A Trend of Plasma Renin Activity among Hypertensive Patients in Basra

Abstract

Background: Measurement of plasma renin activity in hypertensive patients is of value in deciding the specific antihypertensive drugs for certain patient's characteristics and in resistant hypertension where it can diagnose different form of secondary hypertension. Certain patient's variables affect plasma renin level.

Objective: To study the relation of many variables with the plasma renin activity among hypertensive patients e.g. patients age, gender, body weight, race, smoking, type & duration of hypertension, comorbidity, controllable state and serum potassium level.

Patients and Methods: A cross sectional study was performed on patients with hypertension attends the private clinic, outpatient's clinic and medical ward in Basra for the period of June 2011 to the June 2012.

Result: The study involved 144 patients. Eighty four (58.3%) patients were male and 60(41.7%) patients were female with an age range of 18-78 years and a mean age of 43.5 +/- 13 SD. Twenty four (16.7%) patients were less than 30 years old, 107(74.3%) patients were between 31-60 years and 13(9%) patients were more than 61 years. Twenty two (15.3%) patients were black and 122(84.7%) were white. Nine (6.3%) patients were obese, 59(41%) were overweight and 76(52.8%) were of normal weight. One hundred twenty four (86.7%) patients have no comorbidity, 7(4.9%) have diabetes, 4(2.8%) have CKD, 6(4.2%) have IHD and 2(1.4%) have stroke. Thirty nine (27.1%) patients were smoker and the rest were non smokers. In all age groups, the plasma renin was frequently high, 58.3 % in age group less than 30 years, 62.2% in age 31-60 years and 61.5% in over 61 years old but no statistical significant correlation (Pearson value = 0.931). In both genders, the plasma renin was frequently high 64.3% in male and 58.3% in female but there is no statistical significant correlation (Pearson value = 0.313). In all BMI groups, the plasma renin was frequently high 57.9% in normal weight, 67.8% in overweight and 55.6% in obese but there is no statistical significant correlation (Pearson value = 0.583). In regard to the race, 68.2% black patients have low plasma renin and 68% white patients have high plasma renin which was statistically significant (Pearson value = 0.000). The plasma renin was high both in hypertension less than 3 years (61.8%) and more than 3 years (61.9%) which was statistically non significant correlation (Pearson value = 0.988). In essential hypertension, 10.5% patients have low renin, 27.4% have normal renin and 62.1% have high renin. In comparison with secondary hypertension, there is no statistical significant correlation (Pearson value = 0.972). The plasma renin was high more frequently in systolic (63.6%), diastolic (58.6%) and systolic and diastolic (62.5%) hypertension but there is no statistical significant correlation (Pearson = 0.350). The plasma renin was high more frequently in smokers (61.5%) and non smokers (61.9%) but no statistical significant correlation (Pearson value = 0.360).

Conclusion: Many variables may affect the plasma renin which in turn guides the specific antihypertensive drugs. High plasma renin was more common in almost all variables and variables subgroups except in black races where the plasma renin is low. There is no significant statistical correlation between plasma renin and age, gender, BMI, duration of hypertension, type of hypertension and type of dominant blood pressure elevation. Smoking has no effect on plasma renin.

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Introduction

Hypertension is the most treatable and prevalent risk factor for heart disease, stroke and kidney failure [1]. It has been more than adequately demonstrated that lowering BP reduces cardiovascular morbidity and mortality. Nevertheless, only 36% of patients with hypertension have adequately controlled BP [2]. It has been estimated that 15% of essential hypertension is

associated with high plasma renin, 25% with low plasma renin and 55-60% with normal plasma renin [3]. Low renin hypertension is characterized by volume excess and a favorable response to either diuretics or calcium channel blockers. High renin hypertension is characterized by vasoconstrictor excess and a favorable response to beta-blockers or angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blockers (ARBs). The normal renin hypertension has the combination of both volume and vasoconstrictor mechanisms [3,4].

