Comparative study of lipid profile & lipid peroxidation in normal pregnant subjects & subjects with pre-eclampsia

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Abstract:

Background: It is the increased responsiveness of the arterial system to pressor substances which probably causes the generalized vasoconstriction and hypertension of pre-eclampsia. In normal human pregnancy, there is decreased blood pressure response to pressor materials, but in pre-eclampsia there is marked increase in response to vasopressin [1] to norepinephrine and to angiotensin.

Objective: To Compare lipid profile & lipid peroxidation in normal pregnant subjects & subjects with pre-eclampsia

Methods: This study has been undertaken to correlate hyperlipidemia with lipid peroxidation with PIH/Eclampsia among 65 women. This study was carried out in the department of Biochemistry and Gynecology and Obstetrics at Osmania Medical College and Hospital Hyderabad.

Results: Pregnancy with pre-eclampsia showed an obvious and significant increase in the mean levels of serum malondialdehyde, serum triglyceride, mean serum levels of cholesterol, mean serum sodium levels when compared to the control group.

Conclusion: Lipid peroxidation as an important factor in pathogenesis of pregnancy induced hypertension is discussed.

Key words: lipid profile, lipid peroxidation, pregnant subjects,

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Introduction

It is the increased responsiveness of the arterial system to press or substances which probably causes the generalized vasoconstriction and hypertension of pre-eclampsia. In normal human pregnancy, there is decreased blood pressure response to press or materials, but in pre-eclampsia there is marked increase in response to vasopressin [1] to norepinephrine and to angiotensin.

Pregnant women develop refractoriness to the pressor effect infused angiotensin II (Abdul Harim and Assali 1961), but in pre-eclampsia there is increased responsiveness of arterial system to pressor substances which causes generalized vasoconstriction and hypertension of pre-eclampsia e.g. Vasopressin (Dieckman and Michael 1937).[1] Gant and co-workers (1973)[2] demonstrated that increased vascular sensitivity to angiotensin II clearly preceded the onset of pregnancy-induced hypertension. Talledo and associates (1968) demonstrated increased vascular reactivity using norepinephrine.

Atrial natriuretic peptide is released, upon atrial wall stretching from the blood volume expansion, it acts upon kidney to promote sodium and water excretion. Report that atrial natriuretic peptide substantively increased in women with pre-eclampsia. As blood volume is substantively decreased in women with pre-eclampsia they concluded that the factors other than volume expansion must play a role in release of this peptide.[3]

With the development of PIH, the capillary narrowing in part and generalized vasoconstriction in part are responsible for the reduction in renal blood flow and GFR. Therefore in milder cases, the plasma creatinine or urea concentration is seldom elevated appreciably above normal non-pregnant values. The plasma uric acid concentration is elevated especially in women with more severe disease, due to decreased renal clearance of uric acid exceeding the reduction in GFR and creatinine clearance[4]. Thiazide diuretics also contribute to increased uric acid.

In some severe cases profound renal involvement, plasma creatinine may be elevated two to three times over non-pregnant normal woman due to intrinsic renal pathology caused by severe vasospasm.[5]Transfield and associates 1987 reported that pre-eclampsia is associated with diminished urinary excretion of calcium as a result of increased tubular reabsorption.

In some way the reduced GFR and the many hormonal changes of pregnancy influencing the renal tubular handling of sodium and water now combine to cause the retention of sodium chloride and water.

Depending on dietary intake this may result in generalized edema. Increased total body stores of sodium always occur in pre-eclampsia according to Chesley.[6] The women with pre-eclampsia can no longer excrete a sodium load expeditiously unlike the women with a normal pregnancy or a pregnancy complicated by essential arteriolar hypertension. Thus the avoidance of high sodium becomes of importance only in presence of pre-eclampsia / eclampsia.

Material and Methods

Selection of subjects: This study has been undertaken to correlate hyperlipidemia with lipid peroxidation with PIH/Eclampsia. This study was carried out in the department of Biochemistry and Gynecology and Obstetrics at Osmania Medical College and Hospital Hyderabad.

Total number of cases was 65. All the women were in the age group of 18 – 30 years and in their third trimester with singleton fetus.

Twenty women had absolute normal pregnancy and forty-five were suffering from pregnancy-induced hypertension: Pre-eclampsia and eclampsia.

Pre-eclampsia was identified as a systolic blood pressure of 140-150 mm Hg and diastolic of 90-100 mm Hg or as increase in 20 mm Hg on two separate occasions and semi-qualitative dipstick testing 3 + or more.

