Original Article

To Determine Frequency of Low Birth Weight in Pregnancies with Hyper-Uricemia and Pre-Eclampsia

Saliha Ghias Ud Din[1], Wajiha Shadab[2], Ayesha Mobeen[2], Sadaf Afzal[2], Farah Javed[2] and Mavra Tufail[2]

ABSTRACT

Objective: To determine frequency of low birth weight in pregnancies complicated with Hyper-uricemia and Pre-eclampsia.

Study Design: Descriptive Cross-Sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Islamic International Medical College Trust, Railway Teaching Hospital, Rawalpindi from September 2014 to March 2015.

Materials and Methods: 80 singleton term pregnant women with preeclampsia and hyperuricemia delivered either by vaginal delivery or caesarian section were included in the study. Non-probability consecutive sampling technique was used. Study group had blood pressure >140/90 mmHg on at least two distinct time 4 hours apart and proteinuria of >300 mg /24 hours measured by urine dipstick method. Fetal weight was measured 10 minutes after delivery of baby. One sample t-test was applied to find out any significant difference regarding the low birth weight in study population. Association of low birth weight with gestational age, parity type, age groups and serum uric acid level was also assessed by applying chi square test.

Results: Mean of age of the subjects was calculated as 26.86 $\pm$4.525 years. Mean birth weight of the neonates was calculated to be 2.382 $\pm$ 0.298 kg. 60 (75%) neonates had birth weight less than 2.5 kg and 20 (25%) neonates had birth weight 2.5 kg or more with the p value of 0.043 indicating a statistically meaningful difference.

Conclusion: Frequency of babies with low birth weight increases in pregnancies that are complicated with hyperuricemia and pre-eclampsia as 75% neonates reported low birth weight.

Key Words: Hyperuricemia, pregnancy induced hypertension, Frequency, Low birth weight

Citation of article: Ghias Ud Din S, Shadab W, Mobeen A, Afzal S, Javed F, Tufail M. To Determine Frequency of Low Birth Weight in Pregnancies with Hyper-Uricemia and Pre-Eclampsia. Med Forum 2022;33(3):137-140.

INTRODUCTION

Pre-eclampsia accounts for about three to five percent of all the pregnancies[(1)]. It is second most important cause of maternal mortality and responsible for increase in preterm birth, perinatal mortality and around 30% low birth weight newborns[(2)]. Obesity, anemia, and chronic hypertension are notable risk factors for pre-eclampsia.[(3)]

[1.] Department of Obstetrics and Gynecology, THQ Hazro, District Attock.

[2.] Department of Obstetrics and Gynecology, Islamic International Medical College Trust, Railway Teaching Hospital, Rawalpindi.

Correspondence: Dr. Sadaf Afzal, Senior Registrar, Department of Obstetrics and Gynecology, Islamic International Medical College Trust, Railway Teaching Hospital, Rawalpindi.
Contact No: 0333-7158088
Email: drsadafafzal76@gmail.com

Received: September, 2021
Accepted: December, 2021
Printed: March, 2022

Pre-eclampsia mainly occurs because of placental dysfunction, and it comprises of vasospasm, endothelial dysfunction, thrombosis of placenta and defective trophoblastic invasion[(4)]. Pre-eclampsia can also result in decreased liquor and non-reactive cardiotocography and bad biophysical profile in the fetus[(5)].

Raised serum uric acid level in first twelve weeks of pregnancy is linked with development of preeclampsia later[(6)]. Increased uric acid level results in oxidative stress that results in reduced uterine contractility and altered vascular relaxation[(7)].Proteinuria is the clinical manifestation which is used to diagnose the disorder[(8)]. Women with pre-eclampsia and raised uric acid levels have high incidence of preterm delivery resulting in increased neonatal intensive care unit admissions. This can be due to low birth weight, hypoglycemia, jaundice, hypoxia, respiratory difficulties, neonatal sepsis and prematurity[(9)]. Proposed etiologies for raised uric acid are altered kidney function, excessive tissue degradation and acidosis[(9)]. In non-pregnant population, raised uric acid is regarded risk factor in causing raised blood pressure, cardiovascular disease and kidney disease[(10)].

According to the study by Kang, in women with pre-eclampsia raised uric acid not only indicates disease

severity but is also involved directly in the pathogenesis of the disorder[11]. Hyperuricemia (>4.5 mg/dL) is the first biomarker seen in the laboratory tests providing early evidence of disease at 20 or less gestational weeks. Hyperuricemia has also demonstrated its usefulness to predict maternal and fetal complications and disease sequelae at a later age for both mother and baby[12].

