ASPARTATE TRANSAMINASE - IS IT USEFUL AS A BIOCHEMICAL MARKER AND AS A PREDICTOR OF SEVERITY OF PREGNANCY-INDUCED HYPERTENSION AND ITS COMPLICATION

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ABSTRACT

OBJECTIVES

To compare serum Aspartate Transaminase of normotensive pregnant women with those of pre-eclamptic and eclamptic women. To determine the relationship of levels of serum Aspartate Transaminase with severity of pregnancy-induced hypertension and its complications.

METHOD

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 the control group as well as study group was estimated for Aspartate Transaminase using standard methods, and a comparison is drawn and analysed using t-test and chi-square test.

RESULTS

Serum Aspartate Transaminase levels were high in the study group. The levels of this enzyme were normal in the control group.

CONCLUSION

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 this enzyme along with other cardiac enzymes in the panel of investigations of pregnant women universally needs further large scale comparative studies.

KEYWORDS

Preeclampsia, Eclampsia, Maternal mortality, HELLP syndrome.

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INTRODUCTION: Maternal mortality is one of the vital parameters to assess the health status of society. Pregnancy-induced hypertension along with its inherent complications comprises one of the major factors contributing to maternal mortality.[1] This is a pregnancy specific condition and it still remains one of the major killers of the pregnant women. A characteristic multisystem disorder of pregnancy, pregnancy-induced hypertension till date remains a therapeutic challenge for obstetricians. It affects 7-10% of all 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 stills remains unknown. Once called 'disease of theories,' the aetiological hypotheses presently forwarded are: [4,5]

1. Placental ischaemic hypothesis,
2. Genetic hypothesis,
3. Immune maladaptation hypothesis,
4. Hypothesis of imbalance between scavengers and free radicals, etc.

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. In search of definite aetiological factor/factors of causation of pregnancy-induced hypertension, more and more researches need to be undertaken.

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MATERIAL AND METHOD: The present clinico-biochemical study "Aspartate transaminase - Is it useful as a biochemical marker and as a 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. Institutional Ethical Committee recommendation was obtained.

The women undertaken for study were divided into the following two groups:

Group A (Control group): 98 healthy normotensive pregnant women.

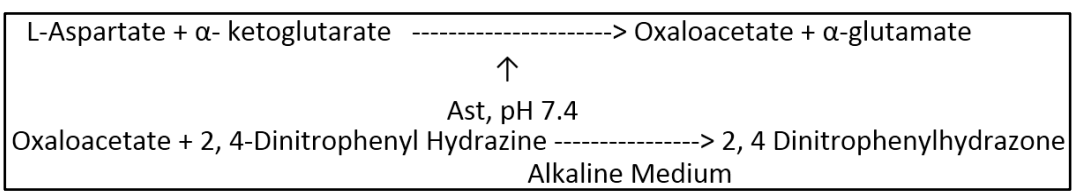
Group B (Study Group): 100 pregnant women with Preeclampsia and Eclampsia. This is further subdivided into:

1. Mild Preeclampsia: BP≥140/90 mm of Hg with proteinuria.
2. Severe Preeclampsia: BP≥160/110 mm of Hg with proteinuria.
3. Eclampsia: PIH with convulsion or coma.

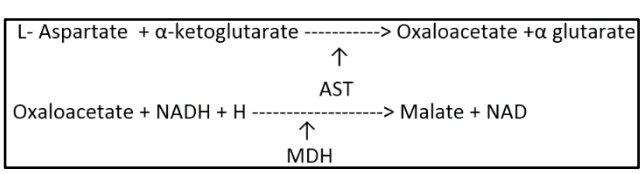
The patients booked before 20 weeks who have crossed 20 weeks of gestation with singleton pregnancy with BP ≥140/90 mm of Hg and proteinuria ≥300 mg/24 Hr of urine or≥ 1+ Dipsticks were included in the study group. Patients hypertensive before 20 weeks of pregnancy with acute urinary tract infection, chronic infections like cardiac, renal, liver, thyroid disease, etc. and with major obstetric complications like antepartum haemorrhage, twins, polyhydramnios were not included in the study.

Method of Estimation of Aspartate Transaminase (AST):

1. **Reitman and Frankel's method-(Reitmans 1957, Henryy J.B. 1974)[5,6]:** 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 colour, 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.



