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Review Article

Hypertensive renal disease: Histological aspects

*Manoj Jain**

Professor, Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Raebareli Road, Lucknow 226014, UP, India

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ABSTRACT

Hypertensive nephropathy is one of the common causes of end-stage renal disease. Hypertension is intimately linked with the kidney as kidney diseases may lead to increased blood pressure and hypertension can be the cause of renal disease. Majority cases of hypertension are primary or essential. Renal parenchymal diseases and renovascular hypertension are important causes of secondary hypertension. Fibrous dysplasia and atherosclerosis constitute majority cases of renovascular hypertension. Renal diseases with hypertension has been divided in to the benign nephrosclerosis and malignant nephrosclerosis. Benign nephrosclerosis is characterized by hyaline arteriolosclerosis and intimal fibrosis and reduplication of internal elastic lamina of arcuate and interlobular arteries. Malignant hypertensive nephropathy is characterized by hyerplastic arteriolitis and fibrinoid necrosis of arterioles and glomeruli.

1. Introduction

Hypertension is intimately linked with the kidney, because kidney disease can be both the cause and consequence of increased blood pressure. According to the 2011 US Renal Data System (USRDS) data, in the year 2009, hypertensive nephrosclerosis (HN) accounted for 28% of patients reaching end-stage renal disease (ESRD). The rate of ESRD attributed to hypertension has grown 8.7% since the year 2000. Hypertensive nephrosclerosis is reportedly the second most common cause of ESRD in white people (23%) and is the leading cause of ESRD in black people (46%).[1] For practical purpose, hypertension has been defined by WHO a systolic blood pressure > 160 mmHg or a diastolic pressure > 95 mmHg or both in adults. In addition, consistent elevation of blood pressure should be established with repeated readings. In children, there is a rise in blood pressure with age; an upper normal limit of 130/80 mmHg is reached by 12–15 years of age. The increased risk associated with high blood pressure is graded, continuous, and present throughout the entire distribution of blood pressure above optimal. Renal risk appears to be more closely related to systolic than to diastolic blood pressure, and black men are at greater risk than white men for developing ESRD at every level of blood pressure. Clinically, macroalbuminuria (a random urine albumin/creatinine ratio > 300 mg/g) or microalbuminuria (a random urine albumin/creatinine ratio 30–300 mg/g) are early markers of renal injury. These are also risk factors for renal disease progression and for cardiovascular disease Table 1.[2]

Hypertension is essential or primary when it cannot be attributed to any underlying condition. When underlying condition can be identified then it is termed as secondary. Majority of the cases of hypertension are primary and estimated prevalence of causes of secondary hypertension are only 5–20% Table 2.[2] Virtually all disorders of the kidney may cause hypertension, and renal parenchymal disease is the most common cause of secondary hypertension. Hypertension is present in >80% of patients with chronic renal failure.

* Tel.: +91 5222494244.
E-mail addresses: mjain@sgpgi.ac.in, mnjjain@yahoo.com.
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Table 1 – Classification for blood pressure for adults > 18 years of age.

Classification	Blood pressure (mmHg)
Normal	<120/80
Pre hypertension	120/80–139/89
Stage I hypertension	140/90–159/99
Stage II hypertension	>160/100

In general, hypertension is more severe in glomerular diseases than in interstitial diseases, such as chronic pyelonephritis. Conversely, hypertension may cause nephrosclerosis, and in some instances it may be difficult to determine whether hypertension or renal disease was the initial disorder. Proteinuria > 1000 mg/day and active urine sediment are indicative of primary renal disease.[3]

