

SIGNIFICANCE OF LACTATE DEHYDROGENASE AND ASPARTATE TRANSAMINASE AS BIOCHEMICAL MARKERS AND AS PREDICTORS OF SEVERITY OF PREGNANCY-INDUCED HYPERTENSION AND ITS COMPLICATIONS

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ABSTRACT

BACKGROUND

To compare serum Lactate Dehydrogenase (LDH) and serum Aspartate Transaminase (AST) of normotensive pregnant women with those of preeclamptic and eclamptic women. To determine the relationship of levels of serum lactate dehydrogenase and serum aspartate transaminase with severity of pregnancy-induced hypertension and its complications.

MATERIALS AND METHODS

The study was carried out on pregnant hypertensive patients attending outpatient department of Obstetrics and Gynaecology department, AMCH, Dibrugarh, Assam from 1st July 2013 to 30th June 2014. Normotensive pregnant women were taken as controls. Each serum sample from both the control group as well as study group was estimated for lactate dehydrogenase and aspartate transaminase using standard methods and a comparison is drawn and analysed using t-test and Chi-square test.

RESULTS

Serum lactate dehydrogenase and serum aspartate transaminase levels were higher in the study group in comparison to the study groups. The mean serum LDH was 198±30.03U/L in control group, whereas in preeclampsia and eclampsia, mean serum levels of LDH were 817±114U/L and 927±108U/L, respectively. The levels of the serum AST were found to be less than 600U/L in normotensive and preeclampsia patients and more than 600 U/L in eclampsia and other complications of PIH.

CONCLUSION

Serum lactate dehydrogenase and serum aspartate transaminase levels in patients suffering from preeclampsia and its complications are consistently higher compared to the normotensive pregnant patients. To determine the usefulness of inclusion of these enzymes along with other cardiac enzymes in the panel of investigations of pregnant women universally needs further large scale comparative studies.

KEYWORDS

Preeclampsia, Eclampsia, Lactate Dehydrogenase, Aspartate Transaminase.

HOW TO CITE THIS ARTICLE: Sonowal R, Kaur R. Significance of lactate dehydrogenase and aspartate transaminase as biochemical markers and as predictors of severity of pregnancy-induced hypertension and its complications. J. Evid. Based Med. Healthc. 2017; 4(20), 1123-1131. DOI: 10.18410/jebmh/2017/221

BACKGROUND

Pregnancy-induced hypertensions, a pregnancy-specific condition still remains one of the major killers of the pregnant women.¹ A characteristic multisystem disorder of pregnancy, pregnancy-induced hypertension remains a therapeutic challenge for obstetricians. It affects 7-10% of pregnancies world over and in India the incidence is reported to be 8-10% of pregnancies.² More than 4 million women across the world develop this disorder every year and an estimated 50,000 to 76,000 women die of this condition every year.³ It accounts for approximately a

quarter of all antenatal admissions and is the leading cause of maternal ICU admissions and causes 15 to 20% maternal deaths worldwide.

The aetiology of pregnancy-induced hypertension still remains unknown. Once called 'disease of theories', the aetiological hypotheses presently forwarded are placental ischaemic hypothesis, genetic hypothesis, immune maladaptation hypothesis, hypothesis of imbalance between scavengers and free radicals, etc.⁴ Oxidative stress seems to be the most acceptable of all these hypotheses in the present day obstetrics. Abnormalities of the lipid profiles and species may have a role in promotion of the oxidative stress and resultant vascular dysfunction seen in pregnancy-induced hypertension. There is increased evidence that the risk of pregnancy-induced hypertension is increased in women having abnormality of lipid metabolism, but the causal relationship of abnormality of lipid metabolism with pregnancy-induced hypertension is not yet definitely determined.

Financial or Other, Competing Interest: None.

Submission 18-01-2017, Peer Review 30-01-2017,

Acceptance 09-02-2017, Published 07-03-2017.

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DOI: 10.18410/jebmh/2017/221



So, this study is undertaken with the following aims and objectives.

- a. Comparison of serum LDH and serum AST levels of normotensive pregnant women with those of preeclamptic and eclamptic pregnant women.
- b. Determination of severity of hypertension during pregnancy in relation to serum LDH and AST levels.

MATERIALS AND METHODS

The present clinico-biochemical study "Significance of lactate dehydrogenase and aspartate transaminase as biochemical marker and as predictor of severity of pregnancy-induced hypertension and its complications" was a prospective study carried out in the pregnant women attending the Outpatient Department of Obstetrics and Gynaecology of Assam Medical College, Dibrugarh. The study was carried out over a period of one year extending from 1st of July, 2013, to 30th June, 2014.

