International Journal of Medical and Health Research
ISSN: 2454-9142
www.medicalsciencejournal.com
Volume 4; Issue 3; March 2018; Page No. 162-165

Studies of serum lipoprotein (a) and lipid profile in preeclampsia patients

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Abstract
Background: Preeclampsia is one of the most important gestational disorders that lead to both maternal and fetal bad outcomes. It is a hypertensive disorder of pregnancy characterized by endothelial dysfunction.
Objective: The objective of this study is to determine the lipid profile pattern among patients with pre-eclampsia. The present study was planned to determined the Lipoprotein (a), serum total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein cholesterol in pre-eclamptic and normal pregnant women. Method: In this present study, serum samples were collected from 30 pregnant females diagnosed as pre-eclampsia and 20 normal pregnant females. Serum levels of lipoprotein (a) [Lp (a)], total cholesterol (TC), triglyceride(TG), high density lipoprotein (HDL) and low density lipoprotein(LDL) and very low density lipoprotein (VLDL) in pre-eclamptic and normal pregnant women were determined.
Results: A significant difference in Lp (a) and lipid profile parameters was observed in preeclamptic patients. Lipoprotein (a) triglyceride and VLDL were significantly increased while HDL was significantly decreased in preeclamptic group compared to normal pregnant women. Positive correlation was found between serum Lp (a) and blood pressure in preeclampsia patients.
Conclusion: The study suggested that lipoprotein (a) [Lp (a)], total cholesterol (TC), triglyceride (TG), high density lipoprotein(HDL) and low density lipoprotein (LDL),and very low density lipoprotein (VLDL) should be considered as important determent risk factors in pre-eclampsia and the obtained data may help in developing strategies for prevention and early diagnosis of the disorder.

Keywords: lipoprotein (a), pre-eclampsia, lipid profile

Introduction

Pre-eclampsia is characterized by hypertension, proteinuria and edema. It usually occurs in the later part of the second trimester and in the third trimester, but can occur in the early part of pregnancy (Tariq *et al.*, 2000: Mikio and Nihiri, 2010) [24, 15]. Eclampsia, in addition to features of preeclampsia, is characterized by epileptiform convulsions (Packer, 2005) [18]. It is usually a sequel to preeclampsia in untreated cases (Lawrence and Amadeo, 1984) [11]. Pre-eclampsia and eclampsia are the most common complications of pregnancy (Tariq *et al.*, 2000) [24] and are said to be the most common cause of fetal and maternal morbidity and mortality worldwide (Solomon and Seely, 2004; Magnussen *et al.*, 2007; Rubina and Tabassum, 2007) [4, 13, 20]. A study carried out in 2009 (Mairiga and Saleh, 2009) [14], among pregnant women study showed that the direct obstetric causes of maternal death accounted for 79.4% and eclampsia accounted for 31.9%. Development of pre-eclampsia/eclampsia is greater in women with family history of essential hypertension and currently metabolic syndrome has also been implicated.

Pre-eclampsia is a type of hypertensive disorder complicating pregnancy and contributes significantly to maternal and perinatal morbidity and mortality (Adegoke *et al.*, 2003) [1]. Pre-eclampsia occurs in 7-10% of pregnancies worldwide (MutluTurkoglu and Ademoglu 1998) [17]. A Ministry of Health maternal deaths' study in 2009 found that the leading direct causes of pregnancy-related deaths in Iraq are haemorrhage (33%), thromboembolism (25%), pre-eclampsia/eclampsia (9%), maternal sepsis (5%) and obstructed labour (4%), One in four delivering women in Iraq faces serious complications during pregnancy and child birth. The government of Iraq has shown a high level of commitment to accelerating the implementation of a cost-effective and evidence-based package of interventions along the continuum of care in full collaboration with partners (WHO, 2013) [26]. Pre-eclampsia affects virtually all maternal organ systems. Early pregnancy dyslipidemia is associated with an increased risk of pre-eclampsia (Enquobahrie, 2004: Caren, 2004) [6, 4]. Women with a history of pre-eclampsia have significant differences in lipid parameters and an increased susceptibility to lipoprotein oxidation when comparedwith women who had normal pregnancy. Disorders of lipoprotein metabolism are reported to be a major cause of hypertension and proteinuria in preeclampsia (Gractacose *et al.*, 2003) [9].

