Biochemical Profile of women with pregnancy induced hypertension

N. Chowdeswari[1,*], M. Girija Menon[2], N. Jaya[3], B.V. Ramarao[4]

[1,3]Associate Professor, [4]Professor & HOD, ACSR Govt. Medical College, Nellore, [2]Associate Professor, Dept. of Biochemistry, Malla Reddy Institute of Medical Sciences, Hyderabad

***Corresponding Author:**
Email: chowdy73@gmail.com

Abstract

Background: Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection. Pre-eclampsia is a syndrome of generalized endothelial dysfunction initiated by abnormal placentation and consequent placental under perfusion, release of cytokines, peroxidants and vasoconstriction and platelet activation. It is characterized by hypertension, reduced uteroplacental blood flow, proteinuria and edema. Pre-eclampsia is associated with increased lipid Peroxidation in maternal circulation and placenta.

Material and Methods: A hospital based cross sectional study was carried out among 65 women of age 18 to 30 years who were in third trimester of pregnancy with singleton fetus. Informed consent was taken from each and every study participant. It was ensured that the study participants did not receive any medication for hypertension. Blood pressure was measured as per the standard guidelines. Urine for protein was determined by Dip sticks method. Serum uric acid, Malondialdehyde and birth weight was measured.

Results: The two groups were similar in the parameters like age, gestational age at blood sampling, and gestational age at delivery. Systolic and diastolic blood pressure, mean arterial blood pressure, proteinuria, serum uric acid and Malondialdehyde were increased in eclampsia group than pre-eclampsia group. These parameters were also increased in pre eclampsia & eclampsia group as compared to the controls. Serum uric acid and Malondialdehyde levels in pregnant women with pre eclampsia & eclampsia showed a statistically significant increase as compared to the control group ($p<0.001$). Mean birth weight was less in eclampsia group than pre-eclampsia group. Induction of labor, preterm delivery and C/Section, were obstetric outcome affecting maternal morbidity.

Conclusion: Serum uric acid & Malondialdehyde were increased in pre eclampsia & eclampsia cases. The eclampsia group was more at risk of delivery by caesarean section than the pre-eclampsia group. The birth weight was also less in eclampsia cases as compared to pre-eclampsia and normal pregnancy.

Key words: Biochemical profile, Eclampsia group, Caesarean section

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-6377.2016.00038.1

Introduction

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection. Pre-eclampsia is a syndrome of generalized endothelial dysfunction initiated by abnormal placentation and consequent placental under perfusion, release of cytokines, peroxidants, vasoconstriction and platelet activation. It is characterized by hypertension, reduced uteroplacental blood flow, proteinuria and edema. Pre-eclampsia is associated with increased lipid peroxidation in maternal circulation and placenta and an increase in serum total lipids& triglycerides[1].

Vasospasm is the basis of pathophysiology of pre-eclampsia and eclampsia[2].

An alternate region of arteriolar constriction and dilatation in nail beds was noted by Hinselmann [3].

Vascular constriction causes a resistance to blood flow and accounts for the development of arterial hypertension. Vasospasm also exerts a noxious effect on the vessels themselves, as circulation in vasavasorum is impaired, leading to vascular damage. Moreover angiotensin – II appears to have direct action on endothelial cells, causing them to contract. These factors could lead to interendothelial leaks through which blood constituents including platelets and fibrinogen, are deposited subendothelially. The vascular changes together with local hypoxia of the surrounding tissues, presumably lead to hemorrhage, necrosis and other end organ disturbances that are sometimes seen with severe pre-eclampsia. Fibrin deposition is prominent in fatal cases[4].

It is the increased responsiveness of the arterial system to pressor substances which probably causes the generalized vasoconstriction & hypertension of pre-eclampsia.

Lipid peroxidation is a process normally occurring at low levels in all cells and tissue.[5]

Uncontrolled lipid peroxidation contributes to certain disease processes via disruption of membrane lipid and other cell components.[6]

The peroxidation chain can become self-perpetuating. If not tightly controlled, the end result is an elevated steady state concentration of lipid peroxides at the expense of oxygen and unsaturated lipid. The mechanism has been extensively reviewed.[7]

The Haematological abnormalities in pregnancy induced hypertension include disseminated intravascular coagulation (DIC) which is not only a characteristic of pre-eclampsia but also plays a dominant role in the pathogenesis of this syndrome. Intravascular coagulation is initiated by the entry of thromoboplastin substances into the blood stream. Rapid DIC & fibrin so formed causes cerebral vascular occlusion & convulsions of eclampsia. Lipid peroxides are elevated in the blood of women with pre eclampsia as first obtained by analysis of serum malondialdehyde, a major break down product split off from lipid peroxides. In normal pregnancy an increase in malondialdehyde was associated with an increase in total serum lipids. In pre-eclampsia, the normal control (anti oxidative) mechanism for lipid peroxidation may not function adequately. The anti-oxidant role of uric acid has been mentioned.

