

A study of renal artery stenosis among hypertensive patients in Basrah (Iraq)

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ABSTRACT

Background: Renal artery stenosis (RAS) is the most common potentially curable cause of secondary hypertension. It accounts for less than one percent of mild hypertension and 10 to 45 percent of severe or malignant hypertension. Atherosclerotic type is the most common form.

Objective: To study the prevalence of renal artery stenosis among hypertensive patients with the aid of clinical criteria suggestive of the diagnosis.

Patients and Methods: A cross-sectional study of patients with hypertension attended a private clinic, outpatient's clinic, emergency department, nephrology ward and coronary care unit in Basrah teaching hospital from the period of January 2010 to January 2012.

Results: The study involved 27 patients with hypertension diagnosed as renal artery stenosis. Atherosclerotic RAS accounted for 77.8% of cases, while fibromuscular dysplastic RAS accounted for 22.2% of cases. The ARAS was more common in female (57.1%) and accounted for 100% of cases more than 60-year old. The FMD type was more common in female (66.7%) and accounted for 100% of cases younger than 30-year old. The most common clinical criteria suggestive for the diagnosis was unexplained renal azotemia (25.9%). Nephrotic range proteinuria was reported in 11.1% while non-nephrotic proteinuria in 51.9%. LVH was reported in 40.7%. The Doppler ultrasound was normal in 96.3. The MRA shows left proximal stenosis in 22.2%, right proximal stenosis in 33.3%, left distal stenosis in 3.7%, right distal stenosis in 18.5% and bilateral stenosis in 22.2%. Hypokalemia was reported in 70.4%. The serum cholesterol was normal in 77.8%.

Conclusion: Renal artery stenosis is more common in whites and rare in blacks. The atherosclerotic type is more common and it is more common in the older age group. The fibromuscular type is more common in the younger age group. Right renal artery stenosis is more common than the left.

دراسة تضيق الشريان الكلوي لدى مرضى ارتفاع ضغط الدم في البصرة (العراق)

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المقدمة: ارتفاع ضغط الدم الناتج عن تضيق الشريان الكلوي هو واحد من أسباب ارتفاع ضغط الدم الثانوي الأكثر شيوعاً والممكن علاجه. انه يمثل اقل من ١% من ارتفاع ضغط الدم البسيط و ١٠-٤٥% من ارتفاع ضغط الدم الشديد. تصلب الشرايين العصيدية هو النوع الأكثر شيوعاً.

الهدف: دراسة مدى انتشار تضيق الشريان الكلوي كسبب لارتفاع ضغط الدم بمساعدة مواصفات سريرية تشخيصية.

الطريقة: دراسة مقطعية أجريت على مرضى مصابين بارتفاع ضغط الدم راجعوا العيادة الخاصة، العيادة الاستشارية الباطنية وعيادة أمراض الكلى، قسم الطوارئ، مركز أمراض الكلى ووحدة إنعاش القلب من شهر كانون الثاني ٢٠١٠ الى كانون الثاني ٢٠١٢.