The study included 198 patients of which 100 were pregnant women with preeclampsia or eclampsia and the remaining were healthy, normotensive pregnant women. Proper recommendation was obtained from the institutional ethical committee.

The women enrolled for study were divided into two groups, Group A (control group) consisting of 98 (ninety eight) healthy normotensive pregnant women and Group B (study group) consisting of 100(one hundred) pregnant women with preeclampsia and eclampsia. The Group B was further subdivided into mild preeclampsia (BP≥140/90 mm of Hg with proteinuria), severe preeclampsia (BP≥160/100 mm of Hg with proteinuria) and eclampsia (PIH with convulsion or coma).

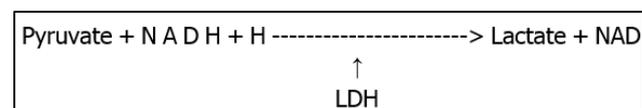
The patients booked before 20 weeks who have crossed 20 weeks with singleton pregnancy with BP ≥140/90mm of Hg and proteinuria ≥300mg/24 hrs. of

urine or ≥1+ dipsticks were included in the study group. The patient is hypertensive before 20 weeks of pregnancy and patients having acute urinary tract infection, chronic infections like cardiac, renal, liver, thyroid disease, etc. and with major obstetric complications like antepartum haemorrhage, twins and polyhydramnios were not included in the study.

Method of Estimation of Serum Lactate Dehydrogenase (LDH)

1) Modified IFCC Method⁵-

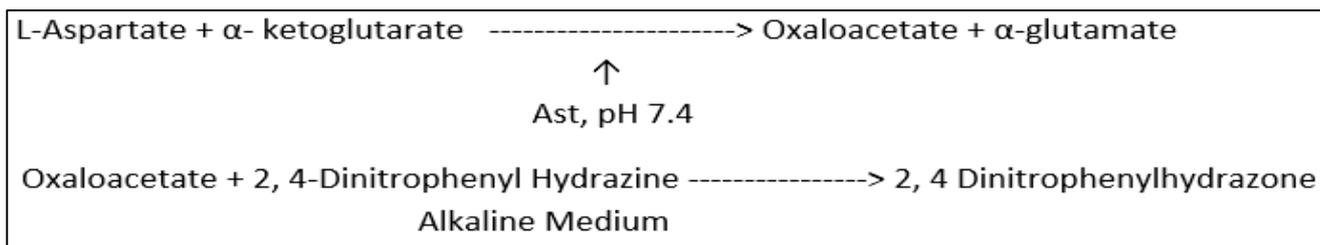
This method devised by Wacker et al in 1980 and Vanderlinde 1982 is based on the reduction of pyruvate to lactate in the presence of NADH by the action of lactate dehydrogenase. The rate of oxidation of NADH to NAD is measured as a decrease in absorbance, which is proportional to the LDH activity in the sample.



Method of Estimation of Aspartate Transaminase (AST)

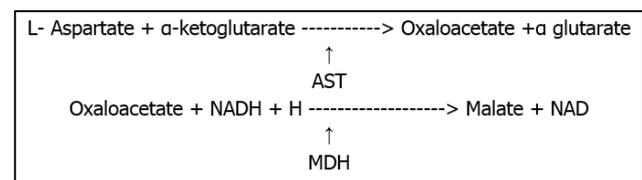
1) Reitman and Frankel's Method⁶-

AST converts L-aspartate and α-ketoglutarate to oxaloacetate and glutamate. The oxaloacetate thus formed reacts with 2, 4 -dinitrophenylhydrazine to produce hydrazone derivative, which in an alkaline medium produces a complex of brown color, the intensity of which is measured. Then, a pyruvate standard is used to plot a calibration curve. The activity of the calibration curve can be read from this calibration curve.



1) Modified IFCC Method⁷-

This method is based on the principle that AST catalyses the transfer of amino group between L-aspartate and α-ketoglutarate to form oxaloacetate and glutamate and the oxaloacetate thus formed reacts with NADH in presence of MDH to form NAD. The rate of oxidation of NADH to NAD is measured as a decrease in absorbance, which is proportional to the AST activity in the serum. This is measured using a biochromatic (3,40,700nm)rate technique.



