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Study Of Serum Lactate Dehydrogenase, Lipid Profile And Serum Magnesium As The Best Predictor For Severity Of Pre-Eclampsia.

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ABSTRACT

Pregnancy causes profound anatomical, physiological, and metabolic changes in maternal tissues. One of the commonest and most dreaded complication is hypertension (preeclampsia (PE)/gestational hypertension (GHTN) which can further complicate into eclampsia (E). Globally, one woman dies every 7 min due to hypertensive disorders of pregnancy (HDOP). Pre-eclampsia complicate 8-10% of all pregnancies. It is the major cause of maternal & perinatal mortality. This is a multisystem disorder & leads to a lot of cellular death. Lactate dehydrogenase (LDH) is an intracellular cytoplasmic enzyme. Cellular enzymes in extracellular space have no metabolic function, although they serve as indicators of disturbances in cellular integrity. Serum Lactate dehydrogenase level is increased in these women due to cellular death. Recent investigations suggest that magnesium deficiency could play an important role in the pathogenesis of preeclampsia, particularly in regulating the tonus of arterioles and veins. The association of altered lipid profile in essential hypertension is well documented. Several studies have shown that endothelial dysfunction is related to hyperlipidaemia. To estimate and compare the serum LDH levels, serum magnesium and lipid profile in normal pregnant women and women with pre-eclampsia and correlating the values of serum LDH levels, serum magnesium and lipid profile as a predictor of severity of pre-eclampsia. 50 pre-eclamptic women (30 with mild & 20 with severe pre-eclampsia) as cases and 50 healthy normotensive pregnant women were taken and serum Lactate dehydrogenase were measured by Method of Henry in fully autoanalyzer. And serum magnesium levels and lipid profile were measured in fully autoanalyzer. Serum Lactate dehydrogenase levels were significantly ($p<0.001$) elevated in mild preeclampsia (530.8 +/- 44.09U/L) & severe preeclampsia (768 +/- 58.16U/l) than in normotensive control subjects (305.38 +/- 45.3 U/L). Mean cholesterol levels were (216.3mg/dl ±30.4 in severe & 170.3mg/dl±32.8 in mild versus 110.6mg/dl±18.6 in control) statistically significantly higher in preeclamptic as compared to normal controls ($p<0.001$). Mean triglycerides levels were (183.4mg/dl±41.3in severe & 118.3mg/dl±29.8 in mild versus 87.3mg/dl±12.4in control) statistically significantly higher in preeclamptic as compared to normal controls ($p<0.001$). Mean HDL-C levels were (38mg/dl±4.7in severe & 43.8mg/dl±4.03in mild versus 51.2mg/dl±6.9in control) statistically significantly lower in preeclamptic as compared to normal controls ($p<0.001$). Mean serum magnesium levels were significantly reduced in women with pre-eclampsia (0.17mg/dl±0.07in severe & 0.62mg/dl±0.29in mild) as compared to normal controls (1.6mg/dl±0.4) ($p<0.001$). From this study we conclude that the assessment of Serum Lactate dehydrogenase, serum magnesium and lipid profile are very useful biochemical markers that reflects the severity of pre-eclampsia to identify the occurrence of the complications of pre-eclampsia in early pregnancy, which may reduce the risk of occurrence of disease.
Keywords: serum Lactate dehydrogenase, Pre-eclampsia, pregnant women, Magnesium, Lipid profile.

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INTRODUCTION

Pregnancy is a crucial period for both mother and foetus. Around 15% of pregnant women are expected to suffer from life-threatening complications either during pregnancy, at delivery or in post-partum period [1]. It is estimated that upto 30% of perinatal deaths are related to hypertensive disorders of pregnancy [2]. Preeclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm, which occurs after gestational age of 20 weeks and can present as late as 4-6 weeks postpartum. Preeclampsia is defined as a blood pressure of at least 140/90 mmHg measured on two occasions each 6 h apart, accompanied by proteinuria of at least 300 mg per 24 h, or at least 1+ on dipstick testing. It is clinically defined by hypertension and proteinuria, with or without pathological edema [3, 4]. This is a multisystem disorder & leads to a lot of cellular death.

