

OPINION

Recommendations for Early Diagnosis of Chronic Kidney Disease

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Abstract

Background: Chronic kidney disease is an important component of chronic non – communicable diseases that are now of pandemic proportions and are the major cause of morbidity and mortality worldwide. Patients with reduced renal function represent a population not only at risk for progression of kidney disease and development of end stage renal disease (ESRD), but also at a greater risk of cardiovascular disease and mortality. Unfortunately, chronic kidney disease is under diagnosed and undetected resulting in lost opportunities for improving the clinical outcome. Early diagnosis with appropriate interventions will improve the quality of care of patients and prevent or delay progression to end stage renal disease. Our objective is to review existing recommendations and examine their adaptation to improving the quality of care for patients with chronic kidney disease in our environment.

Method: Hand searches of published articles and electronic data were the primary sources. Only articles published in the English language were consulted excluding case reports, letters and conference abstracts. Articles of original data were searched from 1980 while review articles and expert committee reports were from 2000.

Results: Early diagnosis of chronic kidney disease is crucial to improving the clinical outcome and reducing the incidence of end stage renal disease. Certain individuals with specific socio demographic and clinical factors are at increased risk of chronic renal disease. All individuals should be assessed as part of routine health encounter, to determine whether they are at increased risk of developing chronic kidney disease based on clinical and socio demographic factors. Individuals at increased risk of developing chronic kidney disease should undergo testing for markers of kidney damage, and to estimate the level of GFR. Individuals found to have chronic kidney disease should be evaluated and treated appropriately. A clinical action plan should be developed for each patient based on the type and stage of renal disease, co-morbid conditions, complications of the disease and risk factors for progression of renal disease or development of cardiovascular disease.

Conclusion: Individuals at increased risk, but found not to have chronic kidney disease, should be advised to follow of risk factor reduction, if appropriate, and undergo repeat periodic evaluation.

Key words: Chronic kidney disease, risk factors, screening, early diagnosis, prevention

Résumé

Introduction: Maladie du rein chronique est un composant important des maladies chroniques non transmissibles qui sont actuellement d'une proportion pandémique et sont des causes majeur de la morbidité et mortalité dans le monde entier. Des patients atteints des fonctions d'une diminution rénale constitue une poplation pas seulement à risque pour une progression de la maladie du rein et du développement de la maladie rénale de la dernière étape (MRDE) mais aussi à un plus grand risque de la maladie cardiovasculaire et mortalité. Malheureusement, la maladie du rein chronique est sous diagnostiquée et sans détecter ce qui mène à la perte des occasions d'améliorer le résultat clinique. Un diagnostique précoce avec des interventions adéquates vont améliorer la qualité des soins pour des patients et éviter une progression tardive pour la maladie rénale de la dernière étape. L'objet de cette étude est de faire une rétrospective des recommandations actuelles et étudier leur adaptation pour pouvoir améliorer la qualité des soins pour des patients atteints de la maladie du rein dans notre milieu.

Méthodes: Recherches des articles publiées et des données électroniques sont des sources de base. Des articles publiées en anglais ont été consultées sans compter des rapports des cas, lettres et des résumés de

la conférence. Des articles des données originales ont été cherchées de 1980 tandis que bilan des articles et des rapports du comité des spécialistes étaient de l'an 2000.

Résultats: Diagnostic précoce pour la maladie du rein chronique est très important afin d'améliorer le résultat clinique et de réduire la fréquence de la maladie rénale de la dernière étape. Certains individus avec des facteurs cliniques et socio-démographiques spécifiques ont une augmentation du risque de la maladie du rein chronique. Tout le monde devrait être examiné comme étant la démarche de la routine sanitaire, pour pouvoir décider s'ils sont à une augmentation de risque d'atteindre la maladie chronique de rein basée sur des facteurs cliniques et socio-démographiques. Des individus qui sont à risque d'atteindre la maladie du rein chronique devraient suivre un test qui va indiquer le dégât du rein, et déterminer le niveau du GFR. Des individus trouvés d'être atteints de la maladie du rein chronique devraient être étudiés et traités convenablement. On devrait établir un plan d'action clinique pour chaque patient d'après le type d'étape de la maladie rénale, conditions co-morbides, complication de la maladie et des facteurs de risque pour progression de la maladie rénale ou développement de la maladie cardiovasculaire.

