

Maternal outcome in Pih Patients in Relation with Serum LDH Levels

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I. Introduction

Pregnancy is a physiological state associated with many alterations in the metabolic, biochemical, physiological, hematological and immunological process. If there are no complications, all these changes are reversible in few days to months after delivery. Hypertension during pregnancy is a major health problem being a leading cause of maternal, fetal & perinatal morbidity and mortality. Fifty percent of women diagnosed with gestational hypertension between 24 and 35 weeks develop preeclampsia (PE). Pre-eclampsia is a multi-system disorder of unknown etiology, unique to pregnancy, with onset after 20 weeks of gestation. Preeclampsia remains poorly characterized with regard to pathophysiology involved in the development of hypertensive disease in pregnancy. It has been described as a two stage disease in which stage I is heralded by poor placental invasion, development, and remodeling. Stage II develops later and involves the clinical recognition of preeclampsia in the form of maternal hypertension, proteinuria, and end-organ disease. Mild preeclampsia occurs in approximately 15% of pregnancies, moderate to severe preeclampsia in around 8% and severe preeclampsia in about 1% to 2%. Preeclampsia is a syndrome, which affects virtually all-maternal organ systems. There is increasing evidence that endothelial cell and altered endothelial cell function play an important role in the pathogenesis of preeclampsia. LDH is most often measured to evaluate the presence of tissue damage. The enzyme LDH is in many body tissues, especially heart, liver, kidney, skeletal muscle, brain, blood cells, and lungs. Dysfunction of endothelial cells can contribute to inappropriate vasoconstriction and platelet aggregation which are early signs of atherosclerosis, hypertension and coronary vasospasm. Acute clinical symptoms that danger fetus life in preeclampsia correlate with distinct activity of AST and LDH.¹ LDH is the earliest marker seen in blood during hypoxia and oxidative stress. It is a useful biochemical marker that reflects the severity of and the occurrence of complications of PE & E.; these are preventable if identified at an early stage and adequately managed. LDH test is easily available, cheap and with good diagnostic & prognostic value. High serum levels of LDH correlate well with the severity of the disease and poor outcomes in PE & E. we conducted this study with the aim to estimate level of LDH in normotensive patients, mild preeclampsia patients, severe preeclampsia patients and to find its correlation with maternal outcome.

II. Materials And Methods

This study was conducted in the Department of Obstetrics and Gynecology, Acharya Vinobha Bhave Rural Hospital (AVBRH) at Sawangi (Meghe), Wardha, Maharashtra, India. Ethical Clearance was taken from the ethical committee of Jawaharlal Nehru Medical College (JNMC), Sawangi, (Meghe), Wardha. Prospective case control comparative study was conducted over total 300 subjects, comprising of 100 with mild preeclampsia, 100 with severe preeclampsia and 100 normotensive pregnant controls.

All eligible pregnant women ≥ 20 weeks of gestation were enrolled in this study and divided into following groups:

- **Group 1**—Healthy normotensive (Normal) pregnant women (**Controls no.=100**)
- **Group-2**—Patients of preeclampsia and eclampsia (**Total no.=200**)
- Group 2 subjects was further subdivided into 2 subgroups -
- **Subgroup 2A**- Mild Preeclampsia (Total no.= 100)
- **Subgroup 2B** - Severe Preeclampsia (Total no.=100)

Refined selection criteria -

- **Sub group 2A- Mild preeclampsia** - Defined as Pregnant female of ≥ 20 weeks of gestation with blood pressure $\geq 140/90$ mm of Hg & $< 160/110$ mm of Hg noted first time during pregnancy on ≥ 2 occasions at least 6 hours apart with proteinuria of $\geq 1+$ (≥ 30 mg/dl) by dipstick method in a random urine sample, would be considered as having mild preeclampsia after excluding urinary tract infection.
- **Sub group 2B- Severe preeclampsia** - Defined as the presence of one of the following symptoms or signs:
- Systolic Blood Pressure of 160 mm Hg or higher or Diastolic Blood Pressure of 110 mm Hg or higher on 2 occasions, at least 6 hours apart, while the patient is resting.
- Proteinuria of 5g or higher in a 24-hour urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart.

- Oliguria of less than 500ml in 24 hours.
- Cerebral or visual disturbances.
- Pulmonary edema or cyanosis.
- Epigastric or right upper quadrant pain.
- Impaired Liver function.
- Thrombocytopenia (platelets <100000/-).
- Intrauterine growth restriction.

Blood samples for serum lactate dehydrogenase levels were collected from preeclamptic cases in plain bulb with aseptic conditions, at the time of diagnosis and before start of treatment. These were analyzed at and by the Department of Pathology and biochemistry Acharya Vinoba Bhave Rural Hospital (AVBRH) at Sawangi (Meghe), Wardha, Maharashtra, with established spectrophotometric pyruvate method, where conversion of pyruvate to lactate takes place in the presence of NADH by the action of lactate dehydrogenase.