From the above literature survey, it is postulated that alteration of lipid metabolism may play a key role in the development of symptoms of pre-eclampsia. The result of this investigation will serve as baseline information for the society and could help in developing strategies for the prevention or early detection of dyslipidemia in preeclampsia in Iraq. The objective of this study is to assess the lipid profile pattern among patients with pre-eclampsia. The present study was planned to determined Serum Lipoprotein (a), serum total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein cholesterol in pre-eclamptic and normal pregnant women.

Materials and Method

In the present Study, 30 pregnant women were selected as cases after confirmed diagnosis of preeclampsia and 20 normal healthy pregnant women as controls. Evaluated the level of serum lipid profile in pre-eclamptic patients and normal pregnant women (controls) admitted in the Obstetric Hospital in Karbala. It was done in the Department of Biochemistry, College of medicine Karbala University in collaboration with the Department of Obstetrics and Gynaecology, Iraq between June 2017 to December 2017. Preeclampsia was diagnosed according to the criteria proposed by Vibha *et al.,* 2011 [25], i.e. systolic blood pressure ≥ 140 mmHg or a rise of 30 mmHg and diastolic blood pressure ≥ 90 mmHg or a rise of 15 mmHg (manifested on two occasion 6 hrs apart) & proteinuria ≥ 300 mg in 24 hour urine samples (manifested on two occasion 6 hrs apart). The cases and controls were matched for maternal age, gestational age and body mass index (BMI). Preeclampsia is of two degree :(9) Mild - diastolic BP < 110 mmHg and Severe - diastolic BP > 110 mmHg. Twenty pregnant women were selected as pre-eclamptic cases. Another 10 normal pregnant women of similar age group and gestational age were also taken as controls. 5 ml of fasting venous blood was drawn from anterior cubital vein and analysed for serum lipids. Enzymatic Colorimetric Test with lipid clearing factor (LCF) was used to determine Serum lipid profile. The total cholesterol was determined by the enzymatic CHOD PAP method of Allain CC *et al.,* 1974. Triglyceride determination carried out by the method adopted by Bucolo G and Harold D. 1973. Estimation of HDL cholesterol done by precipitation technique described by Steele BW *et al.*1976 [23]. Calculation of the LDL and VLDL cholesterol concentrations was done indirectly by using the formulae of Friedwald T *et al.*, 1972 [8]. General physical examinations and systemic examinations with special reference to oedema and blood pressure were carried out. Levels of Lp (a) were determined by immunoturbidometric assay method (Vibha *et al.,* 2011) [25].

Statistical Analysis

The results were analyzed by Graphpad prism software, version 5. The data were expressed as mean ± standard deviation (SD). Differences in demographic characteristics and biochemical parameters were statistically analyzed using one way ANOVA test. Pearson's correlation was used to study the correlation among the parameters (r value). P value < 0.05 was considered statistically significant.

Results and Discussion

The results of the present study of lipid alterations in pregnant patients who developed pre-eclampsia compared with the pregnant women with no pre-eclampsia. In these studies, significantly higher concentrations of serum triglycerides in pre-eclamptic were find out than in the normal pregnant women was find out which is in good agreement with previous larger

Table1: Serum lipoprotein (a) and lipid profile in preeclampsia patients

Sr. No	Biochemical parameters	Normal Pregnancy	Severe Pre-eclampsia	'P' value
1.	Lp (a) (mg %)	19.34 ± 4.67	65.47 ± 3.99	< 0.001*
2.	TG (mg %)	121.10 ± 11.34	241.56 ± 15.57	< 0.001*
3.	VLDL (mg %)	23.54 ± 3.22	52.63 ± 7.41	< 0.001*
4.	TC (mg %)	165.34 ± 12.23	172 ± 11.33	> 0.4
5.	HDL (mg %)	47.2 ± 6.87	38.12 ± 4.14	< 0.05*
6.	LDL (mg %)	118.32 ± 13.44	128.36 ± 13.42	> 0.1

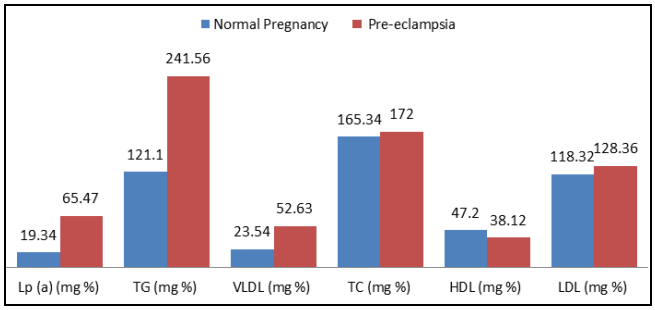

Fig 1: Serum lipoprotein (a) and lipid profile in preeclampsia patients

Pre-eclampsia is a multisystemic, pregnancy specific disorder that is diagnosed by new-onset hypertension and proteinuria after 20 weeks gestation (Korravaran Yodmai, 2007) [10]. It is a common obstetric complication that leads to maternal and perinatal morbidity and mortality in both developed and developing countries (Sibai, 2005) [21].

