Renin-Angiotensin System in Pregnant South African Blacks

NORMOTENSIVE VERSUS HYPERTENSIVE DISEASE CASES

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SUMMARY

Plasma renin activity was measured in the arterial blood, peripheral venous blood, uterine venous blood and in the urine of pregnant South African Blacks, 14 normotensives and 19 with specific hypertensive disease. In addition renin activity was measured in the umbilical venous blood of the babies delivered by Caesarean section of these women. The renin activity was significantly lower in the blood of the specific hypertensive disease subjects than in the normotensives, but significantly higher in the urine of the hypertensive disease cases. Renin activity of the babies of the hypertensive and control subjects did not differ significantly.

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Specific hypertensive disease of pregnancy (pre-eclampsia, eclampsia) is associated *inter alia* with hypertension, increased aldosterone production, sodium retention, oedema, vascular spasm, and increased granularity of the juxtaglomerular cells.[1-4] These manifestations suggest that an imbalance of the renin-angiotensin system might be aetiologically related to the hypertensive syndrome. However, the data reported by different authors are contradictory. Tapia *et al.*[5] for instance, concluded that the plasma renin activity and plasma renin substrate are significantly elevated in both normotensive pregnant women and in women suffering from hypertensive disease of pregnancy, but that the renin-angiotensin system does not differ significantly in normotensive and hypertensive pregnant women. However, these authors also obtained an increase in plasma-angiotensinase activity in normotensive pregnant subjects and suggested that decreased inactivation of angiotensin II may play a role in the pathogenesis of hypertensive disease of pregnancy. Weir *et al.*,[6] on the other hand, found significantly lower renin, renin substrate, angiotensin II and aldosterone concentrations in the venous blood of women suffering from hypertensive disease of pregnancy than in normal pregnant controls, and concluded that raised circulating levels of these substances cannot be incriminated in the pathogenesis of hypertensive disease of pregnancy. In the present article the plasma renin activity of 33 pregnant South African Black women, 19 specific hypertensive disease cases and 14 normotensives, from whom the babies were delivered by Caesarean section, is reported.

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METHODS

Only 2 of the cases who participated in the present study attended an antenatal clinic before admission to hospital. Diagnosis of specific hypertensive disease of pregnancy was arbitrarily based on (*a*) the patient being pregnant for about 34 - 40 weeks; (*b*) a blood pressure exceeding 140/90 mmHg after a period of at least 30 min of recumbency; (*c*) no history of previous urinary tract infection or urinary tract disease; (*d*) the presence of significant proteinuria; and (*e*) a return to normal as far as the blood pressure and urine were concerned, within 12 days after delivery. With few exceptions, the clinical condition of the patients returned to normal within 5 days after delivery. Caesarean section was carried out within 2—24 h after admission and was necessitated by conditions such as placenta praevia and disproportion. The mass of the babies at delivery varied from 2,07 kg to 4,09 kg. Blood pressure measurements were made with a standard sphygmomanometer. The ages of the patients varied from 17 to 35 years (Table I).

Plasma renin activity was measured in the arterial blood, peripheral venous blood, uterine venous blood and in the urine of the mothers, and in the umbilical vein blood of the babies. Follow-up venous renin activity studies were also carried out 10 days postpartum in 3 hypertensive and 7 normotensive subjects. Renin activity was determined by means of the method of Boucher and Genest.[7] However, the plasma and urine were incubated for only 1 hour. Like angiotensin, catecholamines pass through the dowex columns, but the amines do not effect the net pressor response produced by angiotensin II unless they are present in very high concentrations especially noradrenaline. In the latter instance the additional pressor effect produced by noradrenaline can be nullified by the injection of phentolamine[8] into the animal model used for the bio-assay of renin activity. This was done in doubtful cases. As the catecholamine levels of the urine were very high in some of our hypertensive cases, renin

