

Serum Alkaline Phosphatase Activity in Preeclampsia

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Preeclampsia is one of the major causes of maternal mortality in Bangladesh. It is also an important cause of emergency obstetric admission in health care facilities of Bangladesh. Alkaline phosphatase (ALP) activity in the placenta usually increases during normal pregnancy which contributes to increases the plasma level. But it decreases in preeclampsia. Alkaline phosphatase is known to be produced by the liver, bones, small intestine, and kidneys and different alkaline phosphatase isoforms are also expressed by the placenta during pregnancy. Placental isoform of ALP is heat stable. The heat stable ALP is used as an indicator of gestational age, placental function and indirectly as a measure of fetal wellbeing. It can be used as biochemical parameter for documentation of severity of preeclampsia and decision can be made for termination of pregnancy. This study was carried out to analyze the level of serum alkaline phosphatase in preeclamptic patients as well as in healthy third trimester pregnant women to assess the relationship of ALP with preeclampsia. This is a Cross sectional comparative study carried out during the period of December 2008 to May 2009 in the Department of Obstetrics and Gynecology at DMCH and BSMMU, Dhaka. Patients who fulfilled the criteria of preeclampsia were included for the study. During the study period, a total of 100 patients were studied. 50 patients had normal pregnancy and 50 patients were with preeclampsia. The study population was divided into group I and group II. Group I- Included 50 healthy pregnant women of third trimester attending at the above mentioned places were considered as control. Group 2 - Included 50 preeclamptic patients. The results showed that mean total plasma ALP in normal pregnancy was higher than preeclamptic patient. Total plasma ALP in group 1 was 229.37 ± 71.53 and in group 2 was 162.64 ± 15.91 and it was statistically significant ($P < 0.001$). Among preeclamptic patients ALP was significantly decreased in comparison to normal pregnancy. It also showed significant relationship of ALP with mild and severe preeclampsia. So, preeclampsia patients should be screened for ALP.

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Key words: Preeclampsia, Alkaline phosphatase

Introduction

Pregnant women with hypertension can be broadly divided into one of the three categories- chronic hypertension, non-proteinuric hypertension (sometimes

known as pregnancy induced hypertension) and preeclampsia.¹ Compared with normotensive gravida, elevated blood pressure has significantly greater maternal and

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foetal mortality and morbidity specially in developing country like Bangladesh. Preeclampsia occurs in 5-7 percent of pregnant women.² Yet in modern obstetrics services, preeclampsia causes maternal mortality 2-3 percent and perinatal mortality 15 percent³. Unfortunately, in the developing countries incidence of eclampsia is higher due to lack of proper antenatal care, poverty and ignorance. As the cause and pathogenesis is still not well understood, any specific preventive or curative measures have not been possible. Preeclampsia is characterized by hypertension (systolic blood pressure ≥ 140 mm of Hg and diastolic blood pressure ≥ 90 mm of Hg on two separate occasions at least 6 hours apart) that occurs after 20 weeks of gestation in a woman with previously normal blood pressure associated with proteinuria⁴ (defined as urinary excretion of > 0.3 g protein in a 24 hour urine specimen). It may progress to eclampsia, which is a grave situation. HELLP syndrome, abruptio placentae, acute renal failure, DIC is the complication of severe preeclampsia, all of which increase the risk of maternal and perinatal morbidity and mortality⁵. Alkaline phosphatase (AP) is known to be produced by the liver, bones, small intestine, and kidneys and different alkaline phosphatase isoforms are also expressed by the placenta during pregnancy⁶. The average amount of alkaline phosphatase in one human term placenta is 40 mg⁷. Upward and downward trend in placental ALP may presage complications of pregnancy such as hypertension and preeclampsia.⁸ Alkaline phosphatase in the placenta originates exclusively from the syncytiotrophoblast.⁹ Abnormalities such as patchy necrosis, mitochondrial swelling and dilatation of the rough endoplasmic reticulum

have been demonstrated in syncytiotrophoblast of placenta from preeclamptic patient.¹⁰ Such abnormalities, if severe enough, could lead to an overall decreased ALP synthesis in the placenta resulting in decreased maternal serum ALP concentration. Placental isoform of ALP is heat stable. The heat stable ALP is used as an indicator of gestational age, placental function and indirectly as a measure of fetal well being¹¹. So, it is necessary to measure ALP in preeclamptic patient.

