www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i7.22

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Paper

Evaluation of Serum Uric Acid and Lipid Profile in Pre-eclamptic Women: A Hospital Based Study

Authors
Dr Prafula Kumar Mishra[1], Manoj Kumar Yadav[2*], Kedar Prasad Yadav[3], Sankha Simlai[4]
[1]Professor & Head of the Department, Hi-Tech Medical College & Hospital, Rourkela, Odisha, India
[2]Heritage Institute of Medical Sciences, Varanasi, Uttar Pradesh, India
[3]Major S. D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India
[4]K. D. Medical College & Hospital, Mathura, Uttar Pradesh, India
[1,2,3&4]Department of Biochemistry
*Corresponding Author
Manoj Kumar Yadav
Heritage Institute of Medical Sciences, Varanasi, Uttar Pradesh, India

Abstract
Pre-eclampsia is a non-convulsive form of hypertensive disorder of pregnancy. Pre-eclampsia affects approximately 3% of all pregnancies worldwide, with onset of symptoms in the late second or third trimester, commonly after 32nd week. Our aim was to evaluate the biochemical markers i. e.; Lipid profile and serum uric acid for early diagnosis of preeclampsia. This association may be significant in understanding the pathological processes of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia.

Keywords: *BMI, High blood pressure, Lipid profile, Uric acid & Pre-eclampsia.*

Abbreviations Used: *TG: Triglycerides, HDL-c: High Density Lipoprotein Cholesterol, LDL-c: Low Density Lipoprotein Cholesterol, VLDL-c: Very Low Density Lipoprotein Cholesterol, WHO: World Health Organization, BMI : Body mass index, BP : Blood pressure.*

Introduction

Pre-eclampsia is a non-convulsive form of hypertensive disorder of pregnancy.[1] Incidence of preeclampsia in India is reported to be 8-10% of pregnancies. In the United States of America (USA) preeclampsia occurs in 2.6% of pregnancies and eclampsia in 0.056% of pregnancies.[2] Preeclampsia is a pregnancy specific syndrome and a leading cause of maternal and foetal morbidity and mortality. Preeclampsia is a multisystem disorder characterized by hypertension to the extent of 140/90mmhg or more, proteinuria (≥300mg/day) and edema induced by pregnancy after 20th week.[3] However preeclampsia is a complex multisystem syndrome and far more than gestational hypertension and proteinuria.[4] Preeclampsia and related disorders are known to affect function of various organs involved in lipid and lipoprotein metabolism. Several studies have shown that endothelial dysfunction is related to hyperlipidemia.[5,6] Significantly elevated plasma concentration of

Triglycerides (TG), phospholipids and total lipids and decreased high density lipoprotein – cholesterol (HDL-C) concentrations were found in women with preeclampsia in comparison to normal pregnancy.[7,8]

It is proposed that pregnancy mediated changes in serum uric acid are primarily the result of altered renal handling. Increased serum uric acid in women with preeclampsia has been consistently described for more than 80 years. The increase in serum uric acid has been attributed to reduced renal urate clearance because of renal dysfunction.[9] In view of the above; the present study involves evaluation of lipid profile and uric acid levels in preeclampsia.

Material and methods

The present study was conducted in the Department of Biochemistry, Hi-Tech Medical College & Hospital Rourkela, Odisha, India, during the period from November 2012 to October 2013. The study protocol was approved by the Ethics committee of Hi-Tech Medical College & Hospital Rourkela. The present study consists of total 60 women subjects between the age group 20-39 years who are further subdivided into two groups;

i. Group-A**:** Includes Normotensive pregnant women (n= 25) as controls.
ii. Group-B**:** Consists of Pregnant women with preeclampsia (n= 35) as cases.