The untreated patients with newly diagnosed hypertension are more likely to be younger (<50 years of age) and more likely to have stage 1 or 2 hypertension [4]. Choosing therapy based on hormonal profiling, particularly on renin sodium profiling, has been advocated [5]. There are several underlying assumptions to the renin-based strategy. First, the assumption is that measurement of renin accurately identifies hypertensive patients who will have a predictable response to specific antihypertensive therapy [6]. The second underlying assumption is that specific therapy is more effective in different subgroups, e.g., diuretics and calcium channel blockers are more effective in low-renin patients and ACE inhibitors or angiotensin receptor blockers are more effective in high-renin patients [7].

Combination therapy is usually necessary in patients with medium-renin levels, since both vasoconstrictive and volume mechanisms may be involved in the pathogenesis of their elevated BP. Such an approach could lead to earlier recognition of secondary hypertension and mechanistically based therapy that might lower BP in a shorter period of time, with fewer drugs per patient, and hopefully fewer adverse effects. Measuring renin in patients already on therapy is valuable for the physician whether to increase the drugs dosage, add second or third drugs or switch to other drugs [8]. For example, an individual with uncomplicated essential hypertension is taking Lisinopril 40 mg daily and has a BP of 160/95 mm Hg. Measuring a plasma renin level can guide your response in this situation.

If the renin level is very low, then it is unlikely that the Lisinopril is having much of a therapeutic effect, since patients with a reactive renin system should have an increased renin while on ACE inhibitor therapy. A reasonable strategy would be to stop the ACE inhibitor and start a diuretic. If the renin level is high, then it might be reasonable to add either a β blocker or an angiotensin receptor antagonist. Similarly, if a patient taking a diuretic still has elevated BP and the renin level is high, then an ACE inhibitor or angiotensin receptor blocker should be considered. If the renin level is low while on a diuretic, then an aldosterone antagonist could be considered. Measuring renin in patients with resistant hypertension is valuable in diagnosing secondary form of hypertension [9]. For example, low renin and high aldosterone may be the clue for primary aldosteronism as a cause of secondary hypertension.

Patients and Methods

This is a cross sectional study of patients with hypertension attends the private clinic, outpatient's clinic and medical ward in Basra. One hundred forty four patients with hypertension (84(58.3%) male and 60 (41.7%) female) with an age range of 18-78 years and a mean age of 43.5 +/- 13 SD were studied. A history was taken regarding the age, gender, duration of hypertension, controllable state, co-morbid conditions and smoking history. The race of the patients was observed. Body mass index (BMI) using the weight and the height with the formula (BMI=wt./ht.2) and classifying BMI into: normal (15.5-24.9), overweight (25-29.9) and obese (< 30) was measured. Blood pressure was measured using mercury sphygmomanometer in a quiet room; with the patients relax in a seated position, no tea, coffee or smoking for at least 30 min prior to measurement and 1 minute apart for two measurements [10]. Hypertension was classified according to European society of hypertension into:

i. Stage 1 (systolic) 140-159/ (diastolic) 90-99.

ii. Stage 2 (systolic) 160-179/ (diastolic) 100-109.

Stage 3 (systolic) more than 180/(diastolic) more than 110 [11]. A control state was assessed by blood pressure measurement every 2 weeks to assess the efficacy of the drugs and hence the control state. Evidence for secondary hypertension was looked for by history of difficult to control or accelerated hypertension, resistant hypertension or early onset hypertension. Also, by clinical examination and specific investigations e.g. serum aldosterone and plasma catecholamine's. Investigations were done and include the following: fasting blood sugar (70-110 mg/dl), serum creatinine (0.5-1.1mg/dl), serum potassium (3.5-5.3 mEq/l), plasma renin (3.3-30.7 ng/l) in the upright posture by ELISA method. Statistical analyses were performed using SPSS (15) and the Pearson chi-square value of > 0.05 was considered to indicate statistical significance.