Methods

This is a cross sectional comparative study carried out during the period of December 2008 to May 2009 in the Department of obstetrics and gynaecology at DMCH and BSMMU, Dhaka. Biochemical test was carried out in the department of Clinical pathology, DMCH and BSMMU. A total number of 100 pregnant women who fulfilled the inclusion criteria (3rd trimester of pregnancy, single viable pregnancy, single measurement of DBP ≥ 110 mm of Hg or two measurement of DBP 90 mm Hg on two consecutive occasion 6 hours apart, presence of urinary protein detected by heat coagulation test) were selected from patients attending the department of obstetrics and gynaecology at BSMMU and DMCH as indoor admitted patient. Systemic randomized sampling method was followed as per inclusion and exclusion criteria (proteinuria or HTN before conception, gestational age < 20 weeks). Statistical analysis was done by SPSS 11.5 for windows. A P value < 0.05 was taken as minimum level of significance.

Results

A total number of 100 pregnant women were included in the study. The study population was divided into Group 1 and Group 2. Group -1 included 50 healthy pregnant women of third trimester. Group -2 included 50 preeclamptic patients.

Table I: Age of the study subjects

Group	n	Age (Years) (Mean±SD)	P value ^a
Group 1	50	24.4±2.99	0.755 ^{NS}
Group 2	50	24.2±3.38	

^aUnpaired student's 't' test

^{NS}Not significant

Mean age of the subjects of both groups was almost equal.

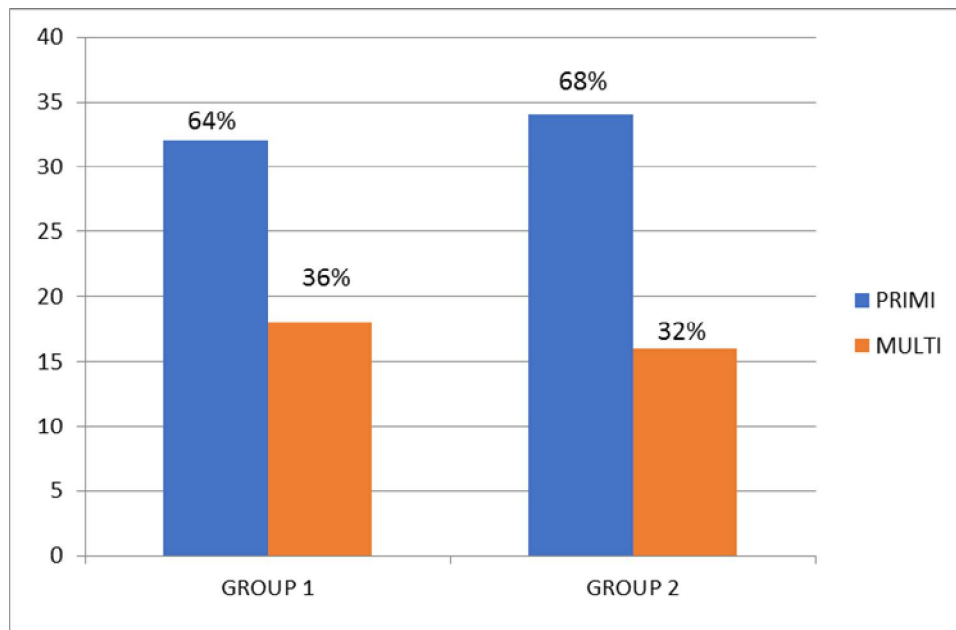


Fig 1. Parity distribution of the study subjects

Chi-square test: $X^2 = 0.178$, $df = 1$, $P = 0.673$ ^{NS}

^{NS} Not significant

Maximum numbers of the women were primiparous in both groups i.e. 64% and 68% in group 1 and group 2 respectively

Table II: Comparison of mean total serum alkaline phosphatase level between parity groups.