Sl. No.	State	Level
1.	Nonpregnant	115-221 IU/L
2.	First trimester	78-433 IU/L
3.	Second trimester	80-447 IU/L
4.	Third trimester	82-524 IU/L

Table 1. Normal Serum LDH Level in Pregnancy⁴

Sl. No.	State	Level
1.	Nonpregnant	12-38U/L
2.	First trimester	3-23U/L
3.	Second trimester	3-33 U/L
4.	Third trimester	4-32 U/L

Table 2. Normal Serum AST Level in Pregnancy^[4]

Other relevant investigations done are Hb%, ABO Rh typing, VDRL, random blood sugar, BT and CT, serum urea, serum creatinine, serum uric acid, platelet count, thyroid function test and liver function tests. Urinary estimation of sugar, protein in 24hrs. urine and culture and sensitivity are done. Besides these, ECG was done to rule out cardiac abnormality.

RESULTS AND OBSERVATIONS

The cases were divided according to the serum LDH and serum AST levels in the following groups-

Serum LDH

1. Serum LDH <600 U/L.
2. Serum LDH 600-800 U/L.
3. Serum LDH >800 U/L.

Serum AST

1. Serum AST <35 U/L.
2. Serum 35-100 U/L.
3. Serum >100 U/L.

Correlation coefficient was obtained by using Pearson correlation and significant values were obtained by using unpaired Student’s t-test, Chi-square test and Fisher exact test, wherever applicable.

Gravida	Group A		Group B	
	No.	Percentage	No.	Percentage
Primigravida	56	57.15	70	70
Multigravida	42	42.85	30	30
Total	98	100	100	100

Table 3. Depicts the Parity Distribution of Cases

Age (Years)	Group			
	A (n=98)		B (n=100)	
	No.	Percentage	No.	Percentage
19-22	22	22.46	28	28
23-26	48	48.97	46	46

27-30	17	17.35	14	14
31-34	10	10.20	9	9
35 and above	1	1.02	3	3

Table 4. Age Wise Distribution of the Cases

Maternal ages varied between 19 to 35 years or more. Number of cases being minimal in the age group 35 years and above.

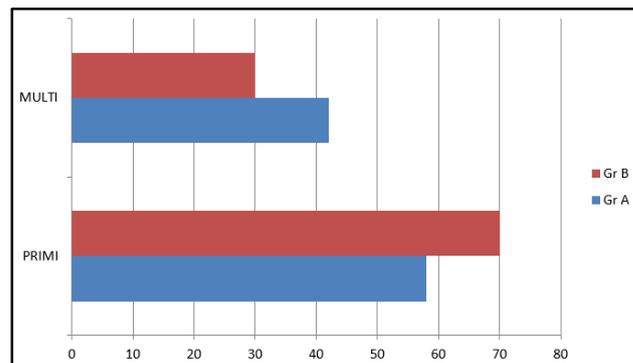


Figure 1. Distribution of Cases According to Gravida

In the control group, 58% were primigravidae and 42% were multigravidae and in the study group the corresponding figures were 70% and 30% respectively with intergroup mean age difference not being statistically significant (p>0.05).

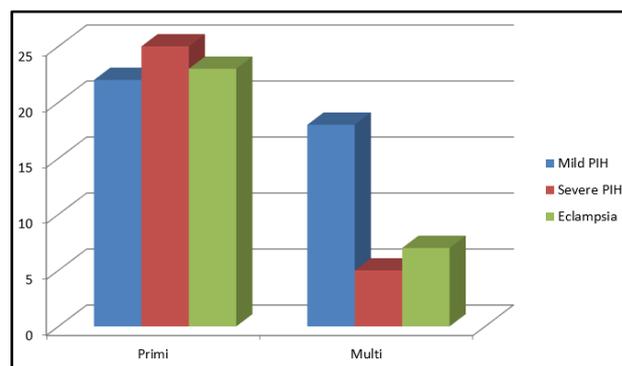


Figure 2. Distribution of Cases According to Gravida in Group B

The above figure depicts the prevalence of the disease according to gravid of the patients in the study group.

Parity	Group A(n=98)		Group B (n=100)					
	Number	Percentage	Mild Preeclampsia		Severe Preeclampsia		Eclampsia	
			Number	Percentage	Number	Percentage	Number	Percentage
Nulliparous	56	57.14	22	55	25	83.34	23	76.6
Para-1	27	27.55	12	30	4	13.33	2	6.66
Para-2	11	11.22	6	15	1	3.33	1	3.33
Para-3	3	3.06	0		0		2	6.66
Para-4	1	1.03	0		0		2	6.66
Total	98	100	40	100	30	100	30	100

Table 5. Distribution of the Cases According to Parity in Both the Groups

The above table makes it clear that out of 30 severe preeclampsia 83.34% cases were nulliparous, 13.33% were in para 1 and 3.33% in para 2. In eclampsia, out of 30 patients, 76.6% were nulliparous.