Neonatal outcome depends primarily on weight at birth[13]. Low birth weight causes significant burden on health services. It can lead to diseases like diabetes, hypertension, obesity, and heart diseases in adulthood leading to profound impact on the society's burden of disease and finances[14]. Serum uric acid has a strong relation with low birth weight in pre-eclamptic women[15]. There is insufficient research data regarding the neonatal outcomes in hyperuricemia and pre-eclampsia complicated pregnancies. This study aimed to assess the occurrence of low birth weight among pregnancies complicated with hyperuricemia and pre-eclampsia. Results of the present study contributed to guiding the obstetrician to recognize the adverse outcomes of the synergistic effect of hyperuricemia and pre-eclampsia and make decision to improve both maternal and fetal outcome.

MATERIALS AND METHODS

A descriptive cross-sectional study was performed in the of Gynecology & Obstetrics department of Islamic International Medical Complex Trust, Railway Teaching Hospital, Rawalpindi from 29th September 2014 to 29th March 2015. Study was conducted with the consent of hospital ethical committee. A total sample of 80 patients was estimated utilizing World Health Organization sample size calculator. Non-probability consecutive sampling technique was used. Singleton, cephalic, term (37>/= completed week) with preeclampsia and hyperuricemia delivered either by spontaneous vaginal delivery or caesarian section were included in the study. All other causes of low-birth-weight babies like anomalous babies, all high-risk pregnancies like diabetes mellitus, multiple gestations, coagulation disorder, moderate to severe anemia and patients taking hyperuricemic drugs like thiazide diuretic, pyrazinamide were not included in the study.

Verbal consent had been taken from the subjects. Study group had blood pressure >140/90 mmHg on two distinct occasions 4 hours apart and proteinuria of >300 mg /24 hour measured by urine dipstick method. Fetal weight was measured 10 minutes after delivery of baby. Serum uric acid was measured by consultant hematologist in Railway Hospital Rawalpindi.

The collected data was entered in SPSS version 20. Descriptive analysis was done for age, uric acid, gestational age, and birth weight. Qualitative variables like low birth weight, parity, were featured as frequencies and percentages. One sample t-test was applied to find out any significant difference regarding the low birth weight in study population. Association of low birth weight with gestational age, parity type, age groups and serum uric acid level was also assessed by applying chi square test. A p-value of ≤ 0.05 was deemed as significant with 95% confidence interval.

RESULTS

80 pregnant women achieving the inclusion and exclusion criteria were registered after informed consent. Mean age of the patients was 26.86 $\pm$ 4.53 years. 29 (36.2%) patients were ranging from 18 to 24 years, 28 (35%) ranged from 25 to 29 years and 23 (28.8%) patients were 30 years or more. Gestational age of the subjects was recorded to be 38.50 $\pm$ 0.35 weeks. Levels of serum uric acid were observed to be 5.38 $\pm$ 0.76 mg/dl. Mean birth weight was calculated to be 2.38 $\pm$ 0.29 kg. 35 (43.8%) females were primigravida, 20 (25%) were para 1 and 25 (31.2%) were para 2 and more.

Regarding frequency of low-birth-weight babies in pregnancies complicated with hyperuricemia and pre-eclampsia, 60 (75%) neonates had birth weight less than 2.5 kg and 20 (25%) neonates had birth weight 2.5 kg or more with the p value of 0.043 indicating a statistically significant difference.

TableNo.1: Association of low birth weight with gestational age, parity type, age groups and serum uric acid levels by applying chi sq test

Factors	Birth Weight		p-value
	Birth weight less than 2.5 kg n=60	Birth weight 2.5 kg or more n=20	
Gestational Age (Weeks)			
less or equal to 38.5 weeks	43 (71.6%)	11 (55%)	0.168
more than 38.5 weeks	17(28.3%)	09 (45%)	
Parity Type			
Primigravida	28 (46.6%)	07 (35%)	0.104
Para 1	17 (28.3%)	03 (15%)	
Para 2 or more	15 (25%)	10 (50%)	
Patients Age (Years)			
18 - 24 years	22 (36.6%)	07 (35%)	0.754
25 - 29 years	22 (36.6%)	06 (30%)	
30 years or more	16 (26.6%)	07 (35%)	
Serum Uric Acid Level (mg/dl)			
less or equal to 5.5	43 (71.6%)	16 (80%)	0.463
more than 5.5	17 (28.3%)	04 (20%)	

In our study 59 (73.8%) women whose uric acid levels was up to 5.5 mg/dl had 43 (71.6%) babies with low birth weight and 21 (26.2%) women with uric acid

more than 5.5 mg/dl had 17 (28.3%) babies with low birth weight. Similarly, according to the gestational age, 54 (67.5%) neonates had gestational age less or equal to 38.5 weeks and 26 (32.5%) neonates had gestational age of more than 38.5 weeks.

