

Correlations of Thrombocytopenia with LDH Level in Patients of Pregnancy Hypertension and Comparison of These Parameters in Normotensive Pregnant Patients

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Abstract

Aim: To correlate the absolute platelet count with lactate dehydrogenase level in patients of pregnancy hypertension and comparison with normotensive pregnant patient

Methodology: A Prospective observational study was conducted from August 2012 to August 2014. All ANC patients diagnosed with raised BP were included in this study. Study was conducted in the department of Obstetrics and Gynaecology in Bharati Hospital having a tertiary care at Bharati Vidyapeeth University Medical College. 150 pregnant women were enrolled in this study who met the inclusion criteria and were divided into two groups: 100 Antenatal women admitted with raised BP were included as study group and 50 Normotensive pregnant women at 36 weeks were included as control group. Patients' progress was observed and perinatal outcome were followed. All the data was collected in MS Excel and analyzed with the help of biostatistician.

Results: 68% of the patients in normotensive group were primigravida, while 60% in mild preeclampsia group were primigravida and 76% in severe preeclampsia group were primigravida but difference was moderately significant. Most common age group was 20-25 years. The difference in mean SBP and DBP in normotensive, mild preeclampsia and severe preeclampsia group was statistically significant. The mean LDH levels were 278.85 ± 114.83 , 498.63 ± 182.26 and 696.78 ± 132.67 respectively in each group and it was statistically significant. Maximum number of patients in severe pre-eclamptic group underwent lower segment caesarean section in which majority had LDH levels >800 IU/l. 44.44% each of the low birth weight babies were seen in LDH levels >800 IU/l and in between 600-800 IU/l. With serum LDH levels <600 IU/l, only 11.11% of babies were seen. Both were statistically significant. Neonatal complications like intra uterine growth retardation, birth asphyxia, still birth and NICU admission were seen in neonates who were born to preeclamptic mothers and majority of the neonatal complications were seen in serum LDH levels >800 IU/l. Neonatal pathological jaundice was seen in neonates who were born to preeclamptic women with serum LDH levels >600 IU/l. Majority of the neonatal sepsis were seen in those neonates who were born to severe preeclamptic women and had serum LDH levels >800 IU/l.

Conclusion: Raised LDH is associated with preeclampsia and higher the LDH levels more are the chances of complications. Hence serum LDH can be measured in all pregnant women to predict preeclampsia.

Keywords: Thrombocytopenia, hypertension, pre-eclampsia, lactate dehydrogenase.

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Introduction

Hypertensive disorders are the most common medical complication of pregnancy and are important cause of maternal and perinatal morbidity and mortality. The most widely used term at present for hypertensive disorder is Pregnancy induced hypertension (PIH). PIH is defined as hypertension that occurs in pregnancy for the first time after 20 weeks of gestation and disappears following delivery [1]. Pre-eclampsia is an important health issue that has to be dealt with especially in developing countries where the incidence and rates of adverse outcomes are higher. Profound changes in the coagulation and fibrinolytic system occur during normal pregnancy and it is associated with hypercoagulable state [2].

Women with pregnancy induced hypertension may develop a variety of hematological aberrations [3]. Out of all the haematological changes that occur in pre-eclampsia and eclampsia, thrombocytopenia is the most common haematological abnormality found [4]. The other tests like prothrombin time, activated partial thromboplastin time, bleeding time and clotting time are more sensitive but expensive. It is known that an underlying coagulation abnormality increases the risk of bleeding complications.

PIH affects approximately 6-8 % of all pregnancies, most often the primigravidas [5]. About 18% of foetal deaths are associated with hypertensive disorders [6]. It is a global problem and complicates approximately 10-17% of pregnancies. The incidence of PIH in India ranges from 5% to 15% [7]. Out of all the haematological changes that occur in PIH, thrombocytopenia is the most common haematological abnormality found.