Locality	Group A(n=98)	Percentage	Group B(n=100)					
			Mild Preeclampsia		Severe Preeclampsia		Eclampsia	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Rural	59	60.20	22	55	18	60	23	76.6
Urban	39	39.80	18	45	12	40	7	23.4
Total	98	100	40	100	30	100	30	100

Table 6. Distribution of Cases According to Locality

The fact that the catchment areas of the hospital are mainly rural areas is reflected in our study.

Gestational Age in Weeks	Group B (n=100)	
	Number	Percentage
≤28	6	6
29-32	29	29
33-37	56	56
≥38	9	9
Total	100	100

Table 7. Gestational Age at Diagnosis of Hypertension

Maximum numbers of cases first detected as hypertensive were between 29 to 37 weeks. So, maximum number of patients of preeclampsia and eclampsia were close to term pregnancy.

Specific Investigations-Serum LDH and AST Levels

Enzymes	Group A (U/L) (Mean ± SD)	Group B (U/L) (Mean±SD)	P-Value
Serum LDH	198.0 ± 30.03	674.3 ± 271.4	<0.001
Serum AST	26.42 ± 5.82	150.8 ± 130	<0.001

Table 8. Comparison of Serum LDH and AST in Both the Groups

The mean values of serum LDH in the control group and in the study group were 198.0±30.03, 674.3±271.4 respectively and the mean value of serum AST in the control group and the study group were 26.42±5.82 and 150.8±130, respectively. This was statistically significant proving higher serum values of LDH and AST in preeclampsia and eclampsia compared to normotensive pregnant patients.

Serum LDH and Systolic Blood Pressure

Systolic BP (mmHg)	LDH<600 U/L		LDH 600-800 U/L		LDH>800 U/L		Total Patients
	Number	Percentage	Number	Percentage	Number	Percentage	
90-139	98	70.50	0		0		98
140-159	37	26.62	2	12.5	1	2.33	40
≥160	4	2.88	14	87.5	42	97.67	60
Total	139	100	16	100	43	100	198

Table 9. Association of Systolic Blood Pressure with Serum LDH in Both the Groups

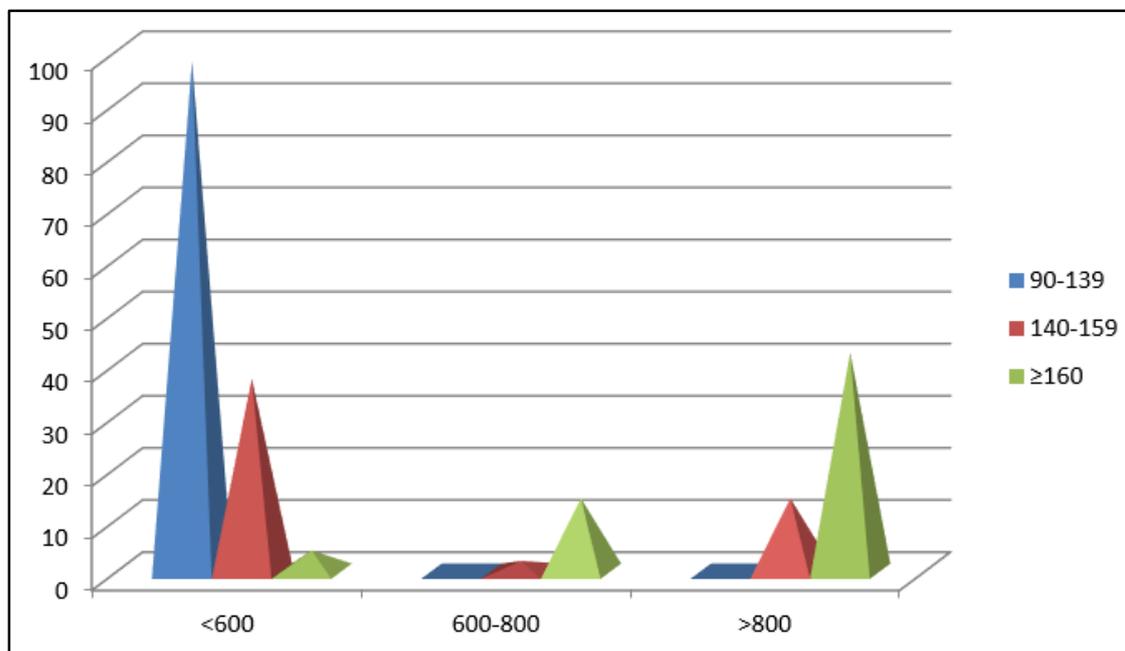


Figure 3. Association of Systolic Blood Pressure with Serum LDH in Both the Groups