النتائج: الدراسة شملت ٢٧ مريض مصابين بارتفاع ضغط الدم الناتج عن تضيق الشريان الكلوي. نوع تضيق الشرايين العصيدية شمل ٧٧.٨% من الحالات، بينما نوع تضيق الشرايين العضلي الليفي شمل ٢٢.٢% من الحالات. نوع تضيق الشرايين العصيدية كان أكثر شيوعاً لدى الإناث بنسبة ٥٧.١% وشكل نسبة ١٠٠% من الحالات في المرضى الأكثر من ٦٠ سنة. نوع تضيق الشرايين العضلي الليفي كان أكثر شيوعاً لدى الإناث بنسبة ٦٦.٧% وشكل نسبة ١٠٠% من الحالات في المرضى الأقل من ٣٠ سنة. أكثر صفة سريرية شيوعاً أدت الى تشخيص الحالة كانت عجز الكلى الغير مشخص بنسبة ٢٥.٩%. زلال الإدرار بالمستوى الكلاني سجل بنسبة ١١.١% بينما زلال الإدرار بالمستوى الغير كلاني سجل بنسبة ٥١.٩%. تضخم عضل القلب سجل بنسبة ٤٠.٧%. سونار الدوبلر كان طبيعياً في ٩٦.٣% من الحالات. رنين الشرايين الكلوية اظهر تضيق الشريان الكلوي الأيسر الداني ب ٢٢.٢% من الحالات، الشريان الكلوي الأيمن الداني ب ٣٣.٣%، الشريان الكلوي الأيسر القاصي ب ٣.٧%، الشريان الكلوي الأيمن القاصي ب ١٨.٥% وكلا الشرايين الأيمن والأيسر ب ٢٢.٢% من الحالات. نقص البوتاسيوم سجل ب ٧٠.٤% من الحالات. نسبة الكوليستيرول كانت طبيعية ب ٧٧.٨% من الحالات.

الاستنتاج: تضيق الشريان الكلوي أكثر شيوعاً لدى ذوات البشرة البيضاء ونادراً لدى ذوات البشرة السوداء. تضيق الشرايين العصيدية هو النوع الأكثر شيوعاً وهو الأكثر شيوعاً في المرضى الأكثر من ٦٠ سنة. تضيق الشرايين العضلي الليفي هو الأكثر شيوعاً في المرضى الأقل من ٣٠ سنة. تضيق الشرايين الكلوية اليمنى هي الأكثر شيوعاً من اليسرى.

INTRODUCTION

Renal artery stenosis (RAS) is the most common potentially curable cause of secondary hypertension. It probably occurs in less than 1 percent of patients with mild hypertension.^[1] By comparison, between 10 and 45 percent of severe or malignant hypertension have renal artery stenosis. It can be detected in patients with other evidence of atherosclerosis, such as coronary artery disease (10-14 percent) and peripheral arterial and aortic disease (24-35 percent).^[2] It is caused by a heterogeneous group of conditions, including atherosclerosis (ARAS), fibromuscular dysplasia (FMD), vasculitis, neurofibromatosis, congenital bands, and extrinsic compression, and radiation.^[3] Atherosclerosis accounts for approximately 90% of the lesions and typically involves the ostium and/ or proximal one-third of the renal artery and often the adjacent aorta.^[4] However, segmental and diffuse intrarenal atherosclerosis may also be observed, especially in advanced cases.^[5] The prevalence of ARAS increases with advancing age and with the presence of traditional cardiovascular risk factors. Among patients with hypertension, ARAS is observed in only 1% to 6%,^[6-8] whereas the incidence of ARAS is more than 30% in patients undergoing cardiac catheterization^[9,10] and more than 50% in elderly patients with known atherosclerotic disease.^[11,12] Atherosclerotic renal artery stenosis results in a progressive loss of renal mass and function over time.^[13,14] Among adult, FMD is more common among females. In most large series, 85-90% of cases are in women. There does not appear to be a female predominance in children.^[15] It accounts for 10-15 percent of cases in adult under the age of 50 years and 35-50 percent of cases in children.^[16-20] The lesion usually involves the mid to distal vessel. It is bilateral in 35 to 50 percent and nearly half of those have extra renal involvement.^[21,22] It can be an incidental finding. In one review, FMD was observed in 71 of 1862 renal arteriogram (4 percent) obtained in kidney potential donors.^[23]

PATIENTS AND METHODS

This is a cross-sectional study of patients with hypertension attended a private clinic, outpatients clinic, emergency ward, nephrology

ward and coronary care unit in Basra teaching hospital from the period of January 2010 to January 2012. A total of three thousand patients with hypertension were studied. Renovascular hypertension was diagnosed in twenty seven patients and was included in this study. Other 2973 patients were excluded from the study. The inclusion criteria as a clinical clue to the diagnosis of renal artery stenosis in hypertensive patients were including:^[24]