Material and Methods

A hospital based cross sectional study was carried out among 65 women of age 18 to 30 years who were in the third trimester of pregnancy with singleton fetus. The study was conducted in the department of Biochemistry & Obstetrics & Gynecology, in the Government Maternity Hospital, Nayapul, Hyd. Institutional Ethics Committee permission was obtained. Informed consent was taken from each and every study participant.

20 women with absolute normal pregnancy & 45 suffering from pregnancy induced hypertension (Pre eclampsia & eclampsia) were included in the study. It was ensured that the study participants did not receive any medication for hypertension. Blood pressure was measured as per the standard guidelines. Pre eclampsia was regarded as systolic blood pressure of 140-150 mm of Hg & diastolic of 90-100 mm of Hg or as increase in 20 mm of Hg on two separate occasions & semi quantitative proteinuria dip stick testing 3 + or more.

The mean arterial pressure was defined as diastolic pressure + 1/3rd (systolic – diastolic blood pressure). Control group consisted of antenatal women between 30 – 36 weeks of gestation with normal blood pressure, with no pedal oedema & no albumin detected in the urine. Urine for protein was determined by Dip sticks method. Normal range of urinary protein loss for pregnant women - upto 300mg/per day. Birth weight of child was measured using a weighing machine immediately after the birth. Serum uric acid was determined by Method of Caraway (1955, 1963)[8]. Normal range - 4.0 – 6.5 mg/dl. Sample volume 500 micro liters. Instrument used is Spectrophotometer. Serum malondialdehyde was determined by Thiobarbituric acid method[9].

Normal range - 247±35 nano moles / 100ml.

Sample volume 10 micro liters. Instrument used is Spectrophotometer.

Sample Collection: 10ml of overnight fasting venous samples from the controls & the cases were collected in sterile clean & dry bottles. Blood centrifuged, serum separated & assay performed.

Statistical Analysis: The collected data was entered and analyzed in Epi Info statistical software version 7. For proportions, chi square test was used. For mean values, student's t test was used. The p value of less than 0.05 was considered as significant.

Results

The following clinical and laboratory parameters were studied in the Controls and Cases

Table 1: Clinical and Laboratory parameters with the description of the Controls and the Cases

Sr. no.	Description	Control	Pre-eclampsia	Eclampsia
1	Age	18-29 yrs	18-29 yrs	18-29 yrs
2	Systolic BP(mm Hg)	110-120	140-160	>160 mm Hg
3	Diastolic BP(mm Hg)	70 – 80	90 – 110	>110 mm Hg
4	Mean arterial BP(mm Hg)	90	113	>126 mm Hg
5	Urinary Protein	0–200 mg/per day	3500–4100 mg/day	6100– 6700 mg/day
6	Gestational age at Blood sampling (weeks)	32±3 weeks	32±3 weeks	32±3 weeks
7	Gestational age at delivery (wks)	36±3 weeks	33±3 weeks	30±3 weeks
8	Birth weight (gms)	2500±600gms	1860±650gms	1340±420gms
9	% of growth retardation birth weight< - 2SD	Nil	All	All
10	Serum uric acid	3.4 mg/dl	Mean 4.76 mg/dl	Mean 6.93mg/dl p<0.001

			p<0.001	
11	Serum Malondialdehyde	271 nm/100ml	Mean 306.00nm/100ml p<0.001	Mean 333.06nm/100ml p<0.001
12	Obstetric outcome which increases maternal morbidity	Nil	Induction of labor, preterm delivery p<0.001	C/Section, induction of labor p<0.001

Table 1 shows the clinical and laboratory parameters of the study subjects. They were similar in the parameters like age, gestational age at blood sampling, and gestational age at delivery. Systolic and diastolic blood pressure, mean arterial blood pressure, Urinary protein, and serum uric acid was more in eclampsia group than pre-eclampsia group. Urinary protein levels were very much above normal range in both pre eclampsia & eclampsia subjects.