Results

The study involved 144 patients. The socio-demographic characteristic of the studied hypertensive patients were presented in (Table 1). Eighty four (58.3%) patients were male and 60(41.7%) patients were female with an age range of 18-78 years and a mean age of 43.5 +/- 13 SD. Twenty four (16.7%) patients were less than 30 years old, 107(74.3%) patients were between 31-60 years and 13(9%) patients were more than 61 years. Twenty two (15.3%) patients were black and 122(84.7%) were white. Nine (6.3%) patients were obese, 59(41%) were overweight and 76(52.8%) were of normal weight. One hundred twenty four (86.7%) patients have no comorbidity, 7(4.9%) have diabetes, 4(2.8%) have CKD, 6 (4.2%) have IHD and 2(1.4%) have stroke. Thirty nine (27.1%) patients were smoker and the rest were non smokers.

Table 2 shows correlation of many studied variable with the plasma renin. In all age groups, the plasma renin was frequently high, 58.3% in age group less than 30 years, 62.2% in age 31-60 years and 61.5% in over 61 years old but no statistical significant correlation (Pearson value = 0.931). In both genders, the plasma renin was frequently high 64.3% in male and 58.3% in female but there is no statistical significant correlation (Pearson value = 0.313). In all BMI groups, the plasma renin was frequently high 57.9% in normal weight, 67.8% in overweight and 55.6% in obese but there is no statistical significant correlation (Pearson value = 0.583). In regard to the race, 68.2% black patients have low plasma renin and 68% white patients have high plasma renin which was statistically significant (Pearson value = 0.000).

Table 1: Socio-demographic characteristic of the hypertensive patients.

Variables		No. (%)
Hypertensive patient No.		144 (100%)
Age in years	> 30	24 (16.7%)
	31-60	107 (74.3%)
	< 61	13 (9.0%)
Gender	Male	84 (58.3%)
	Female	60 (41.7%)
Race	White	122 (84.7%)
	Black	22 (15.3%)
BMI kg/ht 2	15.5-24.9	76 (52.8%)
	25.0-29.9	59 (41.0%)
	<30	9 (6.3%)
Comorbidity	No	124 (86.7%)
	DM	7 (4.9%)
	CKD	4 (2.8%)
	Stroke	2 (1.4%)
	IHD	6 (4.2%)
Smoking	Smokers	39 (27.1%)
	Non smokers	105 (72.9%)

The plasma renin was high both in hypertension less than 3 years (61.8%) and more than 3 years (61.9%) which was statistically non significant correlation (Pearson value = 0.988). In essential hypertension, 10.5% patients have low renin, 27.4% have normal renin and 62.1% have high renin. In comparison with secondary hypertension, there is no statistical significant correlation (Pearson value = 0.972). The plasma renin was high more frequently in systolic (63.6%), diastolic (58.6%) and systolic and diastolic (62.5%) hypertension but there is no statistical significant correlation (Pearson = 0.350). The plasma renin was high more frequently in smokers (61.5%) and non smokers (61.9%) but no statistical significant correlation (Pearson value = 0.360).

Discussion

One hundred forty four patients with hypertension were studied. In regard to age, low plasma renin was seen more in age of 41-60 years (16.9%) which is in the agreements with the most literatures that plasma renin falls with increasing age, normal plasma renin was seen more in age 21-40 years (31.4%) and high plasma renin was seen more in age 21-40 years (64.3%) which is mean that younger patients have high more than normal plasma renin. High plasma renin was more frequent in all age groups. In regard to gender, low plasma renin was more common in female (6.3%) which is in agreements with the most literatures that plasma renin is low in female, normal plasma renin was more common in male (16.7%) and high plasma renin was more common in male (37.5%). In both genders the high plasma renin was more frequent (61.5%). In regard to weight, low plasma renin was more common in 61-80 kg body weight (5.6%), normal plasma renin was more common in 61-80 kg body weight (16.7%)

and high plasma renin was more common in 61-80 kg body weight (28.5%). In all body weight, high plasma renin was more frequent (61.8%).