Parity group	N	Total alkaline phosphatase (IU/L) (Mean ± SD)	P value ^a
Group 1 Primiparous Multiparous	32	226.51 ± 69.81	0.247 ^{NS}
	18	232.19 ± 65.79	
Group 2 Primiparous Multiparous	34	164.32 ± 17.07	0.839 ^{NS}
	16	159.51 ± 15.23	

^aUnpaired student's 't' test

^{NS}Not significant

Mean total alkaline phosphatase level between primiparous and multiparous in group 1 and group 2 do not show any statistically significant difference.

Table III: Blood pressure levels of the study subjects

Group	N	Systolic blood pressure (mm of Hg) (Mean ±SD)	Diastolic blood pressure (mm of Hg) (Mean ±SD)	P value ^a
Group 1	50	108.37 ±9.74	71.63 ±7.08	0.000**
Group 2	50	153.2 ± 11.59	102.02 ± 8.63	

^aUnpaired student's 't' test.

**Significant at P <0.001.

Mean systolic and diastolic blood pressure levels between two groups is statistically significant (P<0.001).

Table IV: Total Alkaline phosphatase level of the study subjects

Group	n	Total alkaline phosphatase (IU/L) (Mean±SD)	P value ^a
Group 1	50	229.37 ± 71.53	0.000***
Group 2	50	162.64 ± 15.91	

^{Unpaired} student's 't' test.

***significant at P <0.001.

Mean total plasma ALP in group 1 was higher than group 2 and it was statistically significant (P<0.001).

Table V: Comparison of Alkaline phosphatase level with severity of pre-eclampsia

Group	n	Total alkaline phosphatase (IU/L) (Mean \pm SD)	P value ^a
Mild	35	166.37 \pm 11.36	0.000**
Severe	15	153.93 \pm 21.36	

^aUnpaired student's 't' test

**Significant at P<0.005

Comparison of alkaline phosphatase with mild and severe preeclampsia shows statistically significant difference.

Discussion

The cause of preeclampsia is still unknown.^{12,13} ALP is an isoenzyme that correlates with maturity of cytotrophoblast. There is progressive increase of ALP with advancement of pregnancy. The cause of progressive increase is still unknown. But there are some theories. Pregnancy increases osteoblastic enzyme activity in the mother and there is passage of foetal osteoblastic enzyme into the maternal circulation causing addition of TALP. This increase in the serum alkaline phosphatase during the second half of pregnancy was recognized and confirmed by many investigators.¹⁴⁻¹⁹ Table I showed that there was no statistically significant difference between the maternal ages of the preeclamptic patients and the control group (P>0.05). Similar findings were published in *Annals of African Medicine*.²⁰ Figure 1 showed maximum numbers of the women were primiparous in both groups. In Table II, comparison of mean total ALP between primiparous and multiparous in group 1 and group 2 did not show any statistically significant difference. Onwuameze et al ²¹ also reported that TALP and PALP had no statistically significant difference in primi and multiparous women. Table III showed that the mean blood pressures (both systolic and diastolic) in the controls were significantly lower (P < 0.001) than in the patients with pre-eclampsia. Table IV showed that mean total plasma ALP in normal pregnancy was

higher than preeclamptic patient and it was statistically significant (P<0.001). Similar findings were reported by Adeniyi and Olatundbosun.²² ALP is significantly higher in normal pregnancy than preeclamptic women between 28-40 weeks of pregnancy. Zuckerman et al ²³, Burtiset al⁸, Spellacy et al ²⁴ and Holmgren ²⁵ reported that PALP contributes to significant increase in TALP during normal pregnancy. Table 5 showed that there was significant relationship of ALP with mild and severe preeclampsia. Sadovsky, Y. Z. Diamant, H. Zuckerman, W. Z. Polishuk established that the activity of the enzyme was unchanged in mild preeclampsia and diminished progressively with advancement of the pathological process, compared with the respective values of normally progressing pregnancy at the same gestational period.²⁶

Conclusion

The study was done between healthy and preeclamptic women to assess the relationship of serum total alkaline phosphatase level with preeclampsia. It has demonstrated negative relationship between blood pressure and the level of serum TALP in patients with preeclampsia. It has also been found that both the systolic and diastolic blood pressures of the patients with preeclampsia correlated negatively with the serum total ALP level. So, it can be concluded that serum total alkaline phosphatase in maternal serum can be one of the biochemical parameter for preeclampsia.

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