variables such as age, gestational age, BMI, BP, proteinuria, uric acid serum level & birth weight were measured as mean ± standard deviation. The categorical variables such as parity and adverse perinatal outcome were measured as frequency & percentage. 2x2 table was generated to calculate the sensitivity, specificity, PPV, NPV and diagnostic accuracy of raised serum uric acid level to predict LBW. Data were stratified for age, BMI, gestational age, parity, severity of pre-eclampsia. Post-stratification, 2x2 tables was generated to calculate the sensitivity, specificity, PPV, NPV and diagnostic accuracy of raised serum uric acid level to predict LBW for each strata.

3. Results

Serum uric acid of 225 patients with pre-eclampsia was taken and patients age was divided in four categories as shown in Table 1.

Table-1 Age distribution of the patients

Age Categories	Frequency	Percent	Mean± SD
<= 25	64	28.4	28.69years ±5.01
26 - 30	93	41.3	
31 - 35	32	14.2	
36.00+	36	16	
Total	225	100	

Descriptive statistics are shown in Table 2.

Table-2 Maternal parameters

	N	Mean	Standard Deviation
Gestational Age	225	41.4222	7.00347
Parity	225	1.94	1.689
BMI(Kg/m)	225	25.63	3.55
Proteinuria	225	49.4133	12.41013

Serum uric acid results of the patients having pre-eclampsia shown in Fig 1 and same 225 patients undergone through delivery, it shows that 42(18.67%) were having positive while 183(81.33%) patients were normal, shown in Fig 2.

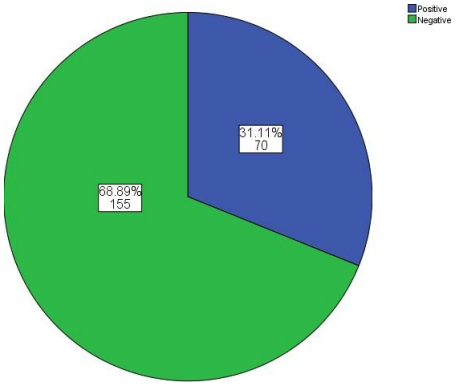

Figure-1 Serum uric acid Results

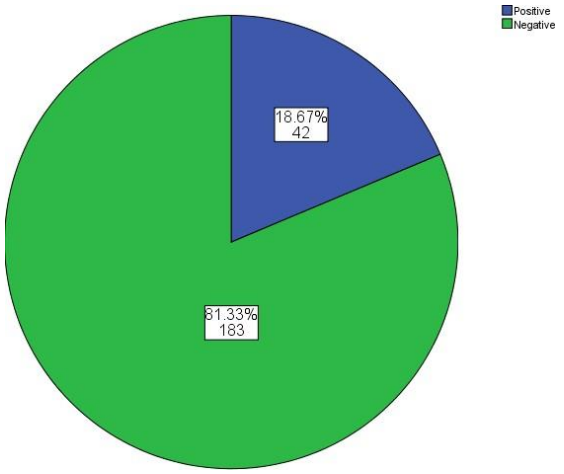

Figure-2 Birth Weight

Age wise distribution of diagnostic accuracy results shows that majority of the patients with low birth weight having accurate diagnosis were presented in lower age group and this accuracy was decrease as the age increase. The age group less than 25 years of age has shown 78.49% accuracy. While this accuracy was 90.63% in the age group of 30-35 years while the age group of more than 35 years have 88.89% accuracy.

Table-5 Diagnostic accuracy of serum uric acid in detecting low birth weight.