In the present study, as more patients studied were in the 61-80 kg body weight and small number of patients were more than 100 kg so we cannot conclude increasing weight is associated significantly with increasing plasma renin. In regard to race, white and black races had high plasma renin more frequently 82(56.9%) and 7(4.9%) respectively. In contrast to all literatures, where plasma renin is low in black race, the present study shows the contrary, because most of our patients are of white races 134(93.1%). In regard to duration of hypertension, high plasma renin was seen more frequently in all duration of hypertension. In contrast to the truth that plasma renin fall with long-standing hypertension, this is because only 7 (4.9%) patients have duration of hypertension more than 5 years.

In regard to comorbidity, most of patients have no comorbidity (86.7%), high plasma renin was more frequent in all co-morbid conditions. In diabetes and chronic kidney disease (CKD), the plasma renin level was high. Patients with CKD have high or normal plasma renin which is in the agreements with the present study, but diabetic patients have low renin which in the contrary to the present study, this is because only 7(4.9%) patients have diabetes so we need more diabetic patients to confer this correlation. In regard to controllable state, low, normal and high plasma renin was more common in controllable hypertension (77.8%). In uncontrolled hypertension, the high plasma renin was more frequent (8.3%) which is in the agreements that resistant hypertension is associated with high plasma renin.

In regard to type f hypertension, high plasma renin was more common in both primary and secondary hypertension (53.5% and 8.3%) respectively. In the present study, 9% of primary hypertensive patients have low renin and 53.5% have high renin. Laragh had estimate the frequency of plasma renin in primary hypertension, about 15% of patients have high renin and 25 % have low renin. The possible explanation could be attributed to different patient's population. In regard to blood pressure elevation, high plasma renin was more common in systolic hypertension (4.9%), this is in contrast to study done by Durukan, Guray, Demirkan and Korkmaz in Torso Hospital, Department of Cardiology, Mersin, Turkey, where they conclude that isolated systolic hypertension is associated with low plasma renin [11]. High plasma renin was more common in diastolic hypertension (11.8%) and also high plasma renin was more common in systolic and diastolic hypertension (45.1%).

High plasma renin was more frequent in diastolic than systolic hypertension (11.8% and 4.9%) respectively. In regard to smoking, both low, normal and high plasma renin were more frequent in non smoker (72.1%). In smokers, plasma renin was high (16.7%) but we need to study more smokers hypertensive patients to assess any causal association. In regard to serum potassium, high plasma renin was associated more with normal serum potassium (49.3%), normal plasma renin was associated more with normal serum potassium (22.2%) and low plasma renin was associated more with normal serum potassium (8.3%). Low serum potassium was seen more with high plasma renin

(11.15). In regard to serum creatinine, high plasma creatinine was associated more with normal plasma renin (2.8%). In regard to fasting blood sugar, high blood sugar was associated more with high plasma renin (61.8%).

Table 2: Distribution of the plasma renin according to the studied variables.