Association of low birth weight was also evaluated with respect to gestational age, parity type, age groups and serum uric acid level as shown in Table-1. There was not any statistically substantial difference found with any of the variables under investigation showing no significant association. Thus, low birth weight of the babies is not corelated with gestational age, parity type, age groups and serum uric acid level.

DISCUSSION

Recently the effectiveness of hyperuricemia has been highlighted not only as a biomarker of preeclampsia but also as a predictor of undesirable fetal and maternal outcomes. The present study shows that finding maternal hyperuricemia nearby delivery is related to adverse maternal and fetal outcomes. Gestational hypertension with the occurrence of hyperuricemia increases the fetal risk as suggested in a study conducted by Hawkin et al[16]. Earlier studies have also indicated a relationship among hyperuricemia and adverse obstetric outcome in hypertensive pregnancy[17][18][19]. Results of our study also strengthen this relationship and it is shown that women with hypertension in pregnancy along with high uric acid results in low-birth-weight babies. Hyperuricemia in women with preeclampsia results in renal disease in mothers and preterm births.

In the present study 59 women whose uric acid level was up to 5.5 mg/dl had a more babies 43 (72.8%) with low birth weight, compared to the women with uric acid above 5.5 mg/dl (n = 17, 28.3%). However, this variation was not significant (p = 0.463). This demonstrated that as the level of serum uric acid increases the incidence of low-birth-weight increases. D' Anna et al, 2000 and Feig et al. 2004 present similar results[20][21].They demonstrated significant relationship among hyperuricemia and fetuses with low birth weight. Another study conducted by Devia et al also revealed similar trend[22]. This tendency of raised uric acid leading to poor outcome as concerned to fetus implies that most likely it's causing growth restriction and the outcome is manifested as low birth weight.

There is a debate concerning whether uric acid is only a biomarker of disease or direct contributory in evolution of preeclampsia and fetal growth restriction [23]. While the exact origin of raised uric acid in preeclampsia is not exactly known decreased renal clearance has been suggested as a plausible cause in studies[24]. This tendency of decrease in clearance of urate generated by the infusing vasoconstrictors like norepinephrine and raised blood uric acid level and decrease clearance detected in glomerulonephritis might imply that the uric acid could become an early indicator of preeclampsia[25]. Beside decreased clearance of uric acid by kidneys increased production by placenta because of ischemia is also seen. Elevated levels of metabolites of purine have been detected in fetuses exposed to hypoxia[26] which enters maternal circulation where they are degraded by maternal xanthine oxidase in preeclampsia. This mechanism explains the link between the raised uric acid levels and restricted fetal growth. Proactive role for uric acid in the evolution of pre-eclampsia has been proposed[27]. The consequent poor fetal outcome in patients with high levels of uric acid implies that it causes growth restriction, reflected as low birth weight[6].

From these findings it can be presumed that adverse fetal consequences in pre-eclampsia, may be the result of hyperuricemia associated with pre-eclampsia. Put differently in pre-eclampsia, the higher the levels of uric acid the higher the chances of adverse fetal effects. Thus, serum uric acid assessment can serve as a good prognostic tool in identifying the gravity of the disease and accordingly decide the time of delivery to ensure safety both for mother and the fetus. Pakistan is a developing country and cannot afford high health budget. Results of this study will guide the obstetrician in recognizing the burden of this disease.

CONCLUSION

Raised uric acid level associated with pre-eclampsia is a significant risk factor for poor fetal outcome. Frequency of babies with low birth weight increases in pregnancies that are complicated with hyperuricemia and pre-eclampsia as 75% neonates reported low birth weight.

Author's Contribution:

Concept & Design of Study:	Saliha Ghias Ud Din, Wajiha Shadab
Drafting:	Saliha Ghias Ud Din, Wajiha Shadab, Farah Javed
Data Analysis:	Saliha Ghias Ud Din, Sadaf Afzal, Farah Javed, Ayesha Mobeen
Revisiting Critically:	Sadaf Afzal, Mavra Tufail
Final Approval of version:	Saliha Ghias Ud Din, Wajiha Shadab

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Laine K, Murzakanova G, Sole KB, Pay AD, Heradstveit S, Räisänen S. Prevalence and risk of pre-eclampsia and gestational hypertension in twin pregnancies: a population-based register study. BMJ Open 2019;9(7):e029908.

