

# Angiotensin-I and Plasma Renin Activity In Pre-eclampsia

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The etiology of pre-eclampsia has not been fully established, it is characterized by the development of hypertension and proteinuria after 20 weeks gestation. This study was designed to measure the plasma Angiotensin-I (Ang-I) and plasma renin activity (PRA) to evaluate the role of renin-angiotensin aldosterone system in pre-eclampsia.

A total of 60 women aged ((19 - 40)) year were included in this study. They were divided into three groups; normal non - pregnant (( n = 20 )) , normal pregnant (( n = 20 )) , and pre-eclamptic women (( n = 20 )) .

Angiotensin-I was measured by the radio immune assay technique and the plasma renin activity (PRA) is calculated as an amount of angiotensin I generated in [(ng/ml)/hr]. The mean  $\pm$  SD of Ang-I in normal non pregnant, normal pregnant and pre-eclamptic women was [(0.5 $\pm$ 0.15), (1.5 $\pm$ 0.2) and (3.1 $\pm$ 0.4) ng/ml] respectively. Statistical analysis (ANOVA) showed that Ang-I was significantly higher in preeclampsia ((P < 0.05)). A significant positive correlation between albuminuria and plasma Ang-I concentration was found in pre-eclampsia. And a positive correlation between albuminuria and PRA concentration was also found in pre-eclampsia.

The results showed there is clear increase in renin activity in preeclamptic women which might be expected to result in higher level of Angiotensin in the plasma, Since angiotensin-II is the most potent of the circulating vasoconstrictors in the human placental so that renin angiotensin (RA) systems plays the key role in blood pressure.

## Introduction

Pre-eclampsia is a disorder that occurs in the 2nd half of pregnancy and is characterized by hypertension and proteinuria (1).

Pregnancy induced hypertension (PIH) is one of the commonest complication of pregnancy. It accounts for 70% of hypertension seen in pregnancy and it is considered as a serious cause of fetal and maternal mortality and morbidity (2).

Renin is an aspartyl protease that specifically catalyzes the hydrolytic release of the decapeptide angiotensin I (Ang-I) from angiotensinogen, it is

released from the juxtaglomerular apparatus in the kidney (that are the site of synthesis, storage and release of renin), when there is severe reduction in sodium concentration or blood volume is detected. Renin acts on angiotensinogen to release Ang I, which is converted by angiotensin – converting enzyme (ACE) to Ang II, Ang II produce a potent rise in blood pressure through several routes, including; Vasoconstriction, Stimulation of the noradrenergic sympathetic nervous system and Stimulation of the adrenals to release aldosterone (3).