All patients were explained in detail about aim, objectives of study and written consent was taken. A detailed obstetric history and examination was done. Height was measured, maintaining an accuracy of 0.5cm.Weight was measured, up to nearest 100gm. Prepregnancy body mass index (Quetelet index) was calculated as weight in kilograms/height in square meters. According to WHO, normal BMI ranges from 18.5 to 24.9 kg/m^2. BMI between 25-29.9 kg/m^2 is overweight, while a BMI > 30 kg/m^2 is considered obese. Blood pressure was measured by sphygmomanometer in right arm in left lateral po-sition after 10 minutes of rest. Preeclampsia was diagnosed as blood pressure >140/90 mmHg on 2 separate occasions 4 hours apart in association with proteinuria (>0.3gm in 24 hours or at least 1+ on dipstick examination).[10]

Biochemical Analysis

An overnight fasting blood sample were collected under all aseptic precautions 5-10 ml of blood was collected and analysed for following parameters.

1. Total Cholesterol (TC) by enzymatic end point CHOD-POD methods.[11]
2. Triglyceride (TG) by enzymatic glycerol phosphate oxidase/peroxidase methods.[12]
3. HDL-Cholesterol by direct enzymatic end point method.[13,14]
4. LDL-Cholesterol by Friedewald's formula.[15]
5. VLDL-Cholesterol by Friedewald' sequtions.
   LDL-c = Tc-HDL-c(TG/5)
6. Uric acid: By modified Trinder method.[16]

Statistical Analysis

All values were expressed as mean±sd. We used student t-test and pearson's correlation coefficient to find the statistical significance. A P-value <0.05 was to be considered statistically significant.

Results and Discussion

The present study was conducted on 60 nulliparous pregnant women in their third trimester between the ages 20 to 39 years; thirty five were patients of pre-eclampsia in study group and twenty five normotensive non-pre-eclamptic women in control group. Pre-eclampsia was diagnosed on the basis of history, clinical examination, blood pressure findings and presence of proteinuria. Table-1 shows the Demographic & Clinical characteristics of the Cases & Controls group. Table-2 shows the Comparison of biochemical parameters between the two groups where TG, VLDL, LDL, cholesterol, serum uric acid level were significantly higher in preeclamptic women ($p<0.001$), while serum HDL was significantly low in preeclamptic women ($p <0.001$).

Table 1: Demographic & Clinical characteristics of the Cases & Controls group:

Parameters	Controls (n=25) (mean±sd)	Cases (n=35) (mean±sd)
Age (yrs)	22.06 ± 10.16	29.06 ± 10.16
Weight (kg)	44.06 ± 10.16	47.8 ± 7.7
Height (cm)	76.03 ± 6.90	77.85 ± 6.88
BMI (Kg/m^2)	27.0 ± 2.1	29.4 ±2.8
Systolic BP	114.76 ±0.43	152 ±0.47
Diastolic BP	68 ±0.82	104 ±0.26

**Statistically Significant (P<0.05)*

Table 2: Comparison of biochemical parameters between the two groups:

Parameters	Controls (n=25) (mean±sd)	Cases (n=35) (mean±sd)
Total Cholesterol(mg/ dl)	176.4 ±12.07	218.34 ± 24.88
Triglycerides (mg/ dl)	129.84 ±11.32	187.4 ± 29.2
LDL-c(mg/ dl)	96.17 ±14.75	137.10 ±13.75
HDL-c(mg/ dl)	41.5 ± 7.9	29.6 ±4.80
VLDL-c(mg/ dl)	25.79 ±2.41	31.4 ±4.57
Uric acid (mg/ dl)	5.4 ±1.03	7.3 ± 0.6

***All parameters Statistically Significant at (P<0.05)*

Pre-clampsia is a multisystem endothelial disease that leads to glomeruloendotheliosis, and in severe cases it may lead to renal impairment and failure.[17]The present results showed that the clinical characteristics and
maternal serum uric acid, triglycerides, total cholesterol, HDL-cholesterol (HDL-C), LDL-cholesterol and VLDL-cholesterol levels in normotensive pregnant women (group-A) and pre-eclamptic women (group-B).

Mean maternal age, weight & height of pre-eclamptic women (group-B) was statistically significant than normotensive pregnant healthy women (group-A), ($p < 0.05$). The mean systolic and diastolic blood pressure in pre-eclamptic women (group-B) was significantly higher than normotensive pregnant women (group-A) (Table-1).