		Low birth Weight		
		Positive	Negative	Total
Serum Uric Acid	Positive	36	34	70
	Negative	6	149	155
Total		42	183	225

Sensitivity	85.71%
Specificity	81.42%
Positive Predictive Value	51.43%
Negative Predictive Value	96.13%
Diagnostic Accuracy	82.22%

Stratification of accuracy of serum uric acid in detecting low birth weight shows that accuracy has no such role over parity, BMI, gestational age and proteinuria. Serum uric acid plays a key role in predicting low birth weight. The sensitivity and specificity of serum uric acid in diagnosis of low birth weight are 85.71% and 81.42% respectively while it has positive predictive value of 51.43% and negative predictive value is 96.13%. Overall, the diagnostic accuracy of serum uric acid in diagnoses of low birth weight is 82.22%. (Table 5)

5. Discussion

In our study Hyperuricemia in patients was associated with adverse fetal outcomes in form of progression in preeclampsia & perinatal morbidity especially low birth weight. Criteria that differentiate between high and lower risk patients with hypertension during pregnancy are arbitrary. Hypertension and proteinuria due to pre eclampsia could be precursors to eclampsia. [8, 9] That's why preeclampsia carries importance in rise in risk to both mother & infant. But it was never been established that, among other symptoms, signs & biochemical disturbances that occurs in preeclampsia, proteinuria & hypertension are good indicators to determine outcome. Hyperuricemia also occurs in preeclampsia & it is earliest & consistent detectable change in preeclampsia & being considered a good predictor of risk to fetus than blood pressure.[10] Xanthine oxidase enzyme synthesizes uric acid in purine metabolism. Preeclampsia leads to oxidative stress resulting in Hyperuricemia & kidney function impairment due to the ischemiac injury in placenta and decreased patient glomerular filtration. Increase in uric acid production effects placenta and is associated with both activity and levels of enzymes xanthine oxidase & dehydrogenase. Increase in uric acid blood level is a result of various different mechanisms[11]. Mazzali et al in his study observed that elevated uric acid in Serum results in hypertension through crystal independent mechanism. Decrease in uric acid in blood was associated with a hypotension through nitric oxide & renin/angiotensin system. Uric acid rising level causes renal vasoconstriction & resulting in hypertension that itself results decline in nitric oxide level in endothelial cells and renin angiotensin system activation .[12] Study conducted by Bellos I et al, the various uric acid threshold values were described and it was concluded that uric acid levels is helpful in predicting poor outcomes in preeclampsiac patients. 196 studies were included & analyzed, comprising total of 39540 women & results showed Preeclampsia association with elevation in uric acid in the 1st trimester (MD:

0.21 mg/dl & 95% confidence intervals: 0.06-0.35) .During 2nd trimester (MD: 1.4 mg/dl & 95% CI: 0.78-2.05) & during 3rd trimester (MD: 2.26 mg/dl & 95% CI: 2.12-2.40). Hyperuricemia leads to preeclampsia severity, eclampsia, hemolysis, deranged hepatic enzymes and thrombocytopenia. Poor perinatal outcome prediction sensitivity ranged from 67.3% - 82.7% and the specificity ranged from 47.7% -70.7%. Study concluded that uric acid levels in serum are raised in preeclampsia and & predicts disease severity and pregnancy complications which are all in consistent with our study. [13]

A study conducted by Yassaee F compared two groups & concluded that hyperuricemia in preeclampsiac women was risk factor for perinatal complications & high risk of fetal demise by 30.4, cesarean section by 6 & mortality in mother by 21.5, growth restriction of fetus by 6 & eclampsia by 14.3 in patients with blood uric acid level of 6mg/dl or above as compared to those with level below 6mg/dl [14] & these findings are in consistent with our study.

Redman in his study demonstrated that risk of fetal death rises in preeclampsia patients with hyperuricemia levels and this rise has been related to eclamptic seizures [15]. In another study conducted by D anna et al increase in SGA among women with hypertension with Hyperuricemia with proteinuria & nonproteinurea and conclusion was made that uric acid level in serum is sensitive index of preeclampsia severity & these findings are in consistent with our study.[16]