2. **Modified IFCC method-(Schumann et al 2002)[7]:** 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 bichromatic (340, 700 nm) rate technique.



Normal serum AST level in pregnancy[8,9,10,11]

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

Table 1

Other relevant investigations done were: -

1. Blood–Hb%, ABO Rh typing, VDRL, Blood Sugar, BT and CT, Urea, Creatinine, Uric Acid, Platelet Count, Thyroid function test and Liver Function test.
2. Urine- Sugar, Culture and Sensitivity.
3. ECG.

RESULTS AND OBSERVATIONS: The cases were divided according to Serum AST levels in the following groups: -

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 t test, chi square test and Fisher exact test, wherever applicable.

Group	No. of cases	Percentage
Group A	98	49.49
Group B	40	20.20
Mild Preeclampsia	30	15.15
Severe Preeclampsia	30	15.15
Eclampsia		
Total	**198**	**100**

Table 2: Distribution of cases

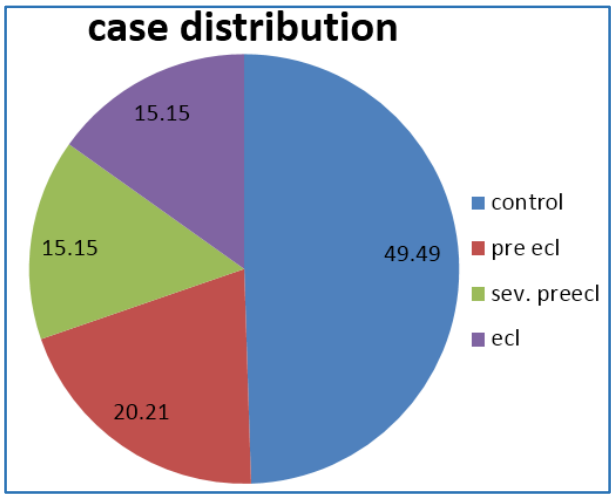


Fig. 1: Pie diagram of case distribution

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: Distribution of cases according to gravida in both the groups

In the study, primigravidae were more compared to the multigravidae as evident from the above table.

Age Distribution: Maximum numbers of cases were between 20 to 25 years of age in both the groups. In group A, 51% of the cases and in group B, 47% of the cases were in this range. The number of patients in various groups is shown in the table 2.

Age (Years)	Group			
	A(n=98)		B(n=100)	
	No.	%	No.	%
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 & ABOVE	1	1.02	3	3

Table 4: Age-wise distribution of the cases

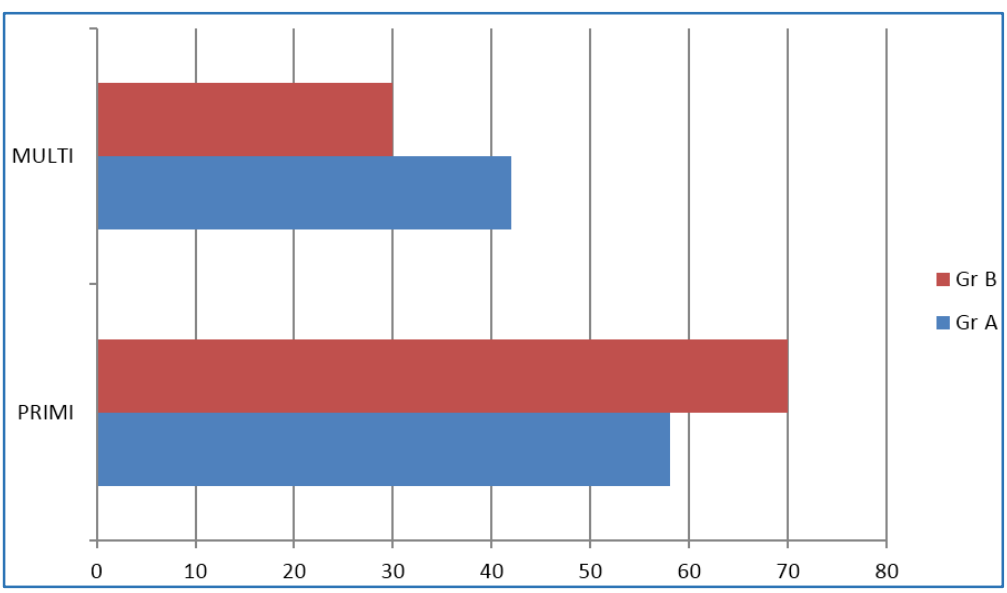


Fig. 2: Distribution of cases according to gravida

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).