Serum LDH and Diastolic Blood Pressure

Diastolic BP (mm of Hg)	LDH<600U/L		LDH600-800U/L		LDH >800		Total Patients
	Number	Percentage	Number	Percentage	Number	Percentage	
60-89	94	67.62	0	-	0	-	94
90-109	42	30.22	5	31.3	10	23.3	57
≥110	3	2.16	11	68.7	33	76.7	47
Total	139	100%	16	100%	43	100%	198

Table 10. Association of Diastolic Blood Pressure with Serum LDH in Both the Groups

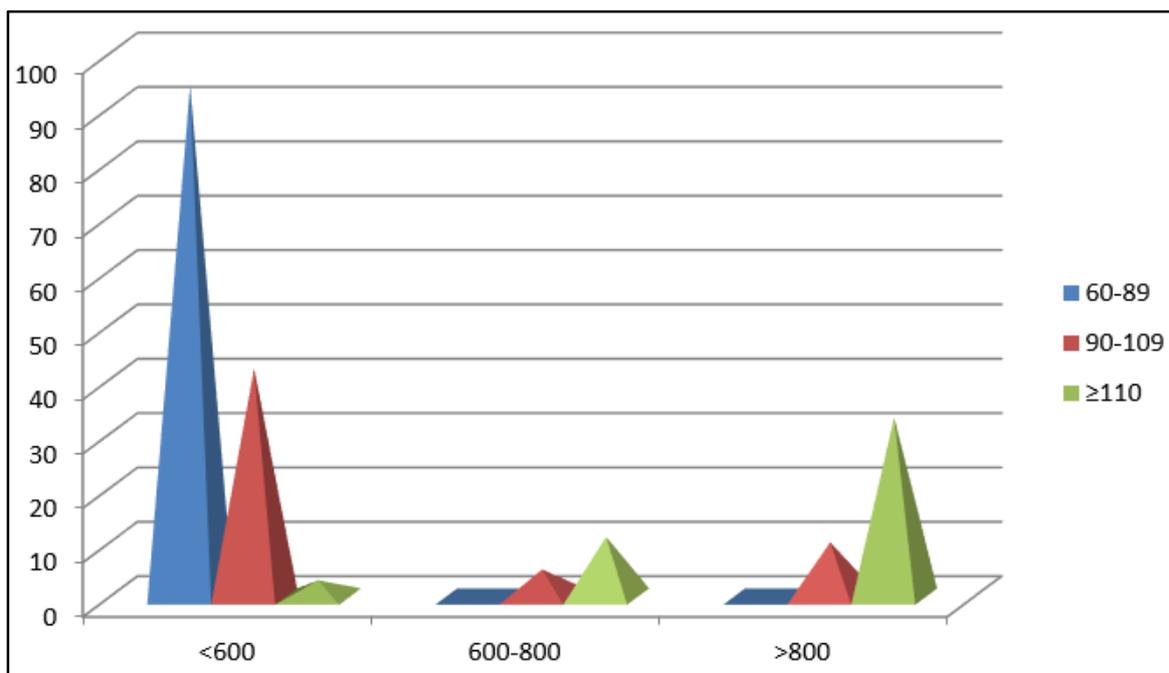


Figure 4. Association of Diastolic Blood Pressure with Serum LDH in Both the Groups

LDH level is low in the normotensive control group in contrast to the comparatively higher levels of LDH in the study groups of preeclampsia and eclampsia. This is clearly depicted in the above table.

Serum AST Level

Groups		AST Level(U/L)(Mean±SD)	Range
Group A (n=98)		26.42 ± 5.82	17-38
Group B (100)	Mild preeclampsia	34.2 ± 14.4	20-78
	Severe preeclampsia	150.6 ± 92.1	68-388
	Eclampsia	306.6 ± 71.2	78-402

Table 11. Comparison of Serum AST Levels in Both the Groups

The AST values in the Group B show higher values than the Group A, which is statistically significant (p<0.0001).