TABLE I. AGE, BLOOD PRESSURE, PLASMA AND URINE RENIN ACTIVITY IN NORMOTENSIVE AND HYPERTENSIVE DISEASE SUBJECTS

	Normotensive pregnant women		Hypertensive disease subjects		
	No. of subjects	$\bar{X} \pm SD$	No. of subjects	$\bar{X} \pm SD$	*P*
Age (years)	14	24,43 ± 3,77	19	25,11 ± 6,56	
Systolic BP (mmHg)	14	115 ± 8,23	19	163,68 ± 25,59	
Diastolic BP (mmHg)	14	75,36 ± 6,11	19	112,37 ± 17,19	
Plasma renin activity (ng Ang/ml/h)					
Arterial plasma	14	4,34 ± 2,65	19	1,89 ± 0,64	<0,01
Peripheral venous plasma	14	3,94 ± 2,29	19	1,86 ± 0,78	<0,01
Uterine venous plasma	14	4,49 ± 3,03	19	2,49 ± 1,05	<0,05
Umbilical venous plasma	14	6,04 ± 2,99	19	5,06 ± 3,02	>0,1
Urine renin activity (RIA) (ng Ang/ml/h)					
(a) RIA (4°C)	12	1,31 ± 1,70	16	2,43 ± 2,06	>0,1
(b) RIA (37°C)	12	2,15 ± 2,19	16	4,49 ± 4,47	<0,1
Difference between (b) and (a)		0,84 ± 0,68		2,09 ± 2,15	<0,05

$\bar{X}$ = arithmetic mean; SD = standard deviation.

activity of the urine was determined by bio-assay and by radio-immunoassay (RIA).[9] In the latter case renin activity was determined in urine samples kept at 4°C and again on aliquots of the same samples which had been incubated for 1 hour at 37°C. The difference in these 2 values was used for statistical analysis. The bladder was emptied just before operation and a urine sample collected during operation in a cooled tube containing 1 mg EDTA/ml urine. The results obtained by the 2 methods correlated well and consequently only those obtained by the immunoassay are presented (Table I, Fig. 1).

RESULTS

The renin activity was significantly lower in the arterial blood ($P<0,01$), peripheral venous blood ($P<0,01$) and in uterine venous blood ($P<0,05$) of the hypertensive disease cases, than in the normal subjects, but significantly higher in the urine of the hypertensive disease cases ($P<0,05$) than in the urine of the controls. The plasma renin activity of the uterine venous blood of the specific hypertensive disease cases was significantly higher than the plasma renin activity of their peripheral venous blood ($P<0,05$), but did not differ in the normotensives. The plasma renin activity of the peripheral venous blood of 3 hypertensive and 7 normotensive subjects (results pooled), was significantly lower ($P<0,01$) 10 days postpartum compared with the results obtained at delivery.

The renin activity of the venous umbilical blood of babies of the hypertensive and control subjects did not differ significantly, and hence cannot be invoked to explain differences in plasma renin activity in our hypertensive disease and normotensive subjects. The renin activity of the umbilical venous blood of babies of hypertensive disease mothers was significantly higher than the renin activity of the peripheral venous blood of their mothers ($P<0,01$). This difference was not present between normotensive mothers and their babies (Table I, Fig. 1).

DISCUSSION

Our results for plasma renin activity of hypertensive disease and control pregnant subjects are similar to those of Weir *et al.*[8] and Bonar *et al.*[10] The renin-angiotensin system of pregnant South African Blacks, therefore, does not behave differently from that of pregnant Europeans or Americans, notwithstanding considerable differences in dietary habits and in blood chemistry. The staple food of South African Blacks is maize, which is eaten in a variety of forms and in large quantities. The fat intake of these people is generally low and the crude fibre content of their diet high. The plasma albumin levels of this population group tend to be lower and the globulin levels higher than in the case of White South Africans.[11] The plasma renin activity of normotensive South African Black and White males, and of hypertensive Black and White males likewise, does not differ significantly (unreported observations).

The lower renin activity of the circulating blood in hypertensive disease of pregnancy may conceivably be traced back to excessive sodium retention[12,13] and the associated increase in total peripheral vascular resistance[14] and reduction in arterial compliance[15] in this condition. According to our results, increased urinary excretion of substrate or renin, or both, are contributory factors. A lower renin activity of the circulating blood does not, however, exclude an aetiological relationship between the renin-angiotensin system and hypertensive disease of pregnancy, since the sensitivity of these patients to angiotensin II is raised,[12,16] the biological half-life of angiotensin II increased,[5] and excretion of angiotensin I, as reflected by