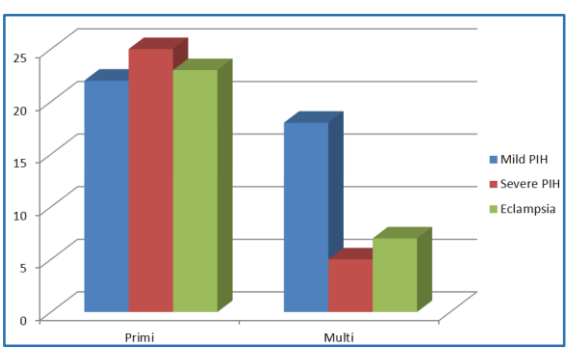


Fig. 3: Distribution of cases according to gravida in group B

The above figure depicts the prevalence of the disease in the primigravidae.

Parity	Group A (n=98)		Group B (n=100)					
			Mild Preeclampsia		Severe preeclampsia		Eclampsia	
	No	%	No	%	No	%	No	%
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%

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 and 6.66% were in majority of the other groups.

Locality	Group A (n =98)		Group B (n=100)					
			Mild preeclampsia		Severe preeclampsia		Eclampsia	
	No	%	No	%	No	%	No	%
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

Majority of the cases in both the groups were from the rural area. This is clear from the above table.

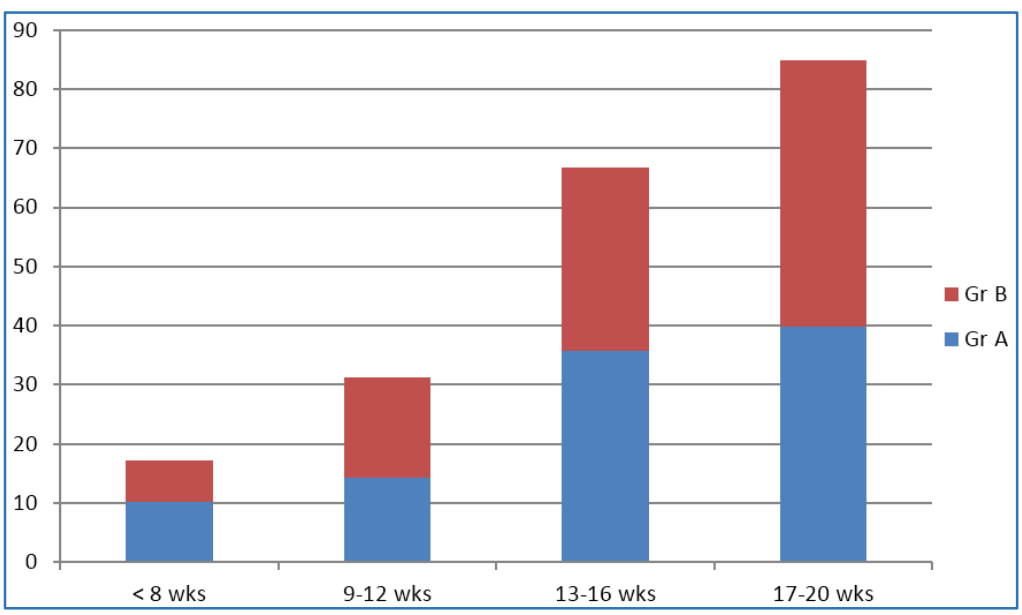


Fig. 4: Booking weeks of the cases taken for study

Highest number of cases was booked between 13 to 20 weeks of pregnancy. All of these cases were normotensive at the time of booking.

Gestational age in weeks	Group B (n =100)	
	No	%
≤ 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 number 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 INVESTIGATION: - SERUM AST LEVELS

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

Table 8: Comparison of serum AST in both the groups

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 AST in preeclampsia and eclampsia compared to normotensive pregnant patients.