Serum AST and Systolic Blood Pressure

Systolic BP (mmHg)	AST<35U/L		AST 35-100U/L		AST >100 U/L		Total Patients
	Number	Percentage	Number	Percentage	Number	Percentage	
90-139	90	76.27	8	24.24	0	--	98
140-159	28	23.73	8	24.24	4	8.51	40
≥160	0	--	17	51.52	43	91.49	60
Total	118	100	33	100	47	100	198

Table 12. Association of Systolic Blood Pressure With Serum AST Levels in Both the Groups

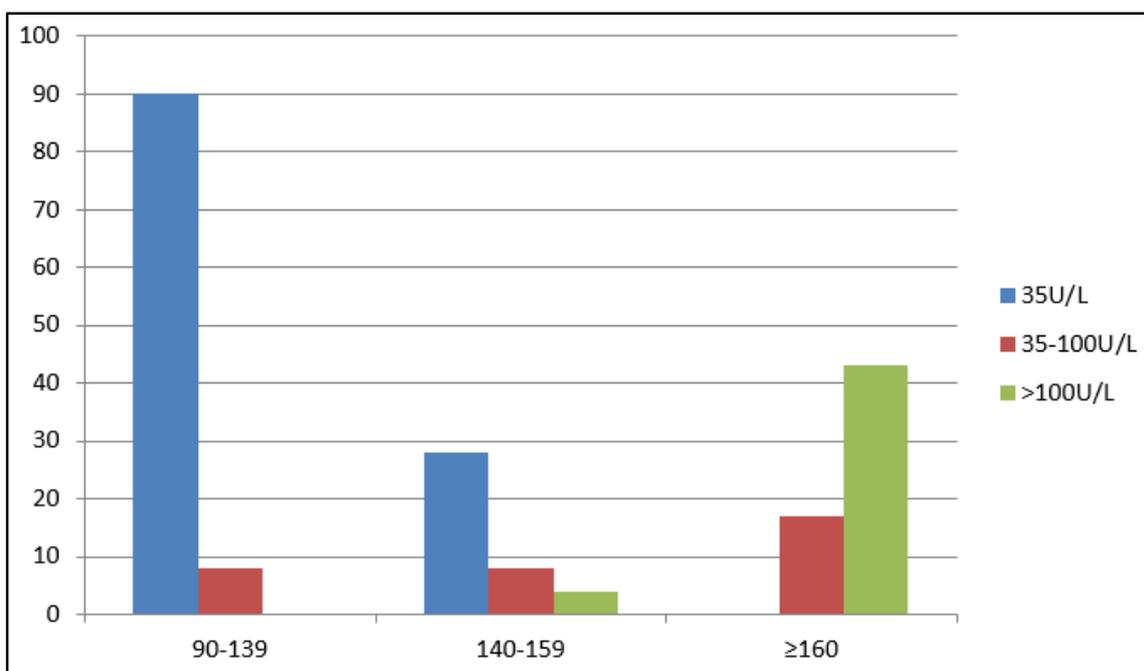


Figure 5. Association of Systolic Blood Pressure with Serum AST Levels in Both the Groups

The AST level was 35u/L in the blood pressure group 90 to 139 mm of Hg, but was high in 140 to 159 mmHg group and >160 mmHg group (p<0.0001).

Serum AST and Diastolic Blood Pressure

Diastolic BP (mmHg)	AST<35 U/L		AST 35-100 U/L		AST>100 U/L		Total Patients
	Number	Percentage	Number	Percentage	Number	Percentage	
60-89	86	72.88	8	24.24	0	--	94
90-109	29	24.57	15	45.46	13	27.66	57
≥110	3	2.55	10	30.30	34	72.34	47
Total	118	100	33	100	47	100	198

Table 13. Association of Diastolic Blood Pressure with AST Levels in Both the Groups