Currently, there is no screening test that would help in identifying which pregnancy

will be associated with PIH or assess its severity [8]. Some investigators have proposed biochemical markers to predict the severity of PIH like Placental tissue protein 13 and Endoglin's; but these tests cannot be used for simple, low-cost screening. Therefore, there is a need to identify a simple test specifically designed for routine use in a hospital environment [9] in particular those suitable at a rural setup. Other tests fibronectin level, decrease antithrombin III level, decrease in α 2 antitrypsin, increase in sFlt-1 (soluble Fms – like tyrosine kinase – 1) concentration, decrease in circulating free placental growth factor (PlGF) and vascular endothelial growth factor (VEGF) are though more sensitive but expensive, time consuming, require well equipped laboratory and not suitable for routine purpose [1]. Blood platelets are essential parameters used in assessing thrombosis [10].

The analysis of biochemical markers particularly markers related to vascular dysfunction such as LDH, AST, and uric acid may enrich the ability to predict and prevent preeclampsia in near future [3]. Lactate dehydrogenase (LDH) is an intracellular enzyme which converts pyruvic acid to lactic acid during glycolysis. LDH gene expression and activity are higher in placentas of preeclampsia than normal pregnancy. LDH has five is forms and among this LDHA4 seen in preeclampsia is most responsive to hypoxia. Elevated levels of LDH indicates cell damage and dysfunction. The multiorgan dysfunction in preeclampsia caused by vascular endothelial damage leads to excessive LDH leakage and elevated levels in serum due to cellular dysfunction, which may cause the occurrence of preeclampsia [4]. So it can be used as a biochemical marker as it

reflects the severity of the disease, occurrence of complications and fetal outcome [5].

Present prospective study is carried out to co-relate severity of pre-eclampsia with actual platelet count and LDH level in comparison with the levels in normotensive pregnant mothers at 36 weeks.

Methodology:

A Prospective observational study was conducted from August 2012 to August 2014. All ANC patients diagnosed with raised BP were included in this study. Study was conducted in the department of Obstetrics and Gynaecology in Bharati Hospital having a tertiary care at Bharati Vidyapeeth University Medical College. 150 pregnant women were enrolled in this study who met the inclusion criteria and were divided into two groups:

Study group – 100 Antenatal women admitted with raised BP.

Control group – 50 Normotensive pregnant women at 36 weeks.

Inclusion Criteria

All pregnant mothers with hypertension
All normotensive healthy mothers at 36 weeks

Exclusion Criteria

Twin pregnancy
Patients with past history of SLE and ITP.
Thrombocytopenia due to other causes.

Measurement of blood pressure: Blood pressure of the patients was measured on right upper limb in the semi recumbent position with the arm at the heart level with a mercury sphygmomanometer. Two-third arm was covered and the arm cuff

was above cubital crease (half inch) and the tubes were above brachial artery. Blood pressure was measured by sphygmomanometer. Systolic blood pressure was recognized by the appearance of tapping sounds (Korotkoff I). Korotkoff V (disappearance of the sound) was used to determine diastolic blood pressure.

Estimation of serum Lactate Dehydrogenase: Plain blood sample was collected for analysis of LDH which was done in fully automated biochemistry analyzer. Serum LDH levels were done in the biochemistry laboratory. The method is based on the reduction of pyruvate to lactate in the presence of NADH by the action of lactate dehydrogenase. The pyruvate that remains unchanged with 2, 4-Dinitrophenylhydrazine, which is determined calorimetrically in an alkaline medium.

Patients' progress was observed and perinatal outcome were followed. All the data was collected in MS Excel and analyzed with the help of biostatistician.

Results:

68% of the patients in normotensive group were primigravida, while 60% in mild preeclampsia group were primigravida and 76% in severe preeclampsia group were primigravida but difference was moderately significant. Most common age group was 20-25 years. All the cases belonged to the third trimester. In the study majority of the patients in the normal pregnancy group delivered after 37 completed gestational weeks, whereas in the severe preeclamptic group, patients delivered before 34 gestational weeks. The difference was statistically significant.

Table-1: Demographic data of the three groups.