Variables		Plasma Renin in ng/ml			Total	Pearson Chi-Square test
		> 3.2	3.3-30.7	< 30.8		
Age in years	> 30	2 (8.3%)	8 (33.3%)	14 (58.3%)	24 (100.0%)	0.931
	31-60	11 (10.3%)	29 (27.1%)	67 (62.2%)	107 (100.0%)	
	< 61	2 (15.4%)	3 (23.1%)	8 (61.5%)	13 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	
Gender	Male	6 (7.1%)	24 (28.6%)	54 (64.3%)	84 (100.0%)	0.313
	Female	9 (15.0%)	16 (26.7%)	35 (58.3%)	60 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	
BMI kg/ht2	15.5-24.9	8 (10.5%)	24 (31.6%)	44 (57.9%)	76 (100.0%)	0.583
	25.0-29.9	5 (8.5%)	14 (23.7%)	40 (67.8%)	59 (100.0%)	
	<30	2 (22.2%)	2 (22.2%)	5 (55.6%)	9 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	
Race	white	0 (0.0%)	39 (32.0%)	83 (68.0%)	122 (100.0%)	0.000
	black	15 (68.2%)	1 (4.5%)	6 (27.3%)	22 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (16.8%)	144 (100.0%)	
Duration of hypertension in years	>3	13 (10.6%)	34 (27.6%)	76 (61.8%)	123 (100.0%)	0.988
	<3	2 (9.5%)	6 (28.6%)	13 (61.9%)	21 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	
Types of hypertension	Primary	13 (10.5%)	34 (27.4%)	77 (62.1%)	124 (100.0%)	0.972
	Secondary	2 (10.0%)	6 (30.3%)	12 (60.0%)	20 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	
Elevated blood pressure	Systolic	1 (9.1%)	3 (27.3%)	7 (63.6%)	11 (100.0%)	0.350
	Diastolic	6 (20.7%)	6 (20.7%)	17 (58.6%)	29 (100.0%)	
	Both	8 (7.7%)	31 (29.8%)	65 (62.5%)	104 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	
Smoking	Smoker	2 (5.1%)	13 (33.3%)	24 (61.5%)	39 (100.0%)	0.360
	Non smoker	13 (12.4%)	27 (25.7%)	65 (61.9%)	105 (100.0%)	
	Total	15 (10.4%)	40 (27.8%)	89 (61.8%)	144 (100.0%)	

In the present study, there is no correlation between the age and the plasma renin which is in the contrary to study done by Thomas GW and colleagues where they showed significant inverse relationship between plasma renin activity and the age, independent of blood pressure [12,13]. Other study done by Peter Weidmann and colleagues which showed that Plasma renin levels were decreased in the elderly [14]. The possible explanation is that the age groups are not uniformly distributed with fewer patients in the age group of more than 61(9%). The plasma renin was more frequently high in the female which is in disagreement with a study done by Cowley AW and colleagues who showed that plasma renin is low in female [15].

But, the plasma renin in the male was more frequently high which is in the agreement with the study. The possible explanation could be attributed to geographical variation between eastern and western female in regard to renin level. The plasma renin was more frequently high in obese patients who are in disagreement with study done by Franz H and colleagues where they showed that obesity is associated with intravascular volume expansion, low peripheral vascular resistance and low plasma renin [16,17]. This could be attributed to small sample size of the obese patients (6.3%). The black races had low plasma renin which is in agreement with a study Price DA and Fisher ND where they showed that black races had low plasma renin [18].

In the present study, white races had high plasma renin. There is no correlation between duration of hypertension and plasma renin level. In the present study, high renin was account for 62.1% of the studied patients with essential hypertension whereas account for 15% by Laragh study, low renin accounts for 10.5% whereas accounts for 25 % by Laragh and normal renin accounts for 27.8% whereas accounts for 55-60% by Laragh [4]. So, high renin essential hypertension is the most common form in our country. There is no correlation between systolic and diastolic blood pressure with plasma renin. This is in contrast to study done by Licata G and colleagues where they showed that there is positive correlation between diastolic blood pressure and plasma renin [18].

Also, this is in contrast to study done by Durukan and colleagues in Torso Hospital, Department of Cardiology, and Mersin, Turkey, where they conclude that isolated systolic hypertension is associated with low plasma renin [19]. This could be attributed to small sample size of isolated systolic and diastolic hypertension. There is no correlation between smoking and plasma renin in our study which is in agreement with study done by Leslie Baer and Ildiko Radichevich where they conclude that plasma renin is not affected by smoking in contrast to other vasoconstrictor e.g. catecholamines and cortisol where they increased in smokers [20].

Conclusion

Many variables may affect the plasma renin which in turn guides the specific antihypertensive drugs. High plasma renin was more common in almost all variables and variables subgroups except in black races where the plasma renin is low. There is no significant statistical correlation between plasma renin and age, gender, BMI, duration of hypertension, type of hypertension and type of dominant blood pressure elevation. Smoking has no effect on plasma renin.

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