

Review Article

How to Detect Early Kidney Disease in Hypertension?

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Abstract

There is high prevalence of kidney disease among hypertensive patients. Identifying kidney disease in hypertensive patients at the earliest is of paramount importance in preventing progression to ESRD. Simple and cost-effective techniques are available for screening kidney disease and all medical care professionals need to be sensitized to do an early screening for kidney disease in all hypertensive patients at presentation. Treating chronic kidney disease (CKD) significantly improves cardio-vascular mortality in hypertensive patients which increases exponentially when there is co-existing hypertension and CKD.

Key words: Chronic kidney disease (CKD), early screening, hypertension

Introduction

Hypertension and kidney disease have a “cause” and “effect” relationship. Majority of the kidney diseases cause hypertension and hypertension can induce kidney disease. Most often, kidney disease remains silent in the early stages. Early detection of kidney disease in hypertensives is of great significance.

“Hypertension” and “Kidney Disease” - “Cause” and “Effect” Relationship

Almost all the kidney diseases except some forms of chronic tubulointerstitial nephritis cause hypertension. Hypertension in kidney disease is multifactorial. Volume overload, activation of renin-angiotensin-aldosterone system, enhanced sympathetic activity, and altered vascular reactivity comprise the common mechanisms.

Hypertension *per se* can injure kidney. Benign nephrosclerosis and malignant nephrosclerosis are the two well-defined pathologies described. Hypertension, being a major risk factor for atherosclerosis, can contribute for “ischemic nephropathy” occurring due to atherosclerotic renal artery disease. Importantly, hypertension is an independent determinant of renal prognosis irrespective of the etiology of kidney disease!

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The Concept of “Chronic Kidney Disease”

Kidney disease, in early stages, may remain silent. Subclinical early kidney disease often failed to get enough attention when the concept of “chronic renal failure” was in vogue. This formed the basis for the evolution of the concept of chronic kidney disease (CKD). CKD refers to any functional/structural alteration of kidney persisting for >3 months.^[1] Glomerular filtration rate (GFR) is normal in Stage 1 CKD and serum creatinine starts rising only in Stage 3 CKD.

CKD stage	GFR (ml/min/1.73 m ²)
I	≥90
II	60–89
III	30–59
IV	15–29
V	<15

Detection of Kidney Disease

There are two important tests to detect early kidney disease: (1) Urine test for the presence of protein and (2) estimation of GFR (eGFR).



Proteinuria

Proteinuria is detected by urinary dipsticks. This is a semi-quantitative and fairly sensitive screening test for kidney disease.

Microproteinuria

Microproteinuria refers to increased urinary protein excretion, but, not sufficient enough to be detected by dipstick.

Proteinuria is not only a harbinger for progressive kidney disease but also is an indicator of cardiovascular disease risk.^[2] Microalbuminuria is more specific than microproteinuria. Microalbuminuria is defined as urinary albumin excretion of 30–300 mg/day or 20–200 mcg/min or urine spot albumin-creatinine ratio of 30–300 mcg/mg of creatinine in two of three tests done over 6 months in the absence of the known causes of transient proteinuria such as fever, physical exertion, and urinary infection.^[3]

eGFR

eGFR is preferred to measured GFR since the commonly employed test for measuring GFR, namely endogenous creatinine clearance, is fraught with inaccuracies and practical difficulties.

Estimation of GFR is done applying serum creatinine-based formulae. Cockcroft-Gault formula, which was widely adopted in the past, has become obsolete.

The two currently employed formulae are as follows: (a) Modification of diet in renal disease (MDRD) formula and (b) CKD-EPI (CKD Epidemiology Collaboration) formula. Both these formulae use four variables, namely (1) age in years, (2) gender, (3) race, and (4) serum creatinine (mg/dl). Of these, CKD-EPI formula is preferred.^[4] Although these formulae have not been validated in Indian subjects, it is prudent to estimate GFR using these formulae rather than relying on serum creatinine alone due to the following reasons:

1. Serum creatinine is less sensitive in identifying renal failure in the early stages. Elevation in serum creatinine value occurs only when GFR has decreased by 50%.
2. The same value of serum creatinine denotes different GFR in different individuals.