The results of this study present that there are certain risk factors significantly associated and augment the incidence of pre-eclampsia in pregnant women whereas there are other factors insignificantly associated with preeclampsia incidence. In developing countries where access to healthcare is limited, it is responsible for about 60,000 maternal deaths worldwide per year (Lima, 2011) [12]. Endothelial dysfunction has been reported as an important biologic feature in women with preeclampsia (Ekambaram, 2011) [5]

The preeclamptic patients in our study showed dyslipidemia, characterized by high levels of TG and VLDL and decreased HDL. In preeclampsia, there is increase in hepatic lipase and decrease in lipoprotein lipase activities, resulting in increased serum TG and VLDL levels (Phalak *et al.,* 2012) [19]. High triglyceride levels increase the risk of placental vascular disorders, which trigger endothelial dysfunction, atherosclerosis and thrombosis. The development of atherosclerosis in the placental spiral arteries of preeclamptic women indicates that dyslipidemia is involved in this disorder. This also indicates that a common pathophysiological mechanism is operative between the endothelial lesions of preeclampsia and atherosclerosis (Lima, 2011) [12].

In this study, preeclamptic pregnant female have been found

to have highly significantly (P\0.001) deceased levels of HDL cholesterol than the normal pregnant females & the nonpregnant females. Its level started increasing postpartum. This is in consistency with the results of several other studies. In a study of portuguese women, subjects with preeclampsia had a lower HDL cholesterol level compared with healthy pregnant women. Another study conducted at Turkey showed significantly lower HDL-cholesterol levels in preeclamptic females than in normal pregnant women. Preeclampsia is a complex pathophysiological state where regulatory systems of inflammation and endothelial function are stimulated beyond the physiological limits of normal pregnancy. There is increasing evidence that lipids may play an important role in the modifications of the endothelial structure and function.

The concentration of total cholesterol, LDL, VLDL & Triglycerides was found to be significantly increased in preeclamptic females as compared to normal pregnant females & the non-pregnant females. All of these again started to fall postpartum. Elevated triglyceride values may compromise vascular function in several ways. For example, triglyceride rich lipoprotein has a prothrombotic activity. Elevated triglycerides might shift the pattern of LDL subclass towards disproportionate increase in smaller denser, more allergenic LDL particles.

To reduce the healthcare burden associated with preeclampsia and to implement preventive measures, early disease diagnosis is very important. Dyslipidemia and raised blood pressure before conception are the predisposing factors for this disorder. Such women should be motivated for regular health check-up by their obstetrician. (Musleh *et al.*, 2012) [16] Better understanding of abnormal lipoprotein pattern in preeclampsia and its association with endothelial dysfunction is crucial from a public health perspective. (Lima, 2011) [12]

From results of our study, we can hypothesize that preeclamptic lesions may predispose these women to adverse cardiovascular complications later on in their life. Elevated levels of serum Lp (a) has atherogenic potential and may result in adverse cardiovascular outcome. Further studies are needed to establish its usefulness in assessing future cardiovascular risk in preeclampsia patients. These women should be counseled regarding possible health hazards and motivated to adopt healthy lifestyles and to seek periodic checkups, in order to detect cardiovascular disease in its early stages, before irreparable damage or even death ensues.

Conclusion

The study shows that women who develop pre-eclampsia had disturbed lipid profile due to abnormal lipid metabolism. Increased triglycerides levels and delayed triglycerides clearance and high blood pressure are the reasons for the development of pre-eclampsia. This association may be significant in understanding the pathological process of preeclampsia and may help in developing strategies for prevention and early diagnosis of preeclampsia. However, elevated serum triglycerides might be involved in the endothelial damage leading to pre‑eclampsia. Moreover, raised serum triglycerides may have value to be used as screening markers in early stages of pregnancy for the development of pre‑eclampsia later.

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