None of the women had received antihypertensive medication until the study samples were taken. The levels of blood pressure and proteinuria were determined at the time of the sampling. The mean arterial pressure was defined as diastolic blood pressure + 1/3.

Sample Collection: 10 ml of overnight fasting venous samples were collected in sterile clean and dry bottles. Blood centrifuged, separated and assay performed.

Group – I: Consists of 20 healthy antenatal women between 30 – 36 weeks of gestation selected as control group with normal blood pressure with no pedal edema and no albumin detected in urine.

Group – II: Consists of 15 pregnant women with pre-eclampsia with pedal edema and with albuminuria.

Group – III: Consists of 30 pregnant women with eclampsia.

The following parameters were studied on fasting blood sample estimation

1. Serum malondialdehyde
2. Lipid profile – Triglycerides
   Cholesterol
   HDL
   LDL
3. Serum creatinine
4. Total proteins
5. Serum uric acid
6. Electrolytes : Sodium
   Potassium

Results

Table 1: Comparison of various parameters among the two groups

Criteria	Group I	Group II
Malondialdehyde	306.00	333.06
Serum triglycerides	25500 mg/dl	26307 mg/dl
Serum cholesterol	274 mg/dl	281.8 mg/dl
Serum HDL	45 mg/dl	42.17 mg/dl
LDL	185 mg/dl	186 mg/dl
Serum Sodium	145 mEq/L	146.5 mEq/L
Serum creatinine	2.32 mg%	2.63 mg%

Pregnancy with pre-eclampsia showed an obvious and significant increase in the mean levels of serum malondialdehyde (SD $\pm$ 25.8) P=<0.001.

Showed a statistically significant increase in the mean serum triglyceride levels (SD $\pm$ 32.7, P value=<.001) when compared to control.

Showed an obvious and statistically significant increase in the mean serum levels of cholesterol when compared to the control group (S.D $\pm$ 20.6; P value = <0.001).

When compared to control groups showed statistically significant increase in the mean serum levels. (S.D $\pm$ 4.7; P value = <0.001).

Comparison between Group – I and control group showed statistically significant values (SD $\pm$ 28; P = 0 001). Showed a slight increase in the mean serum sodium levels when compared to the control group the increase being statistically significant (S.D $\pm$ 4.2; P value <0.001). Comparison between Group –I and control group showed an increase in the mean serum values.

Discussion

The following elaboration of the hypothesis serves to illustrate a potential avenue by which lipid peroxidation could contribute to development of Pre-eclampsia. The primary defect in pre-eclampsia involves reduced uteroplacental perfusion. In normal pregnancy the diameter of spinal arteries feeding their intervillous space increases greatly and they become refractory to vasomotor agent.[7] In pre-eclampsia such adaptions are limited to the decidual portions of the arteries such that the myometrial portions retain their contractility.[8] The reason for this maladaptation is due to superficial implantation or abnormal immunologic reactions between uterine trophoblastic tissue. The resulting physical constriction presumably produces a region of increased vascular resistance. The placental maldaptations have been correlated with increased incidence of placental infarction fetal distress, fetal growth retardation that often accompany pre-eclampsia

suggesting that placental perfusion is a crucial factor in pregnancy outcome.[7]

There are increased lipid peroxide levels due to placental oxidant, antioxidant imbalance, and altered homeostasis. These are circulated in the form of lipo protein bound peroxides. Circulating peroxides come in contact with endothelial cell membrane lipids and reduces the ability of the endothelium to act as a permeability barrier to plasma components, lysosomalenzymes, thromboxane platelet derived growth factor and serotonin released from aggregating platelets in response to endothelial injury would promote vasoconstriction and further endothelial damage. Superoxide anion produced either during platelet aggregation or during reductive degradation of lipid peroxides couldinactivate endothelium derived relaxing factor and thus further impede the vasorelaxant influence of the endothelium.[9] Exposure of the vascular endothelium to lipid peroxides would begin to shut off production of prostacyclin, increasing the propensity of vasoconstriction and platelet aggregation. A Significant drop in local vascular concentration of prostacyclin and endothelium derived relaxing factor could contribute to the pre-eclamptic rise in peripheral resistance and sensitivity to endogenous vasopressor agonist. Constriction of the placental vasculature would decrease placental perfusion further, promoting damage that would increase output of lipid peroxides from the organ. A serious impact of lipid peroxidation is the increased consumption of oxygen in the course of lipid peroxidative reactions. This can critically deplete the cellular oxygen supply when availability of oxygen is limited.[9]