Renovascular hypertension is hypertension resulting from a renal arterial lesion that is relieved by correction of the offending lesion or removal of the kidney. The vast majority of cases of renovascular hypertension are caused by two entities i.e fibrous dysplasia (FD) which generally occurs in younger patients and atherosclerosis obliterans generally occurs in older patients. Approximately 70% of all renovascular lesions are caused by atherosclerosis. Medial fibroplasia is the most common type of fibromuscular disease and is rarely associated with progression to occlusion of the renal artery or renal function deterioration. Other miscellaneous causes of renovascular hypertension include renal artery aneurysms, middle aortic syndrome, periarterial fibrosis, and post-traumatic intimal or medial disease. Table 3.[4]

2. Histological features of hypertensive renal disease

Whether hypertension is "essential" or of known etiology, it results in the development of intrinsic lesions of the renal arterioles (hyaline arteriolosclerosis) that eventually lead to loss of function (nephrosclerosis). There are two different processes i.e ischemic and hypertrophic lead to glomerulosclerosis. Arterial stiffening with increased pulse pressure down as far as the afferent arteriolar level likely plays an important role in the progression of glomerular lesions. Loss of renal autoregulation with glomerular hypertrophy, hyperfiltration, and focal segmental glomerulosclerosis is now recognized to contribute significantly to nephrosclerosis, particularly in the black population. Ischemic glomerulosclerosis, however, may ultimately be the most important lesion, with consequent hypoxia in the parenchyma beyond, leading to tubular atrophy and interstitial fibrosis.[5]

Classically hypertensive renal disease has been divided in to the benign nephrosclerosis (or arteriolar nephrosclerosis) and malignant nephrosclerosis (or accelerated nephrosclerosis malignant hypertensive nephropathy).

Table 2 – Estimated prevalence of causes of hypertension.

1. Primary, essential – 5–20%
2. Secondary – 80–95%
   a. Renal parenchymal disease 2–5%
   b. Renovascular disease 2–5%
   c. Primary aldosteronism 0.5–13%
   d. Obstructive sleep apnea 1–3%
   e. Pheochromocytoma < 1%
   f. Single gene defect <1%

Table 3 – Classification of renovascular hypertension.

1. Atherosclerosis
2. Fibrous dysplasia
   a. Intimal fibroplasias
   b. True fibromuscular hyperplasia
   c. Medial fibroplasias
   d. Perimedial (subadventitial) fibroplasia
3. Miscellaneous: renal artery aneurysms, middle aortic syndrome, periarterial fibrosis, and post-traumatic intimal or medial disease

3. Benign nephrosclerosis or arteriolar nephrosclerosis

Benign nephrosclerosis is seen in patients who are hypertensive (BP > 150/90 mmHg) for an extended period of time but whose hypertension has not progressed to a malignant form. It occurs usually in the older age group and often discovered to be hypertensive on routine physical examination or as a result of nonspecific symptoms as headaches, weakness, and palpitations. Physical examination may reveal changes in retinal vessels (arteriolar narrowing and/or flame-shaped hemorrhages), cardiac hypertrophy, and signs of congestive heart failure. Renal disease may manifest as a mild to moderate elevation of serum creatinine, microalbuminuria, or proteinuria. The kidneys in benign nephrosclerosis are typically reduced in size and the two kidneys are usually affected equally. The capsular surface is most commonly finely granular, reflecting disease in small arteries and arterioles. In cases of advanced benign nephrosclerosis larger renal arteries show intimal thickening and damage larger clusters of nephrons causing coarser granularity superimposed against a background of fine granularity with scattered V-shaped pits. Such larger scars extend only through the cortex and not the medulla, indicating their relationship to the interlobular or arcuate vessels. This feature differentiates them from pyelonephritic scars, which are larger, U-shaped, and extend through a fibrotic medulla to end in a dilated, distorted and inflamed calyx. The cut surface reveals cortical thinning and glomeruli may be difficult to identify. Cortical cysts may also be present.

The characteristic pathology is in the renal arterioles and small arteries. Two processes participate in the arterial lesions i.e medial and intimal thickening and hyaline (homogenous glassy eosinophilic material) deposition in arterioles (hyaline arteriolosclerosis), caused partly by extravasations of