III. Observations And Result

Table No 1: Showing Age-Wise Distribution of the Groups (Mild Preeclampsia, Severe Preeclampsia and Controls) (N=300)

Age	Groups			Total
	Mild Preeclampsia	Severe Preeclampsia	Control	
<20 Years	13(4.3%)	13(4.3%)	13(4.3%)	39(13%)
21-30 Years	79(26.3%)	80(26.6%)	83(27.6%)	242(80%)
31-40 Years	7(2.3%)	5(1.6%)	4(1.3%)	16(5.3%)
>40 Years	1(0.3%)	2(0.6%)	0	3(1%)
Total	100	100	100	300

Table No 2: Showing Parity-Wise Distribution Of Patients & Controls (N=300)

Parity	Groups			Total
	Mild Preeclampsia	Severe Preeclampsia	Control	
Primigravida	50(16.6%)	59(19.6%)	58(19.3%)	167(55.6%)
Secondary Gravida	42(14%)	35(11.6%)	35(11.6%)	112(37.3%)
Multigravida	8(2.6%)	6(2%)	7(2.3%)	21(9%)
Total	100	100	100	300

Table no 3: showing distribution of ldh levels in patients and control groups.

LDH	GROUPS			TOTAL
	Mild Preeclampsia	Severe Preeclampsia	Control	
<600 IU	50(16.66%)	5(1.6%)	98(32.66%)	153(51%)
600-800 IU	41(13.6%)	19(6.3%)	1(0.3%)	61(20.3%)
>800 IU	9(3%)	76(25.3%)	1(0.3%)	86(28.6%)
Total	100	100	100	300

Table No 10: Showing Maternal Complications According To Ldh In Severe Preeclampsia Group (N=100)

Complications	<600 Iu	600-800 Iu	>800 Iu	Total	P Value
Dic	1(1%)	1(1%)	0	2(2%)	0.006
Eclampsia	1(1%)	0	4(4%)	5(5%)	
Wound Gape	0	0	4(4%)	4(4%)	
Shock	0	0	2(2%)	2(2%)	
Pph	0	0	2(2%)	2(2%)	
Arf	1(1%)	0	10(10%)	11(11%)	
Hellp	1(1%)	2(2%)	7(7%)	10(10%)	
Abruption	0	0	3(3%)	3(3%)	

IV. Results

In this study out of total 300 patients 39 (13%) patients were in age group of less than 20 years, 242 (80%) patients were in age group between 21-30 years, 16 (5.3%) patients were in age group of 31-40 years and 3 (1%) patients were in age group of more than 40 years. In this study out of total 300 patients 167 (55.6%) patients were primigravida, 112 (37.3%) patients were secondary gravida and 21(9%) patients were multigravida. In this study out of 300, in mild preeclampsia group 50(16.66%) patients had LDH value less than 600 IU, 41(13.6%) patients had LDH value between 600-800 IU and 9 (3%) patients had LDH values of more than 800 IU. In severe preeclampsia group 5 (1.6%) patients had LDH value of less than 600 IU, 19 (6.3%) patients had LDH value between 600-800 IU and 76 (25.3%) patients had LDH value more than 800 IU. In

control group 98 (32.66%) patients had LDH value less than 600 IU, 1(0.3%) patient had LDH value between 600-800 IU and 1(0.3%) patient had LDH value of more than 800 IU.

In the present study, in the group of severe preeclampsia 2%(2) patient went into DIC with LDH levels being >600, 600-800 IU respectively, 5% (5) patient developed eclampsia out of which 1 %(1) had LDH level less than 600 IU and 4 %(4) had LDH levels more than 800 IU.4%(4) of patient developed wound gape all of them had LDH levels more than 800 IU. 2 % (2) of patient went into shock LDH level in these patient were >800 IU. 2% (2) patient went into post partumhaemorrhage LDH levels for these patients were observed as more than 800 IU. 11% (11) patient developed acute renal failure 1 % (1) of patient had LDH level less than 600 IU, 10 %(10) of patient developed acute renal failure had LDH level more than 800 IU. 10% (10)of patient developed HELLP 1%(1),2%(2) and 7%(7) patient had LDH levels as less than 600. 600-800 and more than 800 IU.3% (3) patients developed abruption had LDH levels more than 800 IU.

V. Discussion

Preeclampsia is considered to be an idiopathic multisystem disorder that is specific to human pregnancy. Complex cellular toxic endocrinological mechanisms are believed to be responsible for cell destruction leading to multi-organ dysfunction **Error! Bookmark not defined.**In India, Pregnancy induced hypertension is seen mostly in younger age group and in primigravida women. Preeclampsia is primarily regarded as a disease of first pregnancy.¹⁹Preeclampsia may be life-threatening for both mother and child, increasing both fetal and maternal morbidity and mortality. As women with severe preeclampsia have about 5 fold increase in perinatal mortality and morbidity.