In pre-eclampsia the normal control mechanisms for lipid peroxidation may not function adequately or the capacity of the antioxidative system may be overfilled despite the increased antioxidative response. [10] The antioxidant role of uric acid has been mentioned. Raised serum uric acid is not merely a non-specific reflection of kidney damage but a sign of antioxidative response related to the pathogenesis of pre-eclampsia. The data showing diminished uric acid production in patients in first trimester, later increase in 2nd and 3rd trimesters suggested impaired anti-oxidant production. This finding is in good correlation with authors Delong. C.L. Parlberg K. M et. al.[11] In this study there is increase in serum uric acid in pre-eclampsia/ eclampsia. The rise in antioxidants is probably of compensatory nature responding to increased peroxide load in pre-eclampsia. As lipid peroxidation continues to override the counter active capacity of blood antioxidants an ultimate manifestation of this model sequence would be elevated blood pressure.

In normal pregnancy an increase in malondialdehyde levels was associated with increase in total serum lipids, indicating that the ratio of lipid peroxide to total lipid had not changed.[1] placental tissue is a major source of lipid peroxide products in pregnancy. Free radical mediated Lipid peroxidation in human placental tissue microsomes increases as a function of gestational age when fixed concentrations of peroxidation catalysts (reduced nicotinamide adenine dinucleotide, adenosine diphosphate, and ferric chloride) are provided. This had led to speculation that lipid peroxide accumulation invivo occurs with advancing gestation, reaching a Zenith in term placentas. 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 (Carl A. Hubel).[1]

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 will 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. In placental tissue peroxidation was neither stimulated by arachidonate nor inhibited by prostaglandin inhibitors (Carl A. Hubel) [1] the investigators concluded that lipid peroxidation in placenta reflected non-specific unsaturated lipid peroxidation as opposed to prostaglandin endoperoxide generation. High availability of unsaturated lipid contributes to a predisposition of enhanced lipid peroxidation (Yagi et al).[6] Human placental tissue found to produce high amounts of triglyceride. Placentas from women with pre eclampsia have a significantly increased triglyceride content reflecting that placental tissue found to produce high amounts of triglyceride. Placentas from women with pre eclampsia have a significantly increased triglyceride content reflecting that placenta is diseased in this disorder. The human placenta contains a high degree of intrinsic lipooxygenase activity promoting speculation that aberrant lipooxygenase activities leading to increased production of archidonic acid peroxidation products may contribute to complications of pre-eclampsia. Recently Andrzei Ledwozw found that lipid peroxides inhibits lipoprotein lipase activity and there by plasma. Triglyceride hydrolysis. In our study there is an increase in malonaldehyde 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. 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 U.T. Uotila who in his report stated an increase in malondialdehyde levels in pre-eclampsia/eclampsia patients when compared with normal pregnant patients. Carl A Hubel[1] in his report stated that lipid peroxidation as a causative factor in pregnancy induced hypertension. Kharb. S; GulabNetal in their report stated MDA showed high correlation to the level of blood pressure. Serum cholesterol and Triglycerides were increased in normotensives and still higher in pre-eclamptic women. Their study supports the view that increased lipid peroxidation may be involved in vasoconstriction in pre-eclampsia. The increased lipid peroxides considering their aggressive nature formed at one point during development of altered homeostatis could contribute to further disruption.

Conclusion

Concentrations of plasma triglycerides, cholesterol, total lipids and lipid peroxide and serum uric acid, total proteins, sodium and potassium in patients with pregnancy induced hypertension who were divided into groups control, pre-eclampsia and eclampsia groups, were estimated. Statistically significant increases of the estimated compounds were found in all groups in comparison with the controls.

The existence of positive correlation between the lipid profile and lipid peroxidation products and the systolic blood pressure was found.

There was also positive correlation between the level of blood pressure, MDA level to the fetal outcome and maternal outcome.

Lipid peroxidation as an important factor in pathogenesis of pregnancy induced hypertension is discussed. If future work confirms an etiological role for lipid peroxidation in pre-eclampsia antioxidant therapy, perhaps in combination with dietary omega – 3 fatty acids might be of value in shifting thromboxane – Prostacyclin balance towards a less thrombogenic state and preserving the overall integrity of the vascular endothelium.

Conflict of Interest: None

Source of Support: Nil

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