Lactate dehydrogenase (LDH) is an intracellular enzyme which converts pyruvic acid to lactic acid during the process of glycolysis. Glycolysis is the major energy pathway of carbohydrate metabolism in the placenta. Hypoxia in pre-eclampsia further induces glycolysis and increases LDH activity. Studies have shown that LDH activity & gene expression are higher in placentas of pre-eclampsia than normal pregnancy [5-7]. Hypoxia induces LDH isoenzyme activity in trophoblasts resulting in increase lactic acid production. Elevated levels of LDH are indicative of the cellular damage and dysfunction, so it can be used as a biochemical marker because it reflects the severity of the disease & occurrence of complications.

The association of alteration of serum lipid profile in preeclampsia is well documented. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction. The most important feature in preeclampsia is hypertension which is supposed to be due to vasospastic phenomenon in kidney, uterus, placenta and brain [8]. Altered lipid synthesis leading to decrease in PGI2:TXA2 ratio is also supposed to be an important way of pathogenesis in pregnancy induced hypertension [9]. Thus abnormal lipid metabolism seems important in the pathogenesis of preeclampsia. Pre-eclampsia 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 [9]. Significantly elevated plasma concentration of triglycerides (TG), total cholesterol and decreased high density lipoprotein – cholesterol (HDL-C) concentrations were found in women with pre-eclampsia in comparison to normal pregnancy [10, 11]. In this context, the present study has been undertaken to compare the changes in lipid profile in normal pregnancy and preeclampsia.

Preeclampsia in developing countries has been found to have a great impact because the diet of pregnant mothers are not rich enough with essential minerals and vitamins [12]. Inadequate dietary intake is harmful for the mother and the growing fetus. Magnesium is one of the essential intracellular cations and an important cofactor for activation of many enzymes. Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity. Magnesium causes vascular muscle relaxation [13, 14]. Recent investigations suggest that magnesium deficiency could play an important role in the pathogenesis of preeclampsia, particularly in regulating the tonus of arterioles and veins (Seelig et al) [15].

The aim of the study was To estimate and compare the serum LDH levels, serum magnesium and lipid profile in healthy normotensive pregnant women and women with pre-eclampsia and correlating the values of serum LDH levels, serum magnesium and lipid profile as a predictor of severity of pre-eclampsia.

METHODS AND MATERIALS

A total of 50 pregnant women with pre-eclampsia & 50 healthy pregnant women were studied prospectively at Thanjavur medical college.

Pregnant women were divided into the following groups:

- Group 1 (n=50) - Healthy normotensive pregnant women;
- Group 2 (n=30) - Mild Pre-eclampsia → onset of hypertension after 20 wks of gestation with diastolic BP >90 or ≤ 110mmHg with or without proteinuria;
- Group 3 (n=20)- Severe Pre-eclampsia→ Diastolic BP >110mmHg on two occasions 6hrs apart with significant proteinuria (>500mg/24hrs).

Exclusion criteria

The cases with hypertension which were excluded from the study were those with

- Coincidental hypertension in pregnancy. Essential hypertension as suggested by: (i) history or documentation of hypertension in the pre-pregnant state; (ii) hypertensive present before 20 weeks of gestation.
- Renal diseases.
- Coincidental seizures in pregnancy.

History or documentation of epilepsy in pre-pregnant state. II. Space occupying lesion in brain like tuberculoma, or brain tumor. III. Trauma to brain IV. Hyperpyrexia.

Serum LDH level measured using Method of Henry by auto analyzer. Lipid profile was determined by enzymatic colorimetric method. Serum magnesium was measured by the colorimetric method and use of Xylitol Blue by an auto-analyzer Mean and standard deviation were calculated for preeclamptic and control groups. Descriptive statistics were calculated and data was presented as mean & standard deviation. Systolic BP, Diastolic BP, serum LDH levels , lipid levels & serum magnesium levels between preeclamptic and control group were analysed using independent student *t*-test and *p*-value <0.05 was considered statistically significant.

RESULTS

In control group, all had LDH levels of <400 IU/L, the mean value of LDH being 305±45.31 IU/L. Most of the patients with mild pre-eclampsia group had LDH levels <600 IU/L, the mean LDH calculated as 530.8±44.09 IU/L. And severe pre-eclampsia group had LDH level > 600 IU/L, the mean LDH were 768.0±58.16 IU/L. It was found that High systolic & high diastolic BP was associated with high levels of LDH. On analyzing the above data it is clearly observed that there is significant rise in LDH levels with increasing severity of disease (P<0.001) (Table 1).