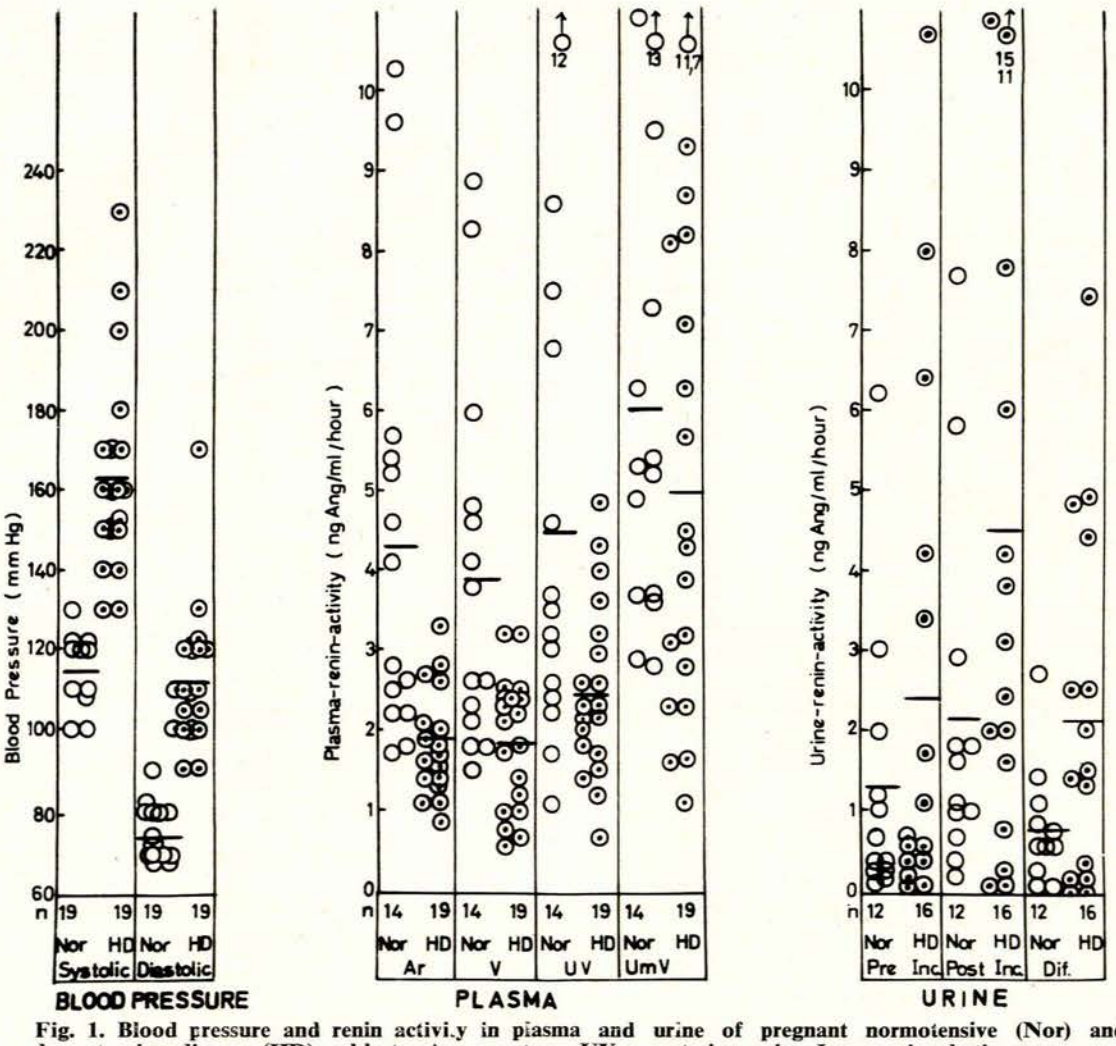

Fig. 1. Blood pressure and renin activity in plasma and urine of pregnant normotensive (Nor) and hypertensive disease (HD) subjects. Ar = artery; UV = uterine vein; Inc. = incubation; —— = arithmetic mean; V = vein; UmV = umbilical vein; Dif. = difference.

the present results, increased. In addition it has been reported that subjects predisposed to specific hypertensive disease of pregnancy have abnormally high plasma renin activity during the early subclinical stage of the disease.[17]

Hypertensive disease of pregnancy may conceivably then be initiated by hypersecretion of renin by the uterus[18,19] or kidneys[4] owing to inadequate blood perfusion or for some other reason. This leads to increased angiotensin II production, which stimulates aldosterone secretion and hence sodium retention. The rise in extra- and intracellular sodium increases the sensitivity of the blood vessels to angiotensin,[12,16] thus raising the peripheral resistance and blood pressures, but suppresses renin secretion through negative feedback. However, in spite of a drop in renin activity, increased vascular resistance and hence hypertension, are maintained through the raised vascular sensitivity to angiotensin.

Once the condition has become established[4] urinary excretion of substrate or renin, or both, may increase and contribute to the reduction in renin activity of the blood.

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