Conclusion: Des individus avec augmentation, mais trouvés de ne pas atteindre de la maladie du rein chronique, devraient être conseillés de suivre une réduction du facteur du risque, si c'est nécessaire, suivre une évaluation périodique répétée.

Mots-clés: Maladie du rein chronique, facteurs du risque, test du dépistage, diagnostic précoce, prévention

Introduction

Chronic non-communicable diseases are now of pandemic proportions and are the major cause of morbidity and mortality worldwide. Chronic kidney disease (CKD), diabetes mellitus, hypertension and cardiovascular disease all contribute to the burden of chronic diseases which are replacing acute and communicable diseases as the dominant public health problem even in the developing world.¹⁻⁴ These diseases appear to have an unholy alliance increasing morbidity and mortality and are expected to increase rapidly in the next two decades.

Chronic kidney disease plays a central role and represents a key element within the network of major chronic diseases. For instance, chronic kidney disease is a major risk factor for cardiovascular morbidity and mortality and is also a major complication of diabetes mellitus and hypertension.⁵ Patients with reduced renal function represent a population not only at risk for progression of kidney disease and development of end stage renal disease (ESRD), but also at a greater risk of cardiovascular disease and mortality. Unfortunately, chronic kidney disease is under diagnosed and undetected resulting in lost opportunities for prevention.⁶ There is paucity of programs for detection, management and prevention of chronic kidney disease globally.

Chronic kidney disease has a prolonged latent period during which the disease is present but asymptomatic with progressive renal damage. There is wide variability in the rate of progression among individuals even when similar risk factors are present.⁷ This suggests the existence of biologically relevant characteristics that influence the occurrence and course of renal disease. This position is clearly illustrated among individuals with autosomal dominant polycystic kidney disease (ADPKD). Family members who inherit the same mutation of the polycystic gene may demonstrate highly variable rate of progression to end stage renal disease.⁷

Combinations of several factors that result in rapid progression to end stage renal disease define the course of the disease.^{7,8} Some of these factors may be causal while others may be associated with but enhance other factors.^{7,9} Some of these factors are modifiable while others are not. Early diagnosis with appropriate interventions will improve the quality of care of patients and prevent or delay progression to end stage renal disease.⁸

Objective

The objective is to review existing expert recommendations and examine their adaptation for improving the quality of care and outcomes of individuals with chronic kidney disease in a poor economic environment.

Method

Hand searches of published literature and searches of electronic data bases were the primary sources. Full journal articles of original data, review articles, meta-analysis and editorials were considered. Case reports, letters and abstracts were excluded. No systematic process was followed to obtain the articles. Only articles published in English language were included in the search. Articles of original data were searched from 1980 while review articles and expert committee reports were searched from 2000.

Definition and Classification of Chronic Kidney Disease

Chronic kidney disease is defined either as kidney damage, evidenced by structural or functional abnormalities, for not less than 3 months or a persistent decline in glomerular filtration rate (GFR) to less than 60ml/min/1.73m² for not less than 3 months (Table 1). This definition has provided a basis for the development of the kidney disease outcome quality initiative (K/DOQI) clinical practice

guidelines for chronic kidney disease evaluation, classification and stratification.¹⁰ Chronic kidney disease is now uniformly defined¹¹ and risk factors for initiation and progression identified (Tables 2, 3). Risk factors are also classified based on response to appropriate intervention programmes and used in cardiovascular disease epidemiology¹⁰ (Table 4).