Women with preeclampsia had significantly higher BMI compared with controls ($p< 0.05$) (Table-1) which is similar to finding of Sharami et al[18]. Probable, mechanism of increased BMI in preeclampsia is increased insulin resistance and a state of inflammation associated with obesity[19]. Insulin resistance leads to lipolysis, leading to increased flux of fatty acids to liver promoting synthesis of TG[20]. Also maternal obesity is independently associated with development of placental endothelial dysfunction and ultimately preeclampsia.[19]

The mean levels of TG, VLDL, LDL and cholesterol were significantly higher in preeclamptic women than in normotensive controls ($p<0.001$). Also there was a significant decrease in HDL in study group as compared to control ($p<0.001$) (Table-2). Hypertriglyceridemia in preeclampsia is also attributed to insulin resistance due to obesity. During early pregnancy, anabolic phase encourages lipogenesis and fat storage in preparation for rapid fetal growth in late pregnancy. Therefore there is physiologic hyperlipidemia with gestational rise in triglyceride and cholesterol as high as two to three times in third trimester[21] Risk of preeclampsia was four times higher in women with elevated TG[22].

Oestrogen induces biosynthesis of endogenous triglyceride by stimulating hepatic lipase.[23] There is decreased activity of lipoprotein lipase which is

responsible for decreased catabolism at adipose tissue level, Thus in preeclampsia, there is hypertriglyceridemia whereas placental VLDL receptors are up regulated. This results in re-routing of TG rich lipoproteins to feto-placental unit. However in preeclampsia the vascularization of fetoplacental unit may be impaired, resulting in yet-undefined compensatory mechanisms that may further increase synthesis of maternal TG levels.[24]As already discussed, obesity and insulin resistance also promotes synthesis of TG.

Another hypothesis is that hypertriglyceridemia is probably a consequence of competition between chylomicrons and VLDL for lipoprotein lipase. Classically, chylomicron clearance occurs in two sequential steps:

1. Triglyceride hydrolysis by lipoprotein lipase
2. Uptake of remnant by liver.

Delay in second step leads to accumulation of TG in plasma and is thought to represent the atherogenic risk of hyper-triglyceridemia.[25]

Abnormal lipid metabolism is not a mere manifestation but is also involved in pathogenesis of disease. Increased serum triglyceride is likely to be deposited in predisposed vessels such as uterine spiral arteries and contributes to endothelial dysfunction, both directly and indirectly through generation of LDL. Hypertriglyceridemia also has prothrombotic activity which may be associated with hyper-coagulability. Altered lipid synthesis leading to decreased in Prostaglandin I2 (PGI2): Thromboxane A2 (TXA2) ratio is also supposed to be an important way of pathogenesis in pre-eclampsia.[23]

VLDL transports TG in peripheral blood therefore hypertriglyceridemia also leads to increased serum levels of VLDL.[19] As already discussed, insulin resistance causes lipolysis, leading to increased flux of fatty acids to liver promoting synthesis of VLDL.[20]

Increased LDL levels are due to elevated estrogen and progesterone levels in preeclampsia. It has been shown that LDL (specially oxidized LDL) increases arterial sensitivity to pressor agents and inhibits endothelium dependant vasodilatation. This endothelial dysfunction, leads to glomerular lesions and subsequently proteinuria, which also gives an indication of its severity. Low HDL in preeclampsia is due to insulin resistance.[26] According to Pirzado et al[27], there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL. This is responsible for low levels of HDL.HDL carries excess, potentially harmful cholesterol from peripheral tissues to liver, where it can be excreted. In addition, it is involved in activating lipoprotein which releases fatty acids that can be oxidized by β-oxidation pathway to provide energy. Low levels of HDL may compromises these functions.