MDRD formula:

$$\text{GFR} = 175 \times (\text{Scr})^{-1.154} \times (\text{age})^{-0.203} \times 0.742 \text{ (if female)} \times 1.212 \text{ (if black)}$$

CKD –EPI Formula:^[5]

$$\text{GFR} = 141 \times \min(\text{Scr}/\kappa, 1)^{\alpha} \times \max(\text{Scr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

$\kappa = 0.7$ if female

$\kappa = 0.9$ if male

$\alpha = -0.3229$ if female

$\alpha = -0.411$ if male

min = The minimum of Scr/ κ or 1

max = The maximum of Scr/ κ or 1

Scr = Serum creatinine (mg/dL)

These formulae ideally use standardized serum creatinine, i.e., serum creatinine assayed using methods that are traceable to IDMS (isotope dilution mass spectrometry).

Serum cystatin is a low-molecular-weight protein produced by all the nucleated cells of the body and degraded by the renal tubular epithelial cells. Its levels are not altered by inflammation, infections, dietary, and constitutional factors. Although CKD-EPI equation, based on serum cystatin, is believed to be more precise, there is no definite evidence for the same. Moreover, due to cost implication, serum cystatin may not be suitable for screening tests.

Various online calculators and mobile applications are available for calculating estimated GFR (https://www.kidney.org/professionals/KDOQI/gfr_calculator).

Significance of Early Detection of the Renal Disease in Hypertension

1. It provides an impetus for better control of hypertension. Most guidelines advocate a lower BP target in hypertensives with proteinuria as compared to non-proteinuric hypertensives.
2. Preferential use of angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists is advised since they are antiproteinuric and renoprotective.
3. Renoprotective strategies like correction of acidosis (if present) may be applied early.
4. Kidney disease in hypertensives confers added risk for cardiovascular disease. Appropriate risk reduction measures can be taken.
5. Nephrotoxic drugs/agents can be strictly avoided.

There are quite a few studies which have documented the prevalence of kidney disease among hypertensives.

I-DEMAND study (Italy-Developing Education and awareness on MicroAlbuminuria in patients with hypertensive Disease) illustrates significant prevalence of kidney disease among hypertensives.

It is an observational, cross-sectional, and multicentric study involving 3534 hypertensives. Of them, 37% had diabetes also. 27% of them had low GFR (eGFR <60 ml/min/1.73 m²) and 26% of them had microalbuminuria (>2.5 mg/mmol [men]; >3.5 mg/mmol [women]) and 42% of them had both.^[6]

European Society of Hypertension and European Society of Cardiology Guidelines on the management of hypertension emphasize to look for evidence for subclinical kidney damage in every hypertensive. Subclinical kidney disease, particularly microalbuminuria, is described as “renal window” opened on the cardiovascular system, signifying the heightened cardiovascular risk in microalbuminuric hypertensives.^[7]

KHA-CARI an Australian working group advocates annual screening for CKD in hypertensive patients. The screening should include both urinary albumin: creatinine ratio to detect proteinuria and serum creatinine to determine eGFR every year.^[8]

In the PREVEND-IT trial, which evaluated the effect of Fosinopril (ACE inhibitor) on the cardiovascular events, the

initial screening for albuminuria was done through postal survey. The study patients were instructed to send by return mail a “vial” containing a portion of the morning spot urine sample and estimation of protein by nephelometry in a nearby laboratory. This strategy can be a cost-effective strategy for screening large group of hypertensive patients for the presence of albuminuria.^[9]

Indian guidelines on hypertension (I.G.H-III) recommends to screen all hypertensive patients with urine albumin-creatinine ratio and serum creatinine to identify patients with target organ damage and reserving urine microalbumin for risk stratification.^[10]

Conclusion

The importance of early detection of the kidney disease in a hypertensive patient cannot be overemphasized. Physicians at all levels of health care need to be sensitized on screening for kidney disease in every hypertensive patient. There are simple and cost-effective techniques that can be performed without much additional resources. The professional bodies and all the stakeholders involved in formulating guidelines on the management of hypertension have to give special emphasis on this important recommendation.

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