The RAA system is a major determinant

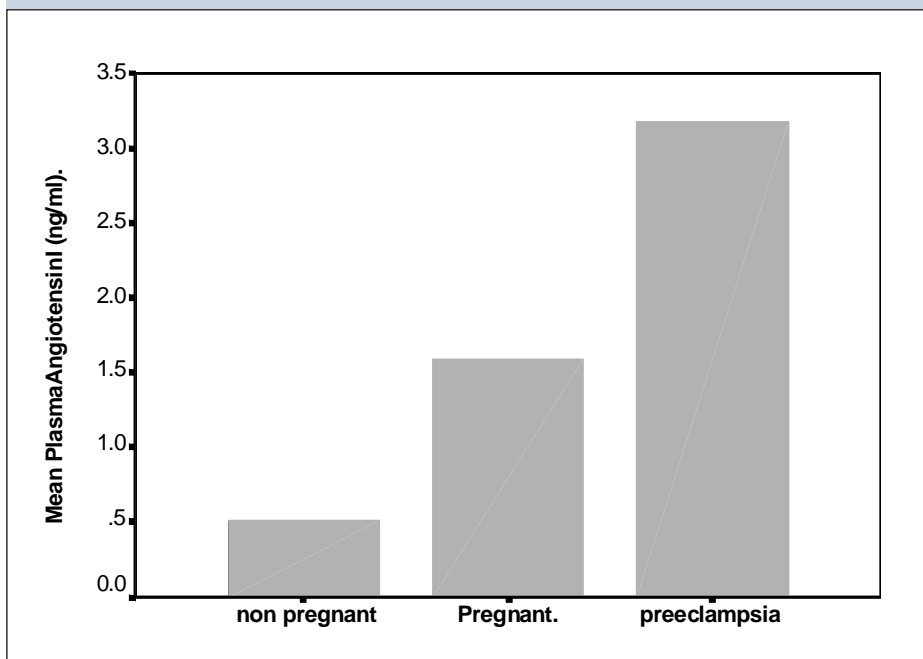


Figure 1 - Bar chart showing the mean plasma Ang-I in three study groups

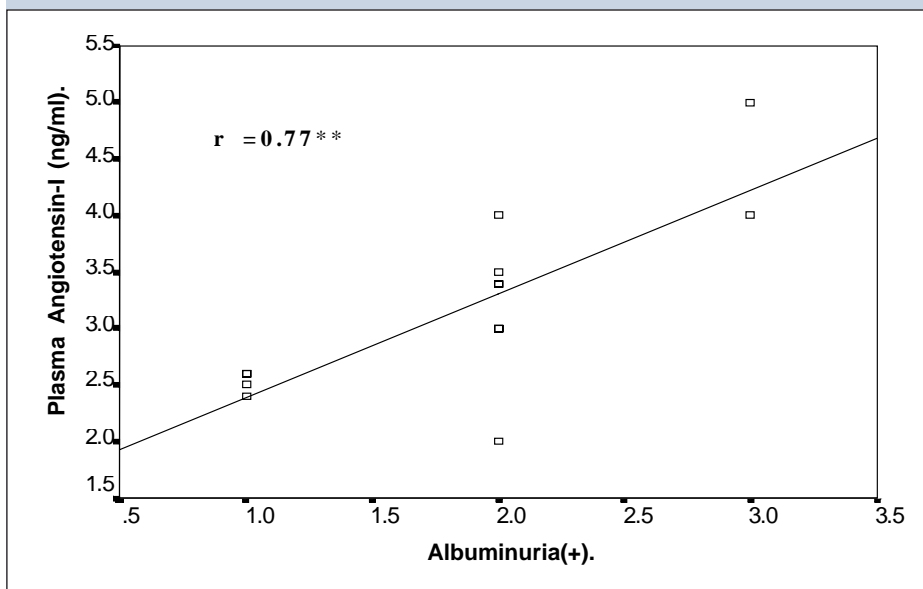


Figure 2 - Scattered plot with a fitted regression line showing the linear association between albuminuria (as a measure of PE severity) and plasma angiotensin I.

of sodium balance in pregnancy, and there is clear increase in renin activity in pregnant women which might be expected to result in higher level of Angiotensin in the plasma. Since angiotensin II most potent of the circulating vasoconstrictors in the human placenta (4).

In addition, it was reported that the concentration of aldosterone in plasma is increased in pregnant and it was about twice than those in control. So that renin angiotensin systems plays the key role in

blood pressure regulation and many investigators have postulated that alteration in the RA system plays a significant role in the pathophysiology of PIH, and recently the association between the angiotensinogen locus and PE/ eclampsia has been found (5).