In mild & severe preeclamptic mean systolic BP were 141±6.3 mm Hg &159±7.9mm Hg, in controls mean systolic BP was 114.2±6.4 mm Hg. In severe preeclamptic mean diastolic BP were 97±4.7mm Hg, in controls mean diastolic BP was 72.2±6.8 mm Hg. Mean Systolic and diastolic BP were statistically significantly higher in preeclamptic as compared to controls (*p*<0.001). (figure2). Mean cholesterol levels were 216.3mg/dl ±30.4 in severe & 170.3mg/dl±32.8 in mild versus 110.6mg/dl ± 18.6 in control, statistically significantly higher in preeclamptic as compared to normal controls (*p*<0.001). Mean triglycerides levels were 183.4mg/dl±41.3in severe & 118.3mg/dl±29.8 in mild versus 87.3mg/dl±12.4in control, statistically significantly higher in preeclamptic as compared to normal controls (*p*<0.001). Mean HDL-C levels were (38mg/dl±4.7in severe & 43.8mg/dl±4.03in mild versus 51.2mg/dl±6.9in control) statistically significantly lower in preeclamptic as compared to normal controls (*p*<0.001). Mean serum magnesium levels were significantly reduced in women with pre-eclampsia (0.17mg/dl±0.07in severe & 0.62mg/dl±0.29in mild) as compared to normal controls (1.6mg/dl±0.4) (p<0.001) (Table 2 and 3).

Table 1: Comparison Of Serum LDH In Normal And Pre-Eclamptic Pregnant Women

GROUPS	LDH LEVEL MEAN ± SD	RANGE	P
Control (n=50)	305.38±45.31	230-397	<0.001
Mild pre-eclampsia (n=30)	530.8±44.09	452-592	
Severe pre-eclampsia (n=20)	768.0±58.16	648-893	

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Table 2: Comparison Of Serum LDH, Lipids Profile & Magnesium In Normal And Mild Pre-Eclamptic Pregnant Women

GROUPS	CONTROL	MILD PRE-ECLAMPSIA	P VALUE
SYS BP mm/Hg	114.2±6.4	141±6.3	<0.001
DIA BP mm/Hg	72.2±6.8	90	<0.001
LDH IU/L	305.4±45.3	530.8±44.1	<0.001
CHO mg/dl	110.6±18.6	170.3±32.8	<0.001
TGL mg/dl	87.3±12.4	118.3±29.8	<0.001
HDL mg/dl	51.2±6.9	43.8±4.03	<0.001
Mg mg/dl	1.6±0.4	0.62±0.29	<0.001

Table 3: Comparison Of Serum LDH, Lipids Profile & Magnesium In Normal And Severe Pre-Eclamptic Pregnant Women

GROUPS	CONTROL	SEVERE PRE-ECLAMPSIA	P VALUE
SYS BP mm/Hg	114.2±6.4	159±7.9	<0.001
DIA BP mm/Hg	72.2±6.8	97±4.7	<0.001
LDH IU/L	305.4±45.3	768±58.2	<0.001
CHO mg/dl	110.6±18.6	216.3±30.4	<0.001
TGL mg/dl	87.3±12.4	183.4±41.3	<0.001
HDL mg/dl	51.2±6.9	38±4.7	<0.001
Mg mg/dl	1.6±0.4	0.17±0.07	<0.001

Figure 1: Comparison Of Serum Ldh In Normal, Mild & Severe Pre-Eclamptic Pregnant Women