In study conducted by Hawkins TL et al and Lim KH et al showed a Hyperuricemia can now be considered as an early feature in preeclampsia and its increases the diagnostic accuracy in patients with preeclampsia. Lim KH concluded that serum uric acid levels correlates directly with severity of renal injury [17,18] The uric acid level >4.5 mg/dl indicates pre eclamptic & such patients require careful and close follow up. Rising levels of uric acid in blood, 5.7 mg/dl, 6.3 mg/dl, and 6.7 mg/dl observed in patients with hypertension and preeclampsia.[19]

Study conducted in Japan in pregnant women with normal blood pressure, Akahori et al showed maternal uric acid level in serum, serum creatinine levels, systolic & diastolic BP with p =0.014 & 0.037 respectively were raised in the SGA group. A negative relation existed between uric acid level in blood & birth weights, r = -0.59; p = 0.006 & positive relation between serum uric acid in mother & serum creatinine levels with r = 0.43; p < 0.05 in severe SGA less than 5th percentile. Analysis showed that uric acid in serum is an independent risk factor for SGA. [20]

Our study suggested that threshold level of uric acid level in mother in prediction of low birth weight delivery is 393mg/dl with sensitivity of 85.71% & specificity of 81.42% & it was supported by a Hawkins TL, which concluded that maternal rise in uric acid resulted in low birth weight and uric acid >5.9mg/dl was associated with poor perinatal outcomes.[17]

In study conducted by Aelie Ryu et al preeclampsiac patients having rising uric acid levels in blood had positive relation with systolic pressure with R=0.321 & P=.014, serum creatinine levels with R=0.505 & P<.001 & proteinuria with P=.014. Among women having labor at term & normal neonate weight at time of delivery, blood uric acid levels were elevated in women who experienced preterm labor with full-term, 5.1±1.3 & preterm, 6.2±1.7 & P=.027 and low birth weight with normal birth weight, 4.8±1.1 & low neonate weight, 6.5±1.6 & P=.001 respectively and these findings are in consistent with our study that serum uric acid plays a key role in predicting low birth weight.[6]

5. Conclusion

Uric acid level in serum is of great diagnostic and prognostic importance in women with pre-eclampsia & helps in predicting low birth weight.

CONFLICTS OF INTEREST- None

Financial support: None to report.
Potential competing interests: None to report
Contributions:
S.A, A.L - Conception of study
A.L, S.H - Experimentation/Study Conduction
S.A, F.H, S.H - Analysis/Interpretation/Discussion
S.A, S.M, A.L, R.A - Manuscript Writing
S.M, F.H, R.A - Critical Review
S.M, F.H - Facilitation and Material analysis

References

[1] Zangana JM, Hamadamen AI. Serum uric acid as a predictor of perinatal outcome in women with pre-eclampsia. Int J Med Res & Health Sci. 2018;7(3):168-74.

[2] Nisa SU, Shaikh AA, Kumar R. Maternal and fetal outcomes of pregnancy-related hypertensive disorders in a tertiary care hospital in Sukkur, Pakistan. Cureus 2019;11(8):2-8. doi:10.7759/cureus.5507

[3] B Shanthirani, A Parimalam. The Study of Serum Uric Acid as a Biochemical Indicator for Maternal and Fetal Outcome in Gestational Hypertension. International Journal of Scientific Study. 2020; 8 (9):53-7.

[4] Rothenbacher D, Braig S, Logan CA, Feike G, Müller M, Koenig W, et al. Association of maternal uric acid and cystatin C serum concentrations with maternal and neonatal cardiovascular risk markers and neonatal body composition. Plos one 2018;13(7). doi.org/10.1371/journal.pone.0200470

[5] Lin J, Hong XY, Tu RZ. The value of serum uric acid in predicting adverse pregnancy outcomes of women with hypertensive disorders of pregnancy. Ginekologia polska 2018;89(7):375-80.doi: 10.5603/GP. a2018.0064

[6] Ryu A, Cho NJ, Kim YS, Lee EY. Predictive value of serum uric acid levels for adverse perinatal outcomes in preeclampsia. Medicine(Baltimore). 2019;98(18). doi: 10.1097/MD.0000000000015462.