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 9: 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 (mm Hg)	AST< 35U/L		AST 35-100U/L		AST >100 U/L		Total Patients
	No	%	No	%	No	%	
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 10: Association of systolic blood pressure with serum AST levels in both the groups

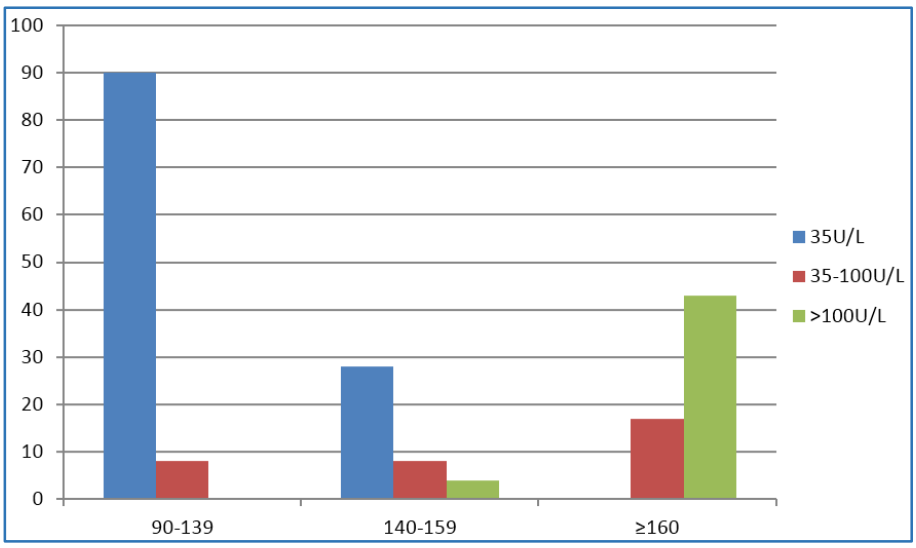


Fig: 5

The AST level was 35 u/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 (mm Hg)	AST<35 U/L		AST 35-100 U/L		AST> 100 U/L		Total Patients
	No	%	No	%	No	%	
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 12: Association of diastolic blood pressure with AST levels in both the groups

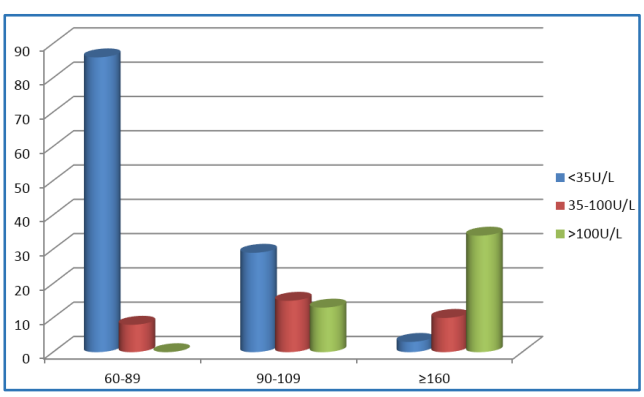


Fig. 6

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).

The main complications detected were as below.

Sl. No.	Complications	No. of patients
1	Pulmonary oedema	20
2	Hypertensive Retinopathy	40
3	HELLP Syndrome	1
4	Disseminated Intravascular Coagulation	2
5	Abruptio Placentae	5
6	Maternal Death	9
7	Acute Renal Failure	3

Table 13

Complications and Serum AST:

Complications	AST 35U/L	AST 35-100U/L	AST>100U/L	No. 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 14: Association of serum AST level and complications of preeclampsia and eclampsia

The AST levels are high in proportion to the complications of Pregnancy-induced Hypertension.

DISCUSSION AND ANALYSIS: 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 common in the primigravidae 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 serum 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 like Walker J J et al, Redman CWG et al, Lardoux H et al etc.[12,13,14]

Serum AST levels were higher in patients with systolic blood pressure 140 mm f 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 AST than normotensive pregnant patients. Likewise, the complications of pregnancy-induced hypertension like pulmonary oedema, abruption placentae, HELLP syndrome, DIC, etc. are higher in the patients with higher levels of serum AST. Similar inferences were seen in all other studies compared with the present study.

SUMMARY AND CONCLUSION: In our study, total number of patients was 198 of which 98 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 AST levels were higher in patients with preeclampsia and eclampsia and in patients with complications of the pregnancy-induced hypertension.

Raised levels of this enzyme 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 this enzyme 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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