Hypercholesterolemia promotes formation of free radicals (free radical theory). Thus several studies have linked 'atherogenic' lipid profile as a potential contributor to increased risk of preeclampsia.[19] Thus, dyslipidemia mediated endothelial dysfunction &placentally derived endothelial disturbing factors like lipid peroxides could possibly contribute in pathogenesis of pregnancy induced hypertension. Thus, estimation of lipid profile may have a predictive role in assessing extent of endothelial damage and may help by preventing or foreseeing complications in pre-eclampsia.[21]

Serum uric acid level were significantly higher in preeclamptic women ($p < 0.001$). This is consistent with previous studies.[28,29] Excessive cellular activity is associated with placental ischemia also leads to overproduction of uric acid which serves as a marker of the disease. Uric acid levels have been consistently reported to be elevated in preeclampsia. Hyperuricemia may predate proteinuria by several weeks.[28,29] Previous studies also indicate that measurement of serum uric acid may be a better indicator of fetal prognosis as compared to blood pressure in preeclampsia.[30] Monitoring of serum uric acid level in those with preeclampsia will help to predict those that will develop eclampsia.[31]

Conclusion

These findings suggest that Total Cholesterol, Triglycerides, LDL-c, VLDL-c, and uric acid levels were raised in pre-eclampsia and statistically significant; while HDL-c levels were raised in these patients but statistically non-significant, it can be concluded that there exists an association in lipid profile and uric acid with pre-eclampsia therefore dyslipidemia and raised uric acid levels are the features of pre-eclampsia in nullipara pregnant women in their third trimester. This association may be significant in understanding the pathological processes of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia.

Bibliography

1. Montan S, Sjoberg N, Svenningsen N. Hypertension in pregnancy—fetal and infant outcome: a cohort study. Hyper tens pregnancy; 6:337-48, (1987).
2. Meculure N, Thompson W. Pre-eclampsia and eclampsia. In: Sengupta BS, Chattopadhyay SK, Thornton JG, Sengupta PS edts. Obstetrics for postgraduate and practitioners. New Delhi: Churchill Livingstone Publications .p: 40-47, (1999).
3. Noris M, Perico N, Remuzzi G. Mechanisms of Disease: pre-eclampsia. Nature Clinical Practice Nephrology 2005;1:98-114.
4. Ness RB, Roberts JM. Heterogeneous causes constituting the single syndrome of preeclampsia: a hypothesis and its implications. American journal of Obstetrics and Gynaecology 1996;175:1365-70.
5. Robert JM, Redman CWG. Preeclampsia: more than pregnancy induced hypertension. Lancet 1993;41:1447-51.
6. Wockhardt Hospitals Blog, Causes, Symptoms and Complications of Pre-eclampsia: Is your Pregnancy at Risk, Thursday, March 12, 2009.
7. Lyall F, Ian AG. The vascular endothelium in normal pregnancy and pre-eclampsia. Reviews of Reproduction 1996;1:107–16.
8. Robert JM, Lain KY. Recent insight into the pathogenesis of preeclampsia. Placenta 2002;23:359-72.
9. F.GaryCummingham, Norman FG, Kenneth et al. Hypertensive disorders in pregnancy, Williams Obstetrics, 22 Edition, Me. Graw Hill 2005:761-764.
10. Tietz Kidney function tests. Tietz textbook of clinical chemistry and molecular diagnostics. 4th edition. Elsevier:807.
11. Richmond W. – Preparation and properties of cholesterol oxidase from Nocardia sp. and its application to the enzymatic assay of total cholesterol in serum. Clin Chem. 19: 1350-1356, 1973.
12. Foosati P. and Prencipe L. – Serum triglyceride determined colorimetrically with an enzyme that produce hydrogen peroxide. Clin Chem. 28: 2077-2080, 1982.
13. Rifai N. and Warnick G.R., Ed.- Laboratory measurements of lipids, lipoproteins and apolipoproteins. AACC press, Washington, DC, USA 1994.
14. Burtis, C.A. and Ashwood, E.R. Ed. – Tietz Textbook of clinical chemistry, 2nd Ed, Saunders, Philadelphia, 1994.
15. Friedewald W.T., Levy R.I., Fredrickson D.S., clin Chem. 18:499, 1972.
16. Trinder PJ. Clin. Pathology. 1949;22:246.
17. Sukonpan K, Phupong V. Serum calcium and serum magnesium in normal and preeclamptic pregnancies. Arch Gynecol Obstet. 273: 12-16 (2005).
18. Sharami SH, Tangestani A, Faraji R, Zahiri Z, Azam A. Role of dyslipidemia in pre-eclamptic overweight pregnant women. Iran J Reprod Med 2012;10:105-112.
19. Ephraim R, Doe PA, Amoah S, Antoh EO. Lipid profile and high maternal body mass index is associated with preeclampsia: A