[7] Le TM, Nguyen LH, Phan NL, Le DD, Nguyen HVQ, Truong VQ, et al. Maternal serum uric acid concentration and pregnancy outcomes in women with pre- eclampsia/eclampsia. Int J Gynecol Obstet. 2019;144(1):21-6. doi: 10.1002/ijgo.12697

[8] Livingston JR, Payne B, Brown M, Roberts JM, Côté AM, Magee LA, et al. Uric Acid as a predictor of adverse maternal and perinatal outcomes in women hospitalized with preeclampsia. J Obstet Gynaecology Canada. 2014;36(10):870-7. doi: 10.1016/S1701-2163(15)30435-7.

[9] T L-A Hawkins , J M Roberts, G J Mangos, G K Davis, L M Roberts, M A Brown.Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: a retrospective cohort study.BJOG 2012;119(4):484-92.doi: 10.1111/j.1471-0528.2011. 03232.

[10] Lüscher BP, Schoeberlein A, Surbek DV, Baumann MU. Hyperuricemia during Pregnancy Leads to a Preeclampsia-Like Phenotype in Mice. Cells.2022;11(22):3703.doi:10.3390/cells11223703.

[11] Sakr HI, Khowailed AA , Al-Fakharany RS , Abdel-Fattah DS , Taha AA .Serum Uric Acid Level as a Predictive Biomarker of Gestational Hypertension Severity; A Prospective Observational Case-Control Study. Rev Recent Clin Trials.2020;15(3):227-39.doi:10.2174/1574887115666200709142119

[12] Mazzali M, Kanellis J, Han L, Feng L, Xia Y, Chen Q. Hyperuricemia induces a primary renal arteriolopathy in rats by a blood pressure-independent mechanism. Am. J. Physiol. Renal. Physiol.2002;282(6):991-97.doi10.1152/ajprenal.00283.2001

[13] Bellos I, Pergialiotis V, Loutradis D, Daskalakis G. The prognostic role of serum uric acid levels in preeclampsia: A meta-analysis. Clin Hypertens. 2020; 22(5):826–34.doi:10.1111/jch.13865.

[14] Yassaee F. Hyperuricemia and perinatal outcomes in patients with severe preeclampsia. Iranian J Med Sci. 2015;28(4):198-99.

[15] Redman CW, Beilin LJ, Bonnar J, Wilkinson RH. Plasma-urate measurements in predicting fetal death in hypertensive pregnancy. Lancet**.** 1976;26(1):1370–73.doi:10.1016/s0140-6736(76)93024-5.

[16] D'Anna R, Baviera G, Scilipoti A, Leonardi I, Leo R. The clinical utility of serum uric acid measurements in pre-eclampsia and transient hypertension in pregnancy. Panminerva Med. 2000; 42(2):101–03. doi:10.1002/pd.2339.

[17] Hawkins TL, Roberts JM, Mangos GJ, Davis GK. Uric acid remains a marker of poor outcome in hypertensive pregnancy. BJOG. 2012; 119(4):484-92. doi: 10.1111/j.1471-0528.2011.03232.

[18] Lim KH, Frideman SA, Ecker JL, Kao L. The clinical utility of serum uric acid measurments in hypertensive diseases of pregnancy. Am J Obstet Gynecol. 1998; 178(5):1067-71. doi: 10.1016/s0002-9378(98)70549-6.

[19] Hosna AU, Bhuiyan M, Ferdous NE, Ahmed K. Effects of hyperuricemia on perinatal outcome in hypertensive disorder of pregnancy. Uni Heart J. 2008;4:36-40.doi:10.3329/UHJ.V4I2.2074

[20] Akahori Y, Masuyama H, Hiramatsu Y. The correlation of maternal uric acidconcentration with small-for-gestational-age fetuses in normotensive pregnant women. Gynecol Obstet Invest. 2012; 73(2):162-7.doi: 10.1159/000332391