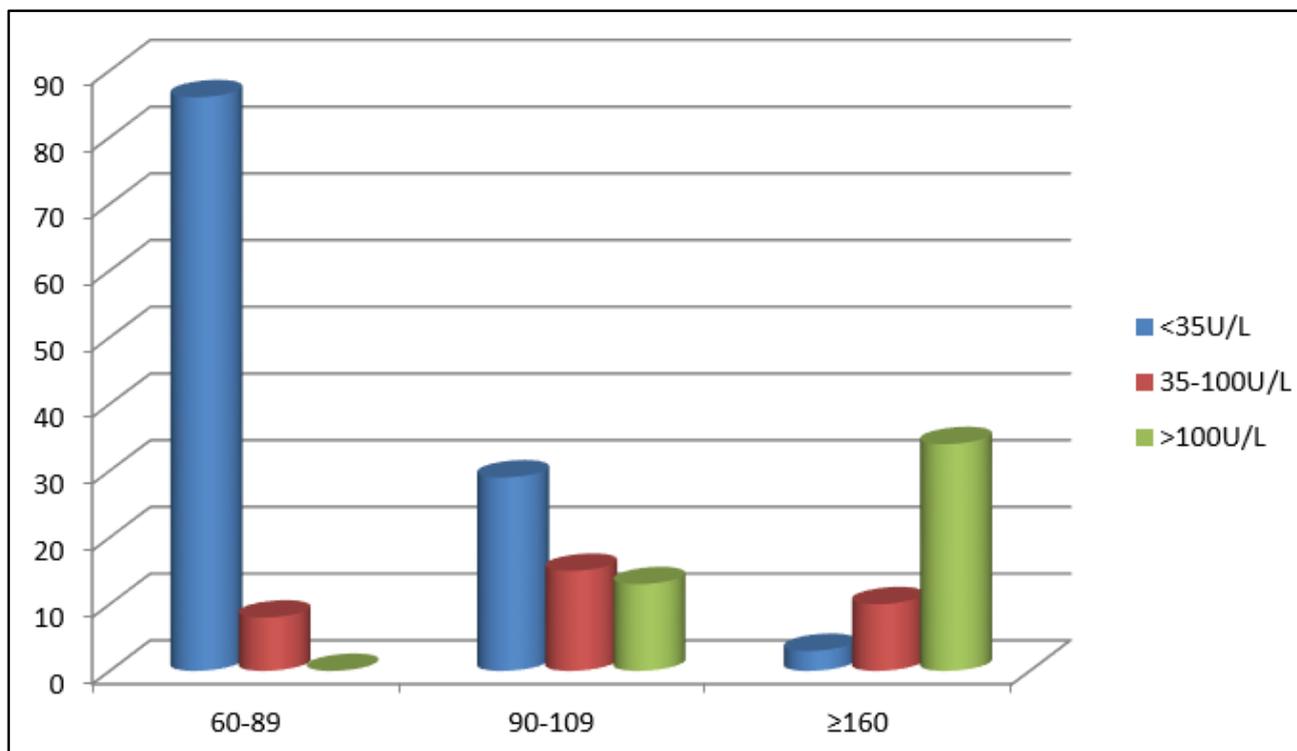


Figure 6. Association of Diastolic Blood Pressure with AST Levels in Both the Groups

The above table shows that AST below 35 U/L is mainly prevalent in the patients with diastolic blood pressure 60 to 89 mm of Hg, whereas in the diastolic blood pressure 90 to 109 mm of Hg and ≥160 mm of Hg groups, the AST level is significantly high(p<0.0001).

Complications were detected in 80 patients of the study group. The main complications detected were as below-

Sl. No.	Complications	Number of Patients,N=80
1.	Pulmonary oedema	20
2.	Hypertensive retinopathy	40
3.	HELLP syndrome	1
4.	Disseminated intravascular coagulation	2
5.	Abruptio placenta	5
6.	Maternal death	9
7.	Acute renal failure	3

Table 14. Complications were Detected in 80 Patients of the Study Group

Complications and Serum LDH

Complications	LDH <600U/L	LDH 600-800 U/L	LDH >800 U/L	Number of Patients
Pulmonary oedema	0	0	20	20
Hypertensive retinopathy	2	6	32	40
HELLP syndrome	0	0	1	1
DIC	0	0	1	1
Abruptio placentae	0	1	5	6
Maternal death	0	0	9	9

Table 15. Association of Serum LDH with Complications of Preeclampsia and Eclampsia

The table clarifies that the complications of preeclampsia and eclampsia are more in the patients who had a high levels of LDH.

Complications and Serum AST

Complications	AST 35U/L	AST 35-100U/L	AST>100U/L	Number of Patients
Pulmonary oedema	0	0	20	20
Hypertensive retinopathy	2	6	32	40
HELLP syndrome	0	0	1	1
DIC	0	0	2	2
Abruptio placentae	0	1	4	5
Maternal death	0	0	9	9
Acute renal failure	0	1	2	3

Table 16. Association of Serum AST Level and Complications of Preeclampsia and Eclampsia

The relationship of the high AST levels with complications is same as high serum LDH level.