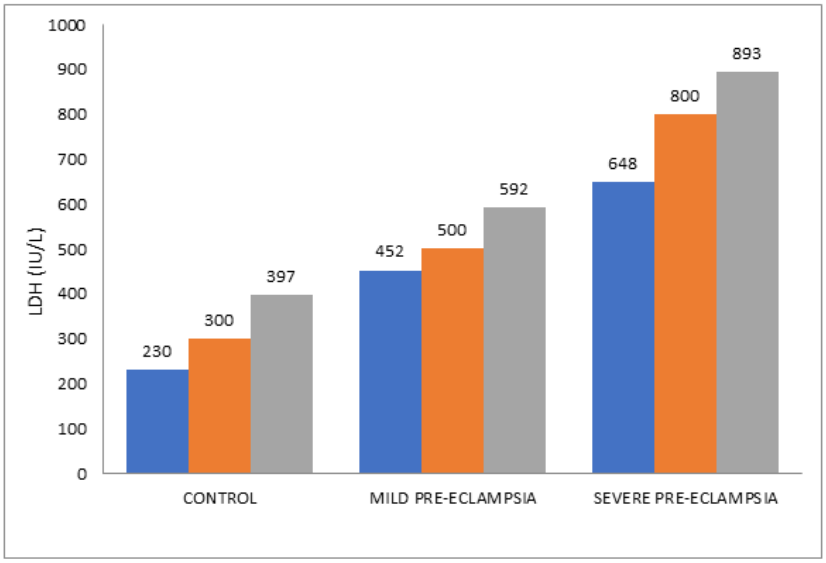

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Figure 2: Comparison Of Serum Ldh And Blood Pressure Between Normal, Mild & Severe Pre-Eclamptic Pregnant Women

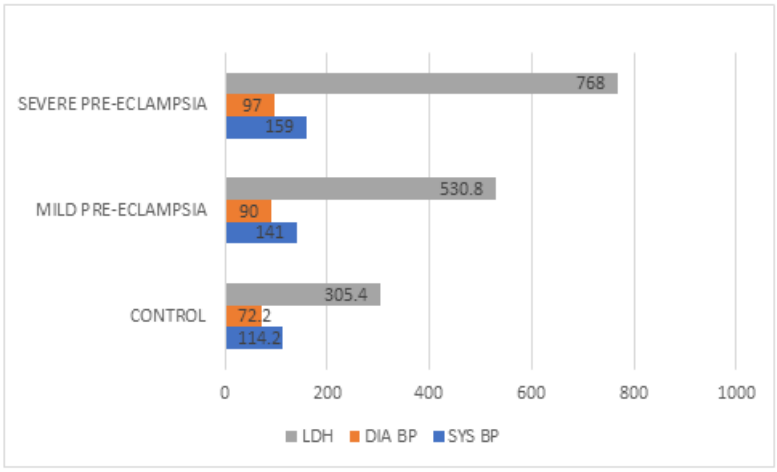


Figure 3: Comparison Of Serum Ldh And Lipid Profile Between Normal, Mild & Severe Pre-Eclamptic Pregnant Women

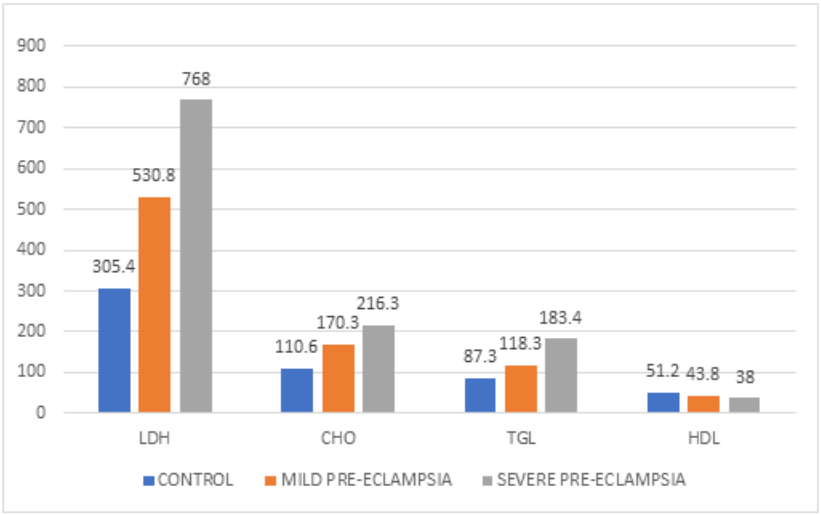
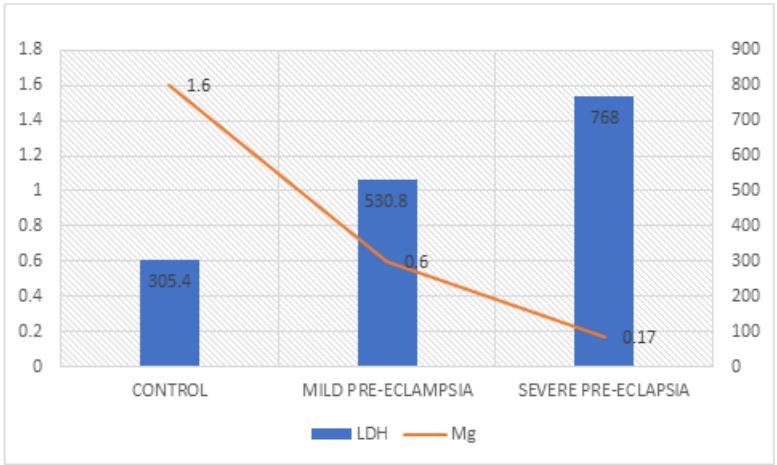