Variables	Normotensive N=50	Mild Preeclampsia N=50	Severe Preeclampsia N=50
Age*	23.12±2.83	23.94±3.71	24.42±2.98
Education Level Illiterate	34 (68%)	33 (66%)	30 (60%)
Literate	20 (40%)	19 (38%)	22 (44%)

Parity	2.5 ± 0.8	2.0 ± 1.1	1.2 ± 0.6
Period of Gestation	39.24 ± 3.05	35.87 ± 2.24	33.05 ± 2.36

The mean SBP in normotensive, mild preeclampsia and severe preeclampsia group were 118.76±10.64, 149.57±8.98 and 167.73±12.83 respectively. The difference was statistically significant. The mean DBP in normotensive, mild preeclampsia and severe preeclampsia group were 74.83±9.74, 95.83±4.83 and 110.84±6.83 respectively. The difference

was statistically significant. The mean LDH levels were 278.85±114.83, 498.63±182.26 and 696.78±132.67 respectively in each group and it was statistically significant. The difference in haemoglobin levels and platelet count were statistically significant. Thrombocytopenia was found in severe preeclampsia

Table-2: Hemodynamics Data

Variables	Normotensive N=50	Mild preeclampsia N=50	Severe preeclampsia N=50
Systolic BP (mmHg)	118.76±10.64	149.57±8.98	167.73±12.83
Diastolic BP (mmHg)	74.83±9.74	95.83±4.83	110.84±6.83
LDH	278.85±114.83	498.63±182.26	696.78±132.67
Haemoglobin	10.42±1.87	8.93±2.05	7.06±2.72
Platelet count(×10 ⁹)	215.74±31.34	118.38±33.84	99.4±70.42

Table-3: Pregnancy Outcome & Level of LDH in severe pre-eclampsia.

Variables		LDH <600 IU/l	LDH 600-800 IU/l	LDH >800 IU/l
		N=8	N=27	N=15
Mode Of Delivery	Normal Vaginal Delivery	3(18.75%)	13(81.25%)	0(0%)
	Cesarean Section	5(14.71%)	14(41.18%)	15(44.12%)
Birth Weight	Low Birth Weight	3(11.11%)	12(44.44%)	12(44.44%)
	Normal	5(21.74%)	15(65.22%)	3(13.04%)

Majority of the patients underwent normal vaginal delivery but maximum number of patients in severe preeclamptic group underwent lower segment caesarean section in which majority had LDH levels >800IU/l. 44.44% each of the low birth

weight babies were seen in LDH levels >800IU/l and in between 600-800 IU/l. With serum LDH levels <600 IU/l, only 11.11% of babies were seen. Both were statistically significant.

Table-4: Complications of Severe Pre-Eclampsia According & LDH level.

Complications	LDH<600IU/l N=8	LDH 600-800IU/l N=27	LDH>800IU/l N=15
Abruptio Placentae	0(0%)	0(0%)	2(13.33%)
Post-Partum Haemorrhage	0(0%)	0(0%)	4(26.67%)
Renal Failure	0(0%)	0(0%)	0(0%)
IPE/PPE	0(0%)	0(0%)	2(13.33%)
HELLP	0(0%)	0(0%)	3(20%)
Cerebral Haemorrhage	0(0%)	0(0%)	0(0%)
Pulmonary Edema	0(0%)	0(0%)	0(0%)
No Other Complications	8 (100%)	27 (100%)	4(26.67%)

Maternal complications like abruptio placentae, post partum haemorrhage, intra partum eclampsia, post-partum eclampsia and HELLP syndrome were seen in severe pre eclamptic group with serum LDH levels >800IU/l.

Neonatal complications like intra uterine growth retardation, birth asphyxia, still birth and NICU admission were seen in neonates who were born to preeclamptic

mothers and majority of the neonatal complications were seen in serum LDH levels >800IU/l. Neonatal pathological jaundice was seen in neonates who were born to preeclamptic women with serum LDH levels >600IU/l. Majority of the neonatal sepsis were seen in those neonates who were born to severe preeclamptic women and had serum LDH levels >800IU/l.