Hence, need has been felt for an inexpensive, easily available biomarker enabling early identification of preeclampsia, which in turn can predict severity and outcome, can be very helpful in lowering the maternal and fetal morbidity and mortality. It should help to identify high risk groups early in pregnancy, so that preventive measures can be instituted without delay to reduce maternal & fetal morbidity and mortality

Earlier studies have suggested possible role of Serum Lactic dehydrogenase (LDH) in the pathogenesis of preeclampsia. Elevated levels of serum LDH indicate the tissue damage related to endothelial dysfunction and endovascular which are main causes of occurrence of preeclampsia. Therefore, serum LDH level seems promising, as it fulfils most criteria for an ideal biomarker, because it is inexpensive, widely available, and it is quickly estimable.

In the present study, mean ages among mild preeclampsia, severe preeclampsia and control groups were 25+5 years, 25+5.41years and 24+3.45 years respectively. Subjects in both groups were almost of equal age groups, and 50 (50%) (50/100) patients were primigravida in mild preeclampsia, and 59 (59 %) (59/100) patients were primigravida in severe preeclampsia group 58 (58%) (58/100) patients were primigravida in the control group. Young age and primigravidity are well-known risk factors for developing pre-eclampsia, .. The patients with severe pre-eclampsia in our study were significantly younger and with significant low gravidity and parity compared with the normotensive and mildly pre-eclamptic women.

This is consistent with other studies. In the study conducted by Sajith et al ¹⁹ the incidence of hypertension in pregnancy was highest among primigravidae. 53.8% (56/104) were primigravida and 46.2% (48/104) were multigravida. Several other authors Aabidha et al, Chan P et al and Mjehed K et al have reported primiparity in 52-73% patients of preeclampsia.

The most important finding in present study was the high frequency of high levels of serum LDH levels in the study population, the mean LDH value was 618.48+- 169.65 IU, 1046.45+- 648.49 IU both in mild preeclampsia and severe preeclampsia groups respectively.50 patients in mild preeclampsia group and 5 patients in severe preeclampsia group had LDH levels less than 600 IU ie. in normal range. There is significant rise in the LDH levels with the increasing severity of the disease (172.37±28.09) normotensive, (356.33±24.47) mild preeclampsia, (609.91±136.92) severe preeclampsia and (854.05±247.45), eclampsia (P<0.0001). it was also observed by Malvino et al ,samara et al

In the present study, study group had more cesarean sections 37 % (74/200) than vaginal deliveries 63% (126/200) as compared to control group who had 13 % cesarean sections (13/100) and 87% (87 /100) vaginal deliveries. Though the levels of LDH were low in subject group who underwent cesarean section in view of scar tenderness/ impending scar dehiscence, no relation was found with LDH and cesarean sections for impending scar dehiscence. In present study, the main indication for cesarean deliveries in study group was impending eclampsia 22(7.3%) ,fetal distress 30(10%), abruption 6(2%), placenta previa 3(1%) and previous LSCS with impending scar dehiscence 13(4.3%) Higher serum LDH levels were associated with increased incidence of maternal complications like abruption placenta, renal failure HELLP syndrome, PPH etc. in the present study. There was a significant increase in maternal morbidity with increasing serum LDH levels (P=0.00). Maternal morbidity was 13 % in patients in study group and this was a significant rise (P =0.00) which was comparable with other study of Hussein et al

Severely pre-eclamptic women with LDH levels of 800 IU/l showed a significant increase in complications in terms of eclampsia, abruption placenta and various other complications compared to women who had lower serum LDH levels, in the study of Qublan et al. A high serum level of LDH ([1,400 IU/l) were shown to have a high predictive value for significant maternal morbidity in a study conducted by Martin et al.^{al}**Error! Bookmark not defined.** Catanzerite et al. reported a subgroup of patients who had elevated levels of LDH manifested with hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome and were at a high risk for developing maternal mortality. Demiretal.concluded that there was a statistically significant relation between maternal complications and high LDH levels. It was noted that in early onset severe preeclampsia, LDH levels before delivery were significantly higher in the abruption group Odendaal et al..

VI. Conclusions

LDH levels are consistently and reliably elevated in PE and E.LDH levels correlate well with the disease severity.LDH levels also correlate reliably with maternal outcomesLDH levels can be a used as a good predictor to identify the high risk patients to improve maternal outcomes. In the meantime, all cases of PE and Eclampsia should be mandatorily screened and risk stratified with LDH estimation. High risk cases with LDH beyond 600/IU should be segregated for management at a higher center

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