1. Onset of hypertension before age of 30-years, particularly, if there is negative family history and no other risk factors for hypertension (e.g. obesity) or severe hypertension after age 55 years.
2. Accelerated, resistant or malignant hypertension.
3. Development of new azotemia or worsening of renal function more than 30 percent from baseline after initiation of angiotensin converting enzyme inhibitors or angiotensin receptor blockers.
4. Unexplained atrophic kidney or size discrepancy > 1.5 cm between kidneys.
5. Sudden, unexplained and recurrent flash pulmonary edema.
6. Unexplained renal dysfunction, including patients starting renal replacement treatment.
7. Multivessel coronary artery disease or peripheral vascular disease.
8. Unexplained congestive heart failure or refractory angina.

Accelerated hypertension was defined as acute rise in blood pressure over a previously well-controlled hypertension. Resistant hypertension was defined as inadequate blood pressure control in a patient adhering to therapeutic doses of three appropriate antihypertensive agents at optimal doses including diuretic. Malignant hypertension was defined as severe hypertension with signs of target organ damage e.g. acute kidney injury, retinal hemorrhages or papilledema, heart failure or neurologic disturbance. Flash pulmonary edema was defined as recurrent episodes of acute pulmonary edema.^[25] History was taken including the age, gender, duration of hypertension, previous controllable state of hypertension, comorbidities 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.^[26] Hypertension was classified according to European society of hypertension^[27] into:

1. Stage 1 (systolic) 140-159/ (diastolic) 90-99.
2. Stage 2 (systolic) 160-179/ (diastolic) 100-109.
3. Stage 3 (systolic) more than 180/ (diastolic) more than 110.

A control state was assessed by blood pressure measurement every 2 weeks to assess the efficacy of the drugs and hence the control state. Abdominal examination for renal artery bruit using deep auscultation at the lateral upper site of the umbilicus or at the lumbar region. Investigations were done and include the following: complete blood count (CBC), fasting blood sugar (70-110 mg/dl), blood urea (16-40 mg/dl), serum creatinine (0.6-1.1 mg/dl), fasting serum cholesterol (<190 mg/dl), serum potassium (3.5-5.3 mEq/l), electrocardiography for evidence of left ventricular hypertrophy or ischemia, chest x-ray for evidence of heart failure and pulmonary edema, abdominal ultrasound for renal size, cortical thickness and parenchymal echogenicity, Doppler ultrasound of the renal arteries for renal resistive index, CT renal angiography or MR renal angiography for anatomic localization of the stenosis and conventional renal angiography in some cases especially prior to intervention provided that eGFR is >30 ml/min/1.73m² in case of renal insufficiency. Statistical analyses were performed using SPSS (version 15), the data were expressed as numbers and percentages. Chi-square was used as a test of significance. value <0.05 is considered as significant.

RESULTS

Twenty seven patients with renal artery stenosis were studied. (Table-1), shows sociodemographic characteristics of the patients. The mean age was 49.7 ± 13.9 SD, 3(11.1%) patients were less than 30 years, 10(37%) were

from 31-60 years and 14(51.9%) were more than 61 years. Eleven (40.6%) were males and 16(59.3%) were females. Fifteen (55.6%) patients were of normal weight, 10(37%) were overweight and 2(7.4%) were obese. All patients (100%) were of white race. Eleven patients (40.7%) were smokers and 16(59.3%) were non smokers. Six (22.2%) patients had CKD, 2(7.4%) had DM, 3(11.1%) had IHD, 1(3.7%) had HF, 2(7.4%) had PVD and 13(48.1%) had no comorbidity.

Table 1. Sociodemographic characteristics of patients with renal artery stenosis.