case-control study of the Cape Coast Metropolis. Ann Med Health Sci Res 2014;4:746-750.
20. NAF Islam, MAR Chowdhury, GM Kibria, S AkhterFaridpur. Study of serum lipid profile in pre-eclampsia and eclampsia. Med. Coll. J. 2010;5(2):56-59.
21. PradnyaPhalak, Mona Tilak. Study of lipid profile in pre-eclampsia. Indian Journal of Basic & Applied Medical Research. 2012; 5, (2) : 405-409.
22. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes (CHAMPS): Population-based retrospective cohort study. Lancet 2005; 366:1797-1803.
23. Swapan Das, Debasish Char, Sanjay Sarkar, PrakashDas,TusharKantiSaha, SuchetaBiswas. Comparison of lipid profiles in normal pregnancy and in pre-Eclampsia: A case control study. IOSR Journal of Dental and Medical Sciences. 2013; 11(4): 53-55.
24. Karl W, Birgit W, Michael M. H et al. Triglyceride rich lipoproteins are associated with hypertension in preeclampsia. The Journal of Clinical Endocrinology & Metabolism 2003;88(3):1162-1166.
25. Kashinakunti S. V. ,Sunitha H , Gurupadappa K, Manjula R. Lipid Profile In Preeclampsia – A Case Control Study. Journal of Clinical and Diagnostic Research 2010 ; 4: 2748- 2751.
26. Cekmen MB. Erhagci AB, Balat A, Duman C, Maral H, Ergen K, et al. Plasma lipid and lipoprotein concentrations in pregnancy induced hypertension. Clin. Biochem. 2003; 36(7):575-578.
27. Pirzado ZA, Sangi SA, Malik R. High density lipoprotein cholesterol metabolism and its role in ischemic heart disease. Pak J Med Res 1999; 38: 38–41.
28. 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. BJOG 2012;119:484-492.
29. Wu Y, Xiong X, Fraser WD, Luo ZC. Association of uric acid with progression to preeclampsia and development of adverse conditions in gestational hypertensive pregnancies. Am J Hypertens 2012;25:711-717.
30. VarmaTR. Serum uric acid levels as an index of fetal prognosis in pregnancies complicated by pre-existing hypertension and pre-eclampsia ofpregnancy. International Journal of Gynecology& Obstetrics 1982;20(5):401-8.
31. Sahijwani D, Desai A, Oza H et al. Serum Uric acid as prognostic marker of pregnancy induced hypertension. Journal of South Asian federationof Obstetrics &Gynecology 2012;4(3):130-3.

Authors Profile

Dr Prafula Kumar Mishra, Professor & Head in the Department of Biochemistry, Hi-Tech Medical College & Hospital, Rourkela, Odisha, India.
Email: *prafula.mishra16@yahoo.com*

Mr Manoj Kumar Yadav, Medical Biochemist in the Department Of Biochemistry, Heritage Institute of medical sciences, Varanasi, Uttar Pradesh, India.
Email: *mkybiochem@hotmail.com*

Mr Kedar Prasad Yadav, Medical Biochemist in the Department Of Biochemistry, Major S. D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India.
Email: *kp.yadav128@hotmail.com*

Mr Sankha Simlai, Assistant Professor in the Department Of Biochemistry, K. D. Medical College & Hospital, Mathura, Uttar Pradesh, India.
Email: *sankha_samlai@yahoo.co.in*