Int J Pharm Bio Sci 2016 April; 7(2): (B) 446 - 450

Original Research Article Biochemistry

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

A STUDY OF SERUM ADENOSINE DEAMINASE ACTIVITY IN PRE-ECLAMPSIA AND NORMOTENSIVE PREGNANT WOMEN AT TERTIARY CARE HOSPITAL IN KARNATAKA

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ABSTRACT

Hypertensive disorders of human pregnancy, such as preeclampsia are a most common medical complication during pregnancy. The aim of this study was to investigate the adenosine deaminase activity in preeclampsia and healthy normotensive pregnant women. This is a hospital based case – control study. Total 120 subjects (60 cases of preeclampsia and 60 healthy normotensive pregnant women) with single foetus in the third trimester were recruited. The serum samples analysed for adenosine deaminase activity by Giusti G. and Galanti B. method. The serum adenosine deaminase activity was significantly increased in preeclampsia patients (26.15 ±4.95 U/L) as compare to healthy normotensive pregnant women (12.47 ±2.93 U/L). ADA is a marker of altered cellular immunity. The serum ADA is increased in preeclampsia due to enhanced cell mediated immune response and endothelial dysfunction. This increased adenosine deaminase activity may be predictive to assess the disease severity in preeclampsia.

KEY WORDS: **Preeclampsia; Adenosine deaminase activity; normotensive pregnancy.**

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INTRODUCTION

Preeclampsia is a multisystem disorder, characterised by hypertension (>140/90 mmHg) with proteinuria (>300mg/24hours urine), oedema or both, induced by pregnancy usually after 20 weeks of gestation. It is seen in 3-10 % of all pregnancies. It is still a major cause of maternal and foetal morbidity and mortality worldwide with multiple etiopathological factors.[1] Several studies are conducted to know the etiopathogenesis of preeclampsia, but it is still unknown. Several factors have been implicated in the development of preeclampsia, those includes abnormal trophoblast invasion of uterine blood vessels, immunological intolerance between feto-placental and maternal tissues.[2, 3] Adenosine deaminase (ADA) is widely distributed in human tissue, especially lymphoid tissues. The enzyme adenosine deaminase catalyses the hydrolytic deamination of adenosine and 2′-deoxyadenosine to inosine and 2′-deoxyinosine, respectively.[4] It plays important role in maturation and activation of human blood monocytes and macrophages. ADA has been considered as an indicator of a non-specific marker of T-cell activation. T-lymphocytes and monocyte-macrophages system have been assumed to be responsible for the increased serum ADA activity.[5, 6] However, the exact mechanism by which serum ADA activity is altered has not been identified. In normal pregnant women, serum total ADA activities were lower than non-pregnant women. It may be associated with depressed cell mediated immunity during normal pregnancy.[7] A large number of studies have shown that serum ADA activity is significantly increased in women with recurrent abortion, preeclampsia and hyperemesis gravidarum where cell-mediated immune response is thought to play important role in etio-pathogenesis.[8,9] In present study, we measured the serum ADA activity in normal pregnant women and pre-eclamptic pregnancies at tertiary care hospital in Karnataka.