Variables		No. (%)
Mean age in years ± SD		49.7 ± 13.9
Age distribution in years	< 30	3 (11.1)
	31-60	10 (37)
	>60	14 (51.9)
BMI distribution	15.5-24.9	15 (55.6)
	25-29.9	10 (37)
	>30	2 (7.4)
Gender	Male	11 (40.7)
	Female	16 (59.3)
Race	White	27 (100)
	Black	0 (0)
Smoking	Smokers	11 (40.7)
	Non smokers	16 (59.3)
Comorbidity	DM	2 (7.4)
	CKD	6 (22.2)
	IHD	3 (11.1)
	HF	1 (3.7)
	PVD	2 (7.4)
	No	13 (48.1)

Table-2, shows renal artery stenosis patient's results. Atherosclerotic RAS accounts for 77.8% of cases, while, fibromuscular dysplastic RAS accounts for 22.2%. The clinical criteria for diagnosis were HT <30 years in 3.7%, recent severe HT >55 years in 11.1%, malignant HT in 3.7%, resistant HT in 14.8%, accelerated HT in 18.5%, flash pulmonary edema in 7.4%, PVD in 3.7%, discrepancy in renal size >1.5 cm in 7.4%, unexplained renal azotemia in 25.9% and incidental in 3.7%. Urine protein was negative in 37%, non nephrotic in 51.9% and nephrotic in 11.1%. The CXR was normal in 77.8% and shows pulmonary congestion in 22.2%. The

ECG was normal in 55.6%, shows LVH in 40.7% and ischemia in 3.7%. The ultrasound shows small left kidney in 25.9%, small right kidney in 51.9% and bilateral small kidneys in 22.2%. The Doppler ultrasound was normal in 96.3% and abnormal in 3.7%. The MRA shows

left proximal stenosis in 22.2%, right proximal stenosis in 33.3%, left distal stenosis in 3.7%, right distal stenosis in 18.5% and bilateral stenosis in 22.2%. The serum K⁺ was normal in 29.6% and low in 70.4%. The serum cholesterol was normal in 77.8% and high in 22.2%.

Table 2. Findings in patients with renal artery stenosis.

Variables		No. (%)
Renal artery stenosis types	Atherosclerotic	21 (77.8)
	Fibromuscular dysplastic	6 (22.2)
Clinical criteria for diagnosis	HT <30 years	1 (3.7)
	Recent severe HT>55 years	3 (11.1)
	Malignant HT	1 (3.7)
	Resistant HT	4 (14.8)
	Accelerated HT	5 (18.5)
	Flash pulmonary edema	2 (7.4)
	PVD	1 (3.7)
	Renal size discrepancy>1.5cm	2 (7.4)
	Unexplained renal azotemia	7 (25.9)
	Incidental	1 (3.7)
Urine for protein	Negative	10 (37)
	Non-nephrotic	14 (51.9)
	Nephrotic	3 (11.1)
Chest x-ray findings (CXR)	Normal	21 (77.8)
	Pulmonary congestion	6 (22.2)
ECG findings	Normal	15 (55.6)
	LVH	11 (40.7)
	Ischemia	1 (3.7)
Ultrasound findings	Left small kidney	7 (25.9)
	Right small kidney	14 (51.9)
	Bilateral small kidneys	6 (22.2)
Doppler ultrasound findings	Normal	26 (96.3)
	Renal artery stenosis	1 (3.7)
MRA findings	Left proximal stenosis	6 (22.2)
	Right proximal stenosis	9 (33.3)
	Left distal stenosis	1 (3.7)
	Right distal stenosis	5 (18.5)
	Bilateral stenosis	6 (22.2)
Serum K ⁺	Normal	8 (29.6)
	Low	19 (70.4)
Serum cholesterol	Normal	21 (77.8)
	High	6 (22.2)

Table-3, shows distribution of renal artery stenosis subtypes according to the age. In younger patients <30 years old, FMD type accounts for 100% of the cases. In 31-60 years old patients, the ARAS was more common than

FMD type 63.6 vs 36.4 respectively. In elderly patients more than 61 years old, the ARAS accounts for 100% of cases. The results were statistically significant.