DISCUSSION

This study conducted over a period of one year included patients attending a referral hospital of Assam. The age of the patients ranged between 17 years to 36 years. Preeclampsia and severe preeclampsia were commoner in the Primigravida than multigravidae.

Preeclampsia is a complex pathophysiological condition where the regulatory system of inflammation and endothelial function is deranged unlike normal physiology of pregnancy. There is increased evidence that increased levels of lipids may play a pivotal role in modification of the endothelial function and structure.

Evidences are also emerging that deranged lipid metabolism in these cases are not a mere coincidence, but are really involved in the pathogenesis of the disease and

complications arising thereof. High levels of lactate dehydrogenase and aspartate transaminases are implicated in these complications of pregnancy.

The patients in the study were mainly from the rural background and from lower middle class family. Majority of the patients in the study group developed hypertension in the third trimester of pregnancy, which is comparable with the other studies.

The mean values of serum LDH were normal (198 ± 30.03 U/L) in the control group in comparison to the study group where levels were high (preeclampsia-817 ± 114 U/L, eclampsia – 927 ± 108 U/L). The following table shows that these findings comparable with various other studies.

Sl. No.	Studies	Serum LDH Levels (u/l) (Mean ± SD)			
		Control	Preeclampsia	Severe Preeclampsia	Eclampsia
1.	Qublan et al 2002 ^[8]	299 ± 79	348 ± 76	774 ± 69.6	-----
2.	R. Aziz and T. Mahbooba 2008 ^[9]	255 ± 79	343.34 ± 59.17	-----	-----
3.	Jaiswar et al 2009 ^[10]	278 ± 119.2	400.45 ± 148.21	646.95 ± 401.6	1648 ± 992
4.	Sonagra AD et al 2012 ^[11]	151.5 ± 47.47	356.46 ± 158.09	356.46 ± 158.09	-----
5.	Present Study	198 ± 30.03	372 ± 76	817 ± 114	927 ± 108

Table 17. Serum LDH Levels

COMPARISON OF SERUM AST VALUES

Sl. No.	Studies	Serum AST Levels (u/l)(Mean ± SD)			
		Control	Mild Preeclampsia	Severe Preeclampsia	Eclampsia
1.	Qublan et al (2002) ⁸	17.3 ± 5.2	22.2 ± 4.8	88.2 ± 9.4	---
2.	R. Aziz and T. Mahbooba (2008) ⁹	22.06 ± 5.10	34.32 ± 10.37		---
3.	B. Munnazza and team (2011) ¹²	24 ± 2.53	41.3 ± 10.76		---
4.	Present study	26.42 ± 5.82	34 ± 14	151 ± 92	307 ± 71

So, it is clear from the above that in cases of normotensive and preeclamptic patients, the serum LDH levels remain below 600 U/L, whereas in severe preeclampsia and eclampsia patients same remain above 600 U/L.

Serum LDH levels were higher in patients with systolic blood pressure 140 mm of Hg or more and diastolic pressure 90 mm of Hg or more. These are the patients who are considered to be suffering from pregnancy-induced

hypertension. In other words, patients with pregnancy-induced hypertension have higher values of serum LDH than normotensive pregnant patients. Likewise, the complications of pregnancy-induced hypertension like pulmonary oedema, abruptio placentae, HELLP syndrome, DIC, etc. are higher in the patients with higher levels of serum LDH.

The serum AST also show higher level in study group in comparison to the control group. Similar inferences were

seen in all other studies compared with the present study. Like serum LDH levels, the serum AST levels were also higher in patients with complications of pregnancy-induced hypertension.

CONCLUSION

In our study, total number of patients was 198, 98 of which were normotensive pregnant patients included in the control group. The study population included mainly primigravida subjects from lower and lower middle class families of 20 to 36 years of age.

Both the serum LDH and serum AST levels were higher in patients with preeclampsia and eclampsia and in patients with complications of the pregnancy-induced hypertension.

Raised levels of these enzymes are attributed to the cellular damage and multiorgan dysfunction occurring during the course of the disease and increasing levels are seen as the disease progresses from mild-to-severe forms.

From our study, it can be concluded that serum levels of these enzymes correlate well with severity of hypertensive disorders of pregnancy and can be considered for inclusion in the panel of investigations for early management and to curb the complications of the disease.

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