MATERIALS AND METHODS

A case control study was conducted to estimate the levels of serum adenosine deaminase in normal pregnant women and pre-eclamptic pregnancies. In this study, we include the sixty clinically diagnosed preeclampsia patients from department of Obstetrics and Gynaecology, C.G. Hospital and Bapuji Hospital attached to J.J.M. Medical College, Davangere (Karnataka) from March 2013 to February 2014. The preeclampsia patients were diagnosed on the basis of development of hypertension (Systolic blood pressure greater than 140 mm Hg and / or Diastolic blood pressure greater than 90 mm Hg on two occasions at least 6 hour apart) and proteinuria of 300 mg or greater in 24 hour urine collection. The diagnosis of preeclampsia was based on the definition given by American College of Obstetrics and Gynaecologists.[10] In this study gestational age of patients was confirmed by ultrasonography examination. Patients with multiple pregnancies, congenital foetal anomaly, and multigravida, history of spontaneous abortion, smoking, diabetes mellitus, and evidence of any acute infections, medication, and history of any medical complication were excluded from study. Sixty healthy normotensive primigravida without any medical complication throughout the pregnancy are recruited as controls. All these controls are examined in the outpatient department of Obstetrics and Gynaecology, C.G. Hospital and Bapuji Hospital attached to J.J.M. Medical College, Davangere (Karnataka). All the subjects are voluntarily participated and gave informed written consent for this study. Under aseptic precaution 5 ml of fasting venous blood samples were collected in plane bulb and serum was separated after clot retraction. Serum adenosine deaminase activity was estimated by spectrophotometric method of Giuseppe Giusti and Bruno Galanti.[11] One unit of ADA was defined as the amount of enzyme required to release one micromole of ammonia per minute from adenosine at standard assay conditions. ADA activity was expressed as unit/ litre (U/L) in serum. Blood pressure was measured by using a sphygmomanometer and proteinuria were measured by using immunoturbidimetric method. Results were expressed as the mean ± SD and as the range. Statistical analyses were carried out using the SPSS statistical software package (SPSS for Windows version 16.0, SPSS Inc., Chicago, Illinois, USA). Student's *t*-test was used to analyse differences between normally distributed data. A p value <0.05 was considered as statistically significant.

RESULTS

The clinical description of the participants in this study is given in table 1. There were no significant difference among normotensive pregnant women and preeclampsia patients in terms of total numbers, maternal age, and gestation period. Changes in the serum ADA activities in normal pregnant women and preeclampsia are shown in table 2.

Table1
Clinical characteristics of normal pregnant women and preeclampsia patients

Variables	Normotensive Pregnant women (n=60)	Preeclampsia patients (n=60)	p-value
Maternal Age in Years (Mean ±SD)	24.97 ±3.49	25.24 ±3.31	0.665
Gestation period in weeks (Mean ±SD)	34.11 ±1.92	34.83 ±1.23	0.605
Systolic BP mmHg (Mean ±SD)	115.08 ±5.14	156.29 ±5.81	0.000*
Diastolic BP mmHg (Mean ±SD)	74.70 ±9.38	103.21 ±3.69	0.000*
Proteinuria in mg/24hour urine (Mean ±SD)	Nil	514.51 ±116.50	0.000*

*p value <0.05 is statistically significant**

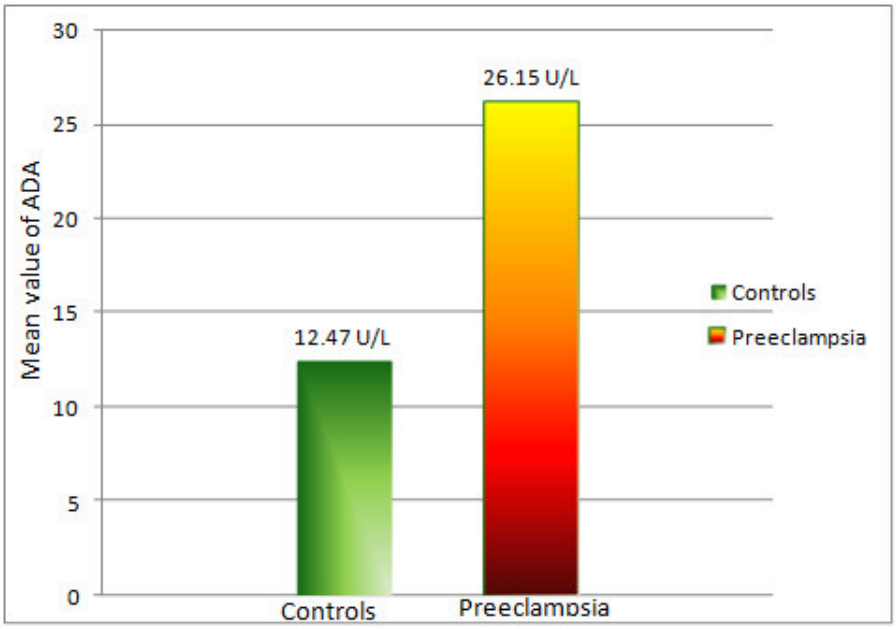
The mean age in years and the mean gestational period in weeks were not bio-statistically different in both the groups of normotensive pregnant women and preeclampsia patients. Systolic blood pressure was significantly higher for the preeclampsia patients (156.29 ±5.81 mmHg) as compare to normal pregnant women (115.08 ±5.14 mmHg). Diastolic blood pressure also significantly elevated in preeclampsia patients (103.21 ±3.69 mmHg) than normal pregnant women (74.70 ±9.38 mmHg).