Table 5: Association of follow up of neonates between 3 groups.

Variables	Normotensive N=50	Mild Preeclampsia N=50	Severe Preeclampsia N=50
Neonatal Pathological Jaundice	0(0%)	5(10%)	9(18%)
Neonatal Sepsis	0(0%)	1(2%)	7(14%)

Discussion:

The analysis of biochemical markers particularly markers related to vascular dysfunction such as LDH may enrich the ability to predict and prevent preeclampsia in near future [11]. Lactate dehydrogenase (LDH) is an intracellular enzyme which converts pyruvic acid to lactic acid during glycolysis LDH gene expression and activity are higher in placentas of preeclampsia than normal pregnancy. LDH has five is forms and among this LDHA4 seen in preeclampsia is most responsive to hypoxia. Elevated levels of LDH indicates cell damage and dysfunction. The multiorgan dysfunction in preeclampsia caused by vascular endothelial damage leads to excessive LDH leakage and elevated levels in serum due to cellular dysfunction, which may cause the occurrence of preeclampsia [12]. So it can be used as a biochemical marker as it reflects the severity of the disease, occurrence of complications and fetal outcome [13].

In the present study majority of patients (60.6%) in the study group were illiterates in all the three groups. Andrews L colleagues (2014) did a similar study and concluded that 56.7% of the patients were illiterate [14]. In the present study, age of most pregnancies occurred in the age

group of 20-30 years and mean age was 23.52±2.85 in all the three groups and which was similar to the studies done earlier by Talwar P et al and Mary VP et al where majority of the patients belonged to younger age group [15, 16]. In the present study thrombocytopenia was found in severe preeclampsia which is a predictor of HELLP syndrome. Greater the severity of preeclampsia, lower will be the platelet count. Similar to this finding was seen in others studies done by Kant RH et al but study done by Qublan HS et al it was not statistically significant. Severe grade of proteinuria is associated with elevated LDH levels [17, 18].

Maternal complications like abruptio placentae, post partum haemorrhage, intra partum eclampsia, post-partum eclampsia and HELLP syndrome were seen in severe preeclamptic group in the study and it was observed that these patients had serum LDH levels >800IU/l. 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 [19]. After following up of mothers upto six all were found to be healthy. Neonates were followed upto one month and in that 2 neonatal death (cause of the death for one neonate was

prematurity and for another one was low birth weight) was noted who were born to severe preeclamptic women and had serum LDH levels >800 IU/l. Neonatal pathological jaundice (NPJ) was seen in neonates who were born to preeclamptic women and all of the neonates mothers who had NPJ in severe preeclamptic group had serum LDH levels >800IU/l. Majority of the neonatal sepsis were seen in those neonates who were born to severe preeclamptic women and had serum LDH levels >800IU/l.

It has been shown by earlier researchers that hematological aberrations such as thrombocytopenia and reduction in some plasma clotting factors may develop in preeclampsia women [20, 21]. A transient mild thrombocytopenia is seen due to increased platelet consumption during pregnancy. Thrombocytopenia is found in approximately 6% of pregnancies and most common cause of thrombocytopenia in pregnancy is preeclampsia and eclampsia. A continuous decline in platelet count as pregnancy advances was shown by Fay et al. [22] and Shah A R et al [23] indicated that there is possibility of platelet hyper destruction during pregnancy. This together with hemodilution and platelet trapping results in decreased platelet. McCrae [24] has suggested that thrombocytopenia may precede the various other manifestations of preeclampsia, and thus should be considered in the event of isolated thrombocytopenia seen in the late second or third trimester. [25]

Conclusion:

From this study, it can be concluded that raised LDH is associated with preeclampsia and higher the LDH levels more are the chances of complications. Hence serum LDH can be measured in all pregnant women to predict preeclampsia. Proper monitoring of serum LDH levels in a high risk pregnant woman may help in early diagnosis and early intervention. As it predicts the severity of the disease it can be used as a reliable biochemical marker to

identify high risk patients for close monitoring, prompt and correct management.

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