**Patients and method**

Sixty women were involved in this study; all patients had no history of medical disorder. The maternal charac-

teristics recorded were age, parity, and gestational age at sampling time, number of abortion, systolic and diastolic blood pressure and proteinuria. They were divided into 3 groups: Group I: 20 normal non pregnant women, as a control, their mean age was 29±5.2 years, the mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were 120±7.3 and 80±5.3 mmHg, respectively. Group II: 20 healthy normotensive pregnant in the third trimester of pregnancy. Their mean age was 28±5.3 years, mean SBP and DBP were 115± 4.3 and 78± 6.2mm Hg, respectively and they had no proteinuria. Group III: 20 pre-eclamptic women in the third trimester of pregnancy. Their mean age was 31 ± 7.5 years, mean SBP and DBP were 150 ± 15.79 and 102 ± 11.73 mm Hg, respectively, the proteinuria was >1.2ml blood was placed into a plan plastic containing anticoagulant (disodium

**The data of this study revealed a significant difference in Ang-I and PRA between the three study groups**

ethylene diamine tetracetic acid). This tube was inverted several times for mixing. Plasma was separated after centrifugation and used for measuring the angiotensin I and then PRA (plasma renin activity).

The radioimmune assay of angiotensin is a competitive immune analytical determination. Unknown samples and standards are incubated together with 1125 angiotensin I in polyclonal anti-angiotensin I antibody- coated tubes. After incubation, the contents of the tubes are aspirated and the bound activity is measured in a gamma counter. The concentration of angiotensin I is reversibly proportionate to the radioactivity measured.

**Calculation of results**

The plasma renin activity (PRA) is calculated as an amount of angiotensin I (A-1) generated in 1ml/hr.

$$PRA[(ng/ml)/hr] = \frac{[(ng/ml)A-1(37^{\circ}C) - (ng/ml)A-1(4^{\circ}C)] \times 2}{incubationTime[hrs]}$$

**Result**

The mean ±SD plasma Angiotensin- I in PE, pregnant women and non pregnant control were 3.1ng/ml, 1.5ng/ml, 0.5ng/ml respectively and statistical analysis showed a significant difference between these three groups (p<0.05) as shown in table 1 and figure 1. There was a significant positive correlation at the 0.01 level between the plasma Angiotensin-I and both of albuminuria and diastolic blood pressure respectively, as illustrated in figure 2 and 3.

The mean±SD plasma renin activity in PE, pregnant women and non pregnant control was 4.9 ± 1.38 (ng/ml)/hr, 1.89± 0.59 (ng/ml)/hr and 0.46±0.15 (ng/ml)/hr respectively, as shown in table 1 and figure 4. Statistical analysis (ANOVA) showed a significant difference between the mean plasma renin activity among the three study groups, (p<0.05).

The data also revealed a significant positive correlation at the level (0.05) between the PRA and both of albuminuria (as a measure of PE severity) and diastolic blood pressure (as a measure of PE severity) at 0.01 level, as shown in Figure 5 and 6.

**Discussion**

The data of this study revealed a significant difference in Ang-I and PRA between the three study groups. Ang-I was significantly higher in PE group (P<0.05) in comparison to pregnant and non pregnant control ;table(1) .These results were in agreement with Symonds, et al ;(6) . They also found a highly significant correlation between the level of Angiotensin I in plasma and the DBP ,which was also confirmed in

our study, as shown in figure(3).

Plasma renin activity is defined as the rate of angiotensin I produced from angiotensinogen by renin in a patient's plasma .Renin released from the kidney

and acts upon angiotensinogen to split off the inactive decapeptide Ang I which is converted primarily by endothelial angiotensin converting enzyme (ACE) to the arterial vasoconstrictor octapeptide (angiotensin II) .Ang II stimulate aldosterone release ,thus Ang II may contribute to maintaining high vascular