Table 3. Distribution of renal artery stenosis subtypes according to age.

Age groups in years	RAS subtypes		Total
	FMD	ARAS	
< 30	2 (100%)	0 (0.0%)	2 (100%)
31-60	4 (36.4%)	7 (63.6%)	11 (100%)
>61	0 (0.0%)	14 (100%)	14 (100%)
Total	6 (22.2%)	21 (77.8%)	27 (100%)

Chi-square value 12.273 degree of freedom 2 P value 0.02

Table-4, shows distribution of renal artery stenosis according to the gender. The ARAS was more common in female in 57.1%. The

FMD type was more common in female in 66.7%. The results were statistically insignificant (P value 0.675).

Table 4. Distribution of renal artery stenosis subtypes according to gender.

Gender	RAS subtypes		Total
	FMD	ARAS	
Male	2 (33.3%)	9 (42.9%)	11 (40.7%)
Female	4 (66.7)	12 (57.1%)	16 (59.3%)
Total	6 (100%)	21 (100%)	27 (100%)

Chi-square value 0.175 degree of freedom 1 P value 0.675

DISCUSSION

In the present study, the ARAS accounts for 77.8% and FMD type accounts for 22.2% of cases. In comparison to study done by Safian and Textor, where they reported that ARAS accounts for 90% and FMD type accounts for 10 % of cases.^[28] Also, a study done by Slovut and Olin, where they reported that FMD type accounted for 10% of cases.^[29] FMD type is more common in younger age patients less than 30-year old in 100% of cases and ARAS type is more common in elderly more than 60-year old in 100% of cases. This is in agreement with a study done by Hansen and colleagues where they showed that the prevalence of ARAS increased with increasing age from 60 onward.^[30] It is also in agreement with a study done by Slovut and Olin, where they showed

that FMD type is more common in younger age patients from 15-50 years.^[29] The FMD type was more common in females; this is in agreement to a study done by Estepa and colleagues where they showed that FMD type is more common in women.^[15] The ARAS was more common in males which is in disagreement with study done by Hansen and colleagues where they showed that ARAS is more common in male.^[30] Both types of renovascular hypertension are more common in whites. This is in agreement to a study done by Svetkey and colleagues, where they showed that renovascular hypertension is more common in whites.^[31] The most common clinical criteria suggestive for diagnosis were unexplained renal azotemia in 25.9%. This is in agreement with a

study done by Wollenweber and colleagues where they showed that 27% of atherosclerotic renal artery stenosis eventually ended with progressive loss of renal function within 6 years.^[32] Peripheral vascular disease was reported in 3.7% which is in disagreement with a study by Choudhri and colleagues where they showed that 24% of PVD patients have bilateral renal artery stenosis.^[33] In resistant hypertension, 14.8% of patients had renal artery stenosis, which is comparable to a study done by Taler and colleagues where they showed that 20% of resistant hypertension had renovascular hypertension.^[34] The prevalence of hypokalemia was 70.4% which is higher than what Maxwell showed in his cooperative study where, the prevalence of hypokalemia was 16%.^[35] The prevalence of proteinuria was 63% which higher than what Maxwell study who showed that 46% of patients with renovascular hypertension had proteinuria.^[35] The nephrotic range proteinuria was 11.1%; Dooci and colleagues showed that renovascular hypertension is occasionally associated with nephrotic range proteinuria.^[36]

Conclusion

A high index of suspicion for diagnosis of renal artery stenosis as a cause of hypertension should be suspected depending on certain clinical criteria. It is more common in whites and rare in blacks. The atherosclerotic type is more common and it is more common in the older age group. The fibromuscular type is more common in the younger age group. Right renal artery stenosis is more common than the left.

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