Mean birth weight was less in eclampsia group than pre-eclampsia group. The birth weight in pre eclampsia & eclampsia were also very much lower when compared to the controls. Growth retardation was thus observed in both pre eclampsia & eclampsia group.

From the above table, it is seen that serum uric acid levels in pregnant women with pre eclampsia & eclampsia showed a statistically significant increase as compared to the control group (p<0.001).

In pregnant women with pre eclampsia, there was a significant increase in the levels of Malondialdehyde (p<0.001). In pregnant women with eclampsia, when compared to the control group & those with pre eclampsia, there is a statistically significant increase in levels of serum Malondialdehyde (p<0.001).

Induction of labor & preterm delivery was seen to be more in pre eclampsia & so also induction of labor & Caesarean section was seen to be more in eclampsia. This also raises the maternal morbidity.

Discussion

In this study, the outcome of 2 groups of Infants, one born to mothers with pre-eclampsia/ eclampsia and the other to, normal pregnant women were compared with the help of a biochemical profile of normal pre eclamptic & eclamptic subjects. The morbidity and mortality of infants born of mothers with pre-eclampsia/ eclampsia was compared with that of normal pregnant women. In this study, it is found that in the infants born to normal pregnant women, the birth weight was 2500±600 gms, gestation age being 36±3 weeks, Apgar score 10±1. In Infants born to mothers with pre-eclampsia, birth weight was 1800±600 gms, gestational age being 32±3 wks and Apgar score 5±1. Neonatal illness was more in pre-eclampsia group and high mechanical ventilation was needed by all. Mortality of infants was low in pre-eclampsia group and high mortality was seen in eclampsia group. This study is in good agreement with the studies that pre-eclampsia/ eclampsia increase the morbidity in the neonatal period[10]. It was seen that obstetric outcome is normal in almost all cases. In pre-eclampsia there is increased propensity for induction of labor due to fetal distress and there were more cases of preterm delivery. In eclampsia there were 5 cases that had fetal distress and fetal death following eclampticfit and all the patients had to undergo caesarean section. Maternal mortality mainly related to eclampsia, accidental hemorrhage and acute renal failure. This is in good agreement with the reports by Perloff D et all[11].

Placental tissue is a major source of lipid peroxidation products in pregnancy. Of the lipid peroxidation products, malondialdehyde is the major break down product. A variety of anti-oxidant mechanisms serve to control lipid peroxidation. Any imbalance between the peroxidant & anti-oxidant forces in which the former dominates is called oxidative stress, of which lipid peroxidation is one important manifestation. This occurs with advancing gestation, reaching zenith in term placenta. The primary defect in pre eclampsia involves reduced utero placental perfusion. In normal pregnancy the diameter of spiral arteries feeding their intervillous space increases greatly. In pre eclampsia these are limited to the decidual portions of the arteries[12]. This maladaptation is due to superficial implantation or abnormal immunologic reactions between uterine trophoblastic tissues. This produces region of increased vascular resistance. The placental maladaptions are correlated with increase incidence of placental infarction, fetal distress & fetal growth retardation as seen in pre eclampsia. Lipofuscin “ageing pigments” have been found in higher concentration in term placentas compared with those less than 32 weeks gestation. This again indicates that placental peroxidation activity increases with gestation, since lipofuscin pigments are generally derived from lipid peroxide. Microsomal membranes from term human placentas are highly susceptible to lipid peroxidation in vitro. In tissues that are proficient in prostaglandin synthesis (uterus, seminal vesicle, Lung)much of the intrinsic lipid peroxidative activity is normally directed toward generation of prostaglandin endoperoxides in the prostaglandin cascade supplying these tissues with arachidonic acid which increase peroxidative processes whereas cyclooxygenase inhibitors decrease peroxidative reactions. Accordingly lipid peroxidation promoted by iron (Fe 2+) plus ascorbate in the uterine tissue was found to be stimulated by arachidonic acid and inhibited by cyclooxygenase inhibitors. The degree of lipid peroxidation induced by iron plus ascorbate was

higher in placental tissue than in uterine tissue. Inplacental tissue peroxidation was neither stimulated by arachidonate nor inhibited by prostaglandin inhibitors. Human placental tissue was found to produce high amounts of triglyceride.