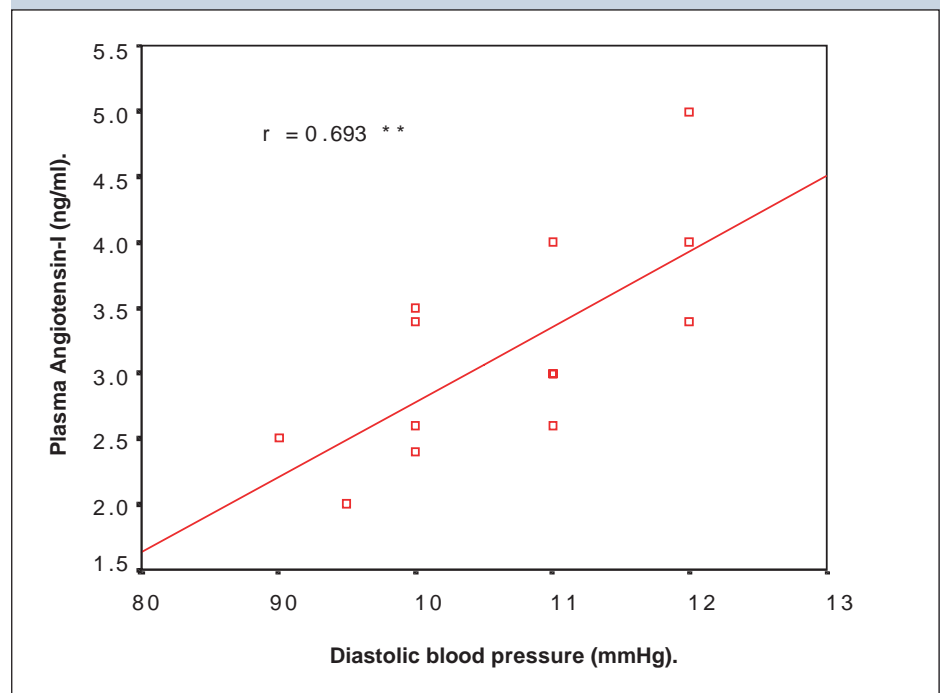
resistance in hypertensive state associated with high plasma renin activity. Intense vasoconstriction will lead to impairment in uterine blood flow, The uteroplacental unit respond by increasing synthesis and release of renin (7) with a consequent rise in Ang II in the systemic circulation, this increases the systemic arterial pressure .So any increase in circulating Ang II as a response to a fall in uteroplacental perfusion pressure will exert a vasoconstrictors, resulting in more reduction of uterine and placental perfusion eventually leads to PE/eclampsia(8).

The PRA is higher in pre-eclamptic patient group than other group, P<0.05 .The increased renin activity during

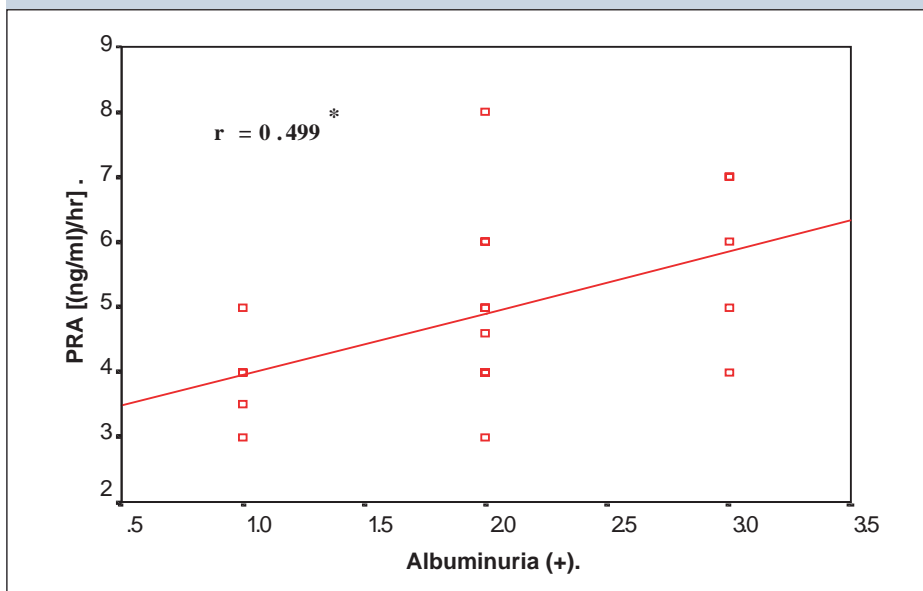
Groups	N	Mean ± SD Ang-I (ng/ml)	Mean ± SD PRA (ng/ml)/hr
Non pregnant control	20	0.5±0.15	0.46±0.15
Pregnant	20	1.5±0.2	1.89±0.59
Pre-eclampsia	20	3.1±0.4	4.9±1.38