Table2
Comparison of mean value of serum ADA in normal pregnant women and preeclampsia patients

Subjects	Serum ADA (U/L)			p-Value
	Mean	SD	Range	Normotensive Pregnant women V/S Preeclampsia patients
Normotensive Pregnant women	12.47	2.93	7.90-20.10	
Preeclampsia patients	26.15	4.95	16.60-38.40	0.000

The pre-eclamptic women showed a bio statistically significant higher (p<0.001) value of serum ADA (26.15 ±4.95 U/L) as compare to normal pregnant women (12.47 ±2.93 U/L). There was no significant correlation between the serum ADA activity and other measured variables such as maternal age, and gestational period.

Graph1
Bar diagram showing mean value of serum ADA in normal pregnant women and preeclampsia patients.



DISCUSSION

ADA is an essential enzyme for the differentiation of lymphoid cells, and changes in ADA activity reflect alteration in immunity. Lower maternal plasma ADA activity has been reported in normal pregnancies compared with non-pregnant women, but the clinical importance of this remains uncertain. In the present study, we observed a significant increase in serum ADA activity in pregnant women with preeclampsia, similar to that described by Yoneyama *et al.*[12, 13] The study conducted by Yoneyama *et al* [14]investigated the serum ADA activity and the pattern of two isoenzymes ADA1

and ADA2 to evaluate the possible role of cell mediated immunity as cause of change in ADA activity in preeclampsia. They found the increased serum total ADA and ADA2 activity in subjects with preeclampsia as compare to normotensive pregnant women. In normal pregnancy the decreased ADA activity reflects the depressed cell mediated immunity throughout gestation as compare to non pregnant women. One possible cause for decreased serum ADA activity in normal pregnancy may be due to increased synthesis of estradiol and cortisol which inhibits the ADA activity.[5, 15] The enzyme ADA is mainly located in haematopoietic cells, such as T-helper cells, monocytes and macrophages. Besides ADA, T-helper cells also produce the basic proinflammatory cytokines interleukin-2, tumour necrosis factor-α (TNF-α) and interferon-γ (IFN-γ). Proinflammatory and anti-inflammatory cytokines (such as IL-4, IL-6 and IL-10, which are produced by Th2 cells) are essential for the growth, differentiation and invasive capabilities of trophoblastic cells.[16] The results of present study are consistent with the study of Oladipo OO, Afolabi BB, and Okorodudu AO.[17] They showed that serum Adenosine deaminase activity increased in subjects with preeclampsia as compare to normotensive pregnant women or non pregnant women. It is due to enhanced cell mediated immunity in preeclampsia. A Study conducted by Karabulut AB, Sibai GM, Kafkasli A, Buruk F, Gozukara EM [18] demonstrate elevated level of serum total ADA and ADA2 activities in maternal serum and fetal cord blood of preeclampsia patients. According to this study, increased ADA activities may indirectly contribute to the maintenance of immune response in preeclampsia by controlling adenosine levels. The major source of circulating adenosine in the blood stream is the platelets, vascular endothelium, and erythrocytes.[19, 20] The result of study conducted by Jacquiti J, David M, Rosario H, Fernado N[21] showed decrease maternal serum ADA activity in normotensive pregnant women as compare to non pregnant women. It is due to depression of cell mediated immunity. In the present study, there was no significant correlation between systolic or diastolic blood pressure and maternal plasma ADA activity.

CONCLUSION

We concluded that increased activity of maternal serum ADA may be due to enhanced cell mediated immune response and endothelial dysfunction in preeclampsia. Reference values of serum ADA in preeclampsia may provide important database for making clinical decisions in high-risk pregnancies where cellular immunity has been altered. In addition, longitudinal studies, beginning from an early gestational age are needed to evaluate the use of ADA activity in maternal plasma as a marker of severity in preeclampsia.

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