Figure 4: Comparison Of Serum Ldh And Magnesium Between Normal, Mild & Severe Pre-Eclamptic Pregnant Women



DISCUSSION

Pre-eclampsia is a pregnancy condition characterized by hypertension, proteinuria & edema occurring late in the 2nd trimester or early in 3rd trimester. LDH is a hydrogen transfer enzyme that catalyzes oxidation of L-Lactate to pyruvate with NAD+ as a hydrogen acceptor. Elevated levels indicate cellular death & leakage of enzyme from the cell. Vascular endothelial dysfunction has been suggested as central pathogenic cause of pre-eclampsia, that results in various clinical complications associated with pre-eclampsia. The multiorgan dysfunction in severe pre-eclampsia caused by vascular endothelial damage; including maternal liver, kidney, lungs, nervous system, blood& coagulation system will lead to excessive leakage & elevated levels in serum due to cellular dysfunction. As severe pre-eclampsia may lead to numerous multisystem complications, we hypothesize that elevated levels of LDH may reflect the severity of pre-eclampsia (Figure 1,2,3,4).

Pre-eclampsia has well known to be associated with abnormal placentation and impaired placental perfusion. However , other conditions that characterized by poor placentation, such as intrauterine growth retardation ,do not necessarily result in pre-eclampsia [16]. This has lead to the growing concept that maternal predisposing factors must combine with the placental disorder to result in preeclamptic maternal syndrome [17]. During pregnancy, there is an increase in the hepatic lipase activity and decrease in lipoprotein lipase activity [18]. Hepatic lipase is responsible for the increased synthesis of the TGs at the hepatic level, whereas the decreased activity of lipoprotein lipase is responsible for the decreased catabolism at the adipose tissue level, the net effect of which will be an increase in circulating TGs [19]. In this study there was a positive correlation between Preeclampsia and lipid parameters as shown in figure 3. Serum triglyceride concentration rise more significantly in pre-eclampsia in our study. The preeclamptic patients in our study presented significantly higher serum concentrations of triglycerides and cholesterol , lower serum concentrations of HDL-C in preeclamptic women indicating a risk factor as compared to controls (Figure3).

Mineral deficiencies like calcium, magnesium, zinc, etc., have been identified to cause significant health problems for women of reproductive age, especially in developing countries due to inadequate dietary intake. The risk of deficiency becomes increased during pregnancy because of increased need of the growing fetus for various nutrients [20]. Changes in levels of these elements could affect pregnancy. One of the problems that may be influenced by nutrient deficiencies is preeclampsia. Recently, more emphasis has been laid on the relationship between maternal serum level of elements and occurrence of preeclampsia [21, 22]. A study by Seydoux J revealed that serum magnesium decreased with progress in pregnancy [23], but the design and method of our study was different from similar previous studies. This was the first investigation, where serum magnesium level was measured in pre-eclampsia women and was compared with the control group since early on in the pregnancy. The present study showed that serum magnesium level was significantly reduced in pre-eclampsia mothers compared with the healthy control group (Figure4).

CONCLUSION

Pre-eclampsia is a pregnancy-specific disease, and in its severe form, serious multisystem complications may occur. Elevated levels of LDH, indicative of the cellular damage and dysfunction can be used as a biochemical marker because it reflects the severity of the disease. Detection of high-risk patients with increased levels of LDH mandate close monitoring and correct management to decrease both maternal and fetal morbidity and mortality. Preeclamptic women had deranged lipid profile due to abnormal lipid metabolism. Increased triglyceride levels and delayed triglycerides clearance and high blood pressure are the grounds for the development of preeclampsia. This relationship may be significant in understanding the pathological process of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia. According to the results from our research, the level of magnesium should be considered as a predicting factor of preeclampsia during the first evaluation of pregnancy. Thus finally the assessment of serum LDH , lipid profile & serum magnesium levels are very useful markers to identify the occurrence of the complications of pre-eclampsia in early pregnancy, which may reduce the risk of occurrence of disease.

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