2. Pankiewicz K, Szczerba E, Maciejewski T, Fijałkowska A. Non-obstetric complications in preeclampsia. Przegląd Menopauzalny= Menopause Rev 2019;18(2):99.
3. Shiozaki A, Saito S. Risk factors for preeclampsia. In: Preeclampsia. Springer;2018.p.3–25.
4. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: pathophysiology, challenges, and perspectives. Circ Res 2019;124(7):1094–112.
5. Chappell LC, Cluver CA, Kingdom J, Tong S. Pre-eclampsia. Lancet 2021;398(10297):341–54.
6. Khaliq OP, Konoshita T, Moodley J, Naicker T. The role of uric acid in preeclampsia: is uric acid a causative factor or a sign of preeclampsia? Curr Hypertens Rep. 2018;20(9):1–9.
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.
8. Bellos I, Pergialiotis V, Loutradis D, Daskalakis G. The prognostic role of serum uric acid levels in preeclampsia: A meta-analysis. J Clin Hypertens 2020;22(5):826–34.
9. Asgharnia M, Mirblouk F, Kazemi S, Pourmarzi D, Keivani MM, Heirati SFD. Maternal serum uric acid level and maternal and neonatal complications in preeclamptic women: A cross-sectional study. Int J Reprod Biomed 2017;15(9):583.
10. George C, Minter DA. Hyperuricemia. StatPearls [Internet]. 2021;
11. Kang DH, Finch J, Nakagawa T, Karumanchi SA, Kanellis J, Granger J, et al. Uric acid, endothelial dysfunction and pre-eclampsia: searching for a pathogenetic link. J Hypertens 2004;22(2):229–35.
12. Khalil S, ElShourbagy S, Hamad S, Abo Zeid E. Hyperuricemia as a predictor of perinatal outcomes in pregnancy induced hypertension. Gynecol Obs Res Open J 2018;5(1).
13. Yu J, Flatley C, Greer RM, Kumar S. Birth-weight centiles and the risk of serious adverse neonatal outcomes at term. J Perinat Med 2018;46(9): 1048–56.
14. Knop MR, Geng T, Gorny AW, Ding R, Li C, Ley SH, et al. Birth weight and risk of type 2 diabetes mellitus, cardiovascular disease, and hypertension in adults: a meta-analysis of 7 646 267 participants from 135 studies. J Am Heart Assoc 2018; 7(23):e008870.
15. Ayankunle OM, Adeniyi AA, Adewara OE, Awoyinka SB, Adebara IO, Adeyemo OT, et al. Maternal serum uric acid: a reliable prognostic indicator of foetal outcome among pre-eclamptic patients in a low resource setting. J Matern Neonatal Med 2021;1–6.
16. Hawkins TL, Roberts JM, Mangos GJ, Davis GK, Roberts LM, Brown MA. Plasma Uric Acid Remains a Marker of Poor Outcome in Hypertensive Pregnancy: A Retrospective Cohort Study. Obstet Anesth Dig 2013;33(3):151.
17. Niraula A, Lamsal M, Majhi S, Khan SA, Basnet P. Significance of serum uric acid in pregnancy induced hypertension. J Natl Med Assoc 2017;109(3):198–202.
18. Schmella MJ, Clifton RG, Althouse AD, Roberts JM. Uric acid determination in gestational hypertension: is it as effective a delineator of risk as proteinuria in high-risk women? Reprod Sci 2015;22(10):1212–9.
19. Pecoraro V, Trenti T. Predictive value of serum uric acid levels for adverse maternal and perinatal outcomes in pregnant women with high blood pressure. A systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2020;252: 447–54.
20. 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):101–3.
21. Feig DI, Nakagawa T, Karumanchi SA, Oliver WJ, Kang D-H, Finch J, et al. Hypothesis: uric acid, nephron number, and the pathogenesis of essential hypertension. Kidney Int 2004;66(1):281–7.
22. Devi N, Rizwan N, Dars S. Fetal outcome in pre-eclamptic women with high serum uric acid level. Online Int Interdiscip Res J 2014;4(Special Issue):86–95.
23. Masoura S, Makedou K, Theodoridis T, Kourtis A, Zepiridis L, Athanasiadis A. The involvement of uric acid in the pathogenesis of preeclampsia. Curr Hypertens Rev 2015;11(2):110–5.
24. Parrish M, Griffin M, Morris R, Darby M, Owens MY, Martin Jr JN. Hyperuricemia facilitates the prediction of maternal and perinatal adverse outcome in patients with severe/superimposed preeclampsia. J Matern Neonatal Med 2010;23(12):1451–5.
25. Bellomo G, Venanzi S, Saronio P, Verdura C, Narducci PL. Prognostic significance of serum uric acid in women with gestational hypertension. Hypertension 2011;58(4):704–8.
26. Lam C, Lim KH, Kang DH, Karumanchi SA. Uric acid and preeclampsia. In: Seminars in nephrology. Elsevier;2005.p.56–60.
27. Sultana R, Ahmed S, Sultana N, Karim SMF, Atia F. Association of serum uric acid with preeclampsia: a case control study. Delta Med Coll J 2013;1(2):46–50.