\*The normal value for Ang-I is 0.5 ng/ml  
\*The normal value for PRA is 0.5-1.9 (ng/ml)/hr at rest, 1.9-6 (ng/ml)/hr after load

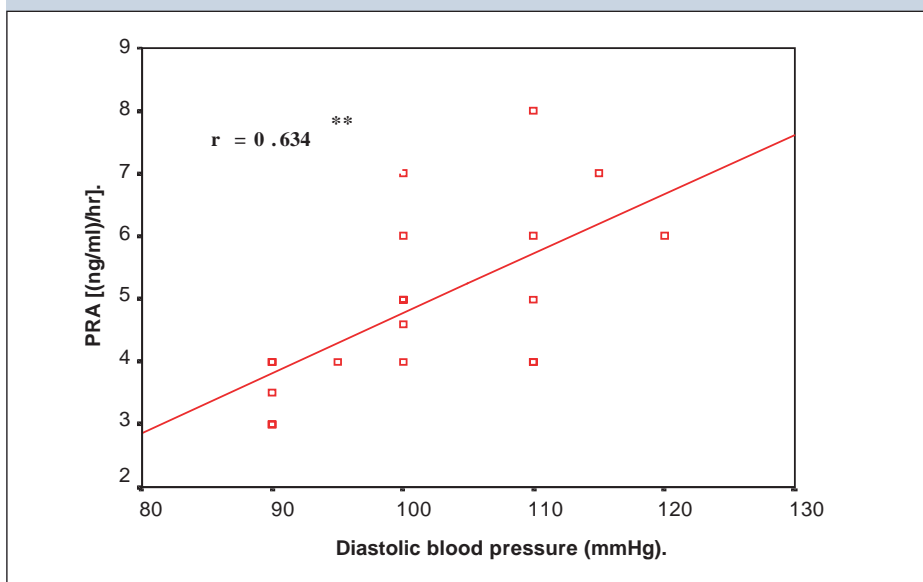
**Table 1** - The mean \*plasma Angiotensin I{PA-I} (ng/ml)and mean \*plasma rennin activity {PRA}{(ng/ml)/hr} ( for each of the three study groups.



**Figure 3** - Scattered plot with a fitted regression line showing the linear association between diastolic blood pressure (as a measure of PE severity) and plasma angiotensin I.



**Figure 5** - Scattered plot showing the linear association between albuminuria (as a measure of PE severity) and plasma renin activity.



**Figure 6** - Scattered plot showing the linear association between diastolic blood pressure (as a measure of PE severity) and the plasma renin activity. [\* the correlation is significant at the 0.05 level(2-tailed).] [\*\*the correlation is significant at the 0.01 level (2-tailed)].

pregnancy might be expected to be result in an elevation of Angiotensin level in the plasma. Our data agree with the data reported by other investigators (9), they found a greater increase in renin activity in hypertensive pregnant women than in normotensive pregnant women. Sunds Jord and Aakvaag (10) suggested that the increase in progesterone during the luteal phase will stimulate the release of renin and presumably angiotensin in the circulating blood and lead to increase secretion of aldosterone. In addition the hepatic extraction of aldosterone is decreased in pregnancy than in non-pregnant subjects (11).

Aldosterone has been suggested as the cause of PE edema as it promotes the retention of Sodium and water, in normal subjects, it has been suggested that the high secretary rate of Aldosterone during pregnancy serves to compensate for the loss of sodium induced by progesterone (11). The result of this study clearly indicated the important role of PRA and Ang-1 in the development of PE, In addition to a significant correlation between them and both of the albumin and DBP (marker of PE severity).

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