In our study there is increase in malondialdehyde levels, a breakdown product of lipid peroxidation in normal pregnant women compared to non-pregnant women and marked increase in pre-eclampsia/eclampsia patients when compared to normal pregnant women. It was seen that all the patients who had high systolic blood pressure were having raised malondialdehyde levels. This is in good agreement with the reports of Uotila J.T.[13] who in his report stated an increase in malondialdehyde levels in pre-eclampsia/eclampsia patients when compared with normal pregnant patients. His report stated that lipid peroxidation is a causative factor in pregnancy induced hypertension. Studies of MDA levels showed high correlation to the level of blood pressure, and increased lipid peroxidation may be involved in vasoconstriction in pre-eclampsia[14]. The increased lipid peroxides considering their aggressive nature formed at one point during development of altered homeostasis could contribute to further disruption.

In this study serum uric acid level is seen to be increasing in the pre eclampsia & eclampsia group which is in good correlation with the study of de Jong C L[15]. Here increase in serum uric acid in pre eclampsia & eclampsia is probably a compensatory mechanism due to increased peroxide load in pre eclampsia as lipid peroxidation continues to override the compensatory effects of anti-oxidants like uric acid. An ultimate manifestation of this sequence would be raised blood pressure.

Conclusion

The two groups were similar in the parameters like age, gestational age at blood sampling, and gestational age at delivery. Systolic and diastolic blood pressure, mean arterial blood pressure, Urinary Protein, and serum uric acid and malondialdehyde levels were higher in eclampsia group than pre-eclampsia group. Mean birth weight was less in eclampsia group than pre-eclampsia group. All these values were also higher compared to the control group.

References

1. Carl. A Hubel Ph. D, James H. Roberts. Lipid peroxidation in pregnancy new perspectives on Pre-eclampsia. Am J Obstet Gynaecol.1989; 161:1025-34.
2. Volhard F. Concept of vasospasm, Williams Text Book of Obst. Gynecology 18th edn. 1918.
3. Hinselmann H. Hypertensive disorders in Pregnancy, Norwalk Conn, Williams Text Book of Obst. Gynecology, 18th edition. US: Appleton & Lange;1989.p.689-705.
4. Brunner H.R, Gavras M. Vascular damage in hypertension. Hosp pract. Norwalk Conn, Williams Text Book of Obst. Gynecology, 18th edition. 1975. p.10-97.
5. Valerian E Kagan. Lipid peroxidation in biomembranes. Valerian E Kagan, Quinn P J, editors. 1st edition. Florida: CRC Press; 1988.p.13-146.
6. Tien M, Aust S.D. Comparative aspects of several model lipid peroxidation systems. In Yagi K ed: Lipid peroxides in biology and Medicine. New York: Academic Press; 1982.p. 23-39.
7. Chance B, Sies H, Boveris A. Hydroperoxide metabolism in Mammalian Organs. Physiol Rev 1979;59:527-605.
8. Harold Varley. Method of Caraway for estimation of serum uric acid. Practical clinical biochemistry, 4th edn. CBS Publisher; 1988.p.205.
9. Mahfouz M. O., Hariprasad I. A., Shaffe, Sadasivudu B. Serum MDA levels in myocardial infarction and chronic renal failure. IRCS Med. Sci. 1986;14:1110–1111.
10. Beke. A, Rigo. J Jr. Effect of preeclampsia on neonatal morbidity. Orvosi Hetilap 1995 Sep 10;136(37):1999-2003.
11. Perloff D. Hypertension and pregnancy related hypertension. Cardiology Clinics 1998;Feb 16(1):79-101.
12. Cooper D.W, Hill J.A, Chesley L.C, Bryams C. Genetic control of susceptibility to eclampsia and miscarriage. Br. J. Obstet Gynaecol 1998;95:644-53.
13. Uotila J T, Tuimala R.J. Findings on lipid peroxidation and antioxidant function in hypertensive complications of pregnancy. Br J Obstet gynaecol 1993;100(3):270-6.
14. Kharb S, Gulati N, Singh V, Singh GP. Lipid peroxidation and vitamin E levels in preeclampsia. Gynecol Obstet Invest 1998;46(4):238–240.
15. De Jong CL, Paarlberg KM, van Geijn HP, Schipper EJ, Bast A, Kostense PJ, Dekker GA. et al; Decreased first trimester Uric acid production in future preclamptic patients. Journal of perinatal medicine, 1997;25(4):347-52.