Chronic kidney disease can be diagnosed early by evaluating individuals with risk factors for initiation and/or progression of kidney disease^{12, 13} and instituting appropriate interventions could either, reverse the disease process, stop or slow down the progression of disease.¹⁴

Table 1: Definition of chronic kidney disease

a.	Kidney damage for not less than three months, defined by structural or functional abnormalities of the kidney with or without decrease in GFR, manifested by either: Pathological abnormalities, or Markers of kidney damage including abnormalities in composition of blood, urine or imaging tests
b.	GFR less than 60mls/min./1.73m ² for not less than three months with or without kidney damage

GFR: Glomerular filtration rate

Table 2: Stages of chronic kidney disease

Stage	Description	GFR (mls/min./1.73m ²)
1	Kidney damage with normal or increased GFR	90 or more
2	Kidney damage with mild decreased GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	Less than 15 or requires dialysis

GFR: Glomerular filtration rate

Table 3: Potential risk factors for susceptibility to and the initiation of chronic kidney disease

Hypertension	Renal stones
Diabetes	Autoimmune disease
Age >60years	Smoking
Recovery from acute renal failure	Illicit drugs use
Male gender	Neoplasm
Low birth weight	Reduced renal mass
Low socio economic status	Access to health care facility
Recurrent or chronic urinary tract infection	Oxidative stress/carbonyl stress
Systemic infections	Insulin resistance syndrome
Obstructive uropathy	Hyperlipidaemia
Obesity	Proteinuria
Familial aggregation	Genetic markers
Lead and other heavy metals	Poverty
Analgesic abuse	
Dietary phytoestrogens	

Table 4: Classification of risk factors based on response to interventions

Classification	Risk factor group
Category I	Factors for which interventions have been proven to lower risk
Category II	Factors for which interventions are likely to lower risk
Category III	Factors for which modification may lower risk
Category IV	Factors for which interventions have been proven to lower risk

Early Diagnosis of Chronic Kidney Disease

The K/DOQI clinical practice guidelines for chronic kidney disease evaluation, classification and stratification, recognize individuals with certain

clinical and socio demographic characteristics to have increased risk of developing chronic kidney disease.¹⁰ In guideline 3 of the clinical practice guidelines,¹⁰ some individuals without kidney damage and with normal or elevated GFR are recognized to be at

increased risk for developing chronic kidney disease and recommend as follows:

- a. All individuals should be assessed as part of routine health encounter to determine whether they are at increased risk of developing chronic kidney disease based on clinical and socio demographic factors.
- b. Individuals at increased risk of developing chronic kidney disease should undergo testing for markers of kidney damage, and to estimate GFR.
- c. Individuals found to have chronic kidney disease should be evaluated and treated as specified in guideline 2.

Evaluate to determine:

- i. Diagnosis (type of disease)

- ii. Comorbid conditions
- iii. Severity of kidney disease
- iv. Complications
- v. Risk of disease progression
- vi. Risk of cardiovascular disease

A clinical action plan should be developed for each patient based on the type and stage of renal disease, comorbid conditions, complications of the disease and risk factors for progression of renal disease or development of cardiovascular disease.

- d. Individuals at increased risk, but found not to have chronic kidney disease, should be advised to follow of risk factor reduction, if appropriate, and undergo repeat periodic evaluation.

Table 5: Recommended steps in screening for chronic kidney disease

Who to screen
Patients at increased risk
Arterial hypertension/cardiovascular disease
Diabetes mellitus and other systemic diseases
Age >60 years
Family history of kidney disease
Recurrent urinary tract infections
How to screen
Dipstick (spot urine) for proteinuria, WBC, RBC
If positive for proteinuria, measure the total protein to creatinine ratio in spot urine sample
If negative for proteinuria, perform specific search for microalbuminuria in patients with diabetes and/or hypertension
If WBC or RBC positive, perform sediment analysis in spot urine sample
Estimate GFR using Cockcroft and Gault formula
Evaluation
If screening is negative, check again every 1-3 years depending on the risk factors
If abnormality is detected on screening, perform diagnostic and therapeutic work up

WBC: White blood cells; RBC: Red blood cells; GFR: Glomerular filtration rate

Table 6: Specific equations for estimating glomerular filtration rate

Adults
MDRD study group equation
$GFR (ml/min/1.73m^2) = 186 \times (Scr \text{ in } mg/dl)^{-1.154} \times (Age \text{ in years})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$
Cockcroft-Gault equation
$Ccr (ml/min) = \frac{(140 - Age \text{ in years}) \times weight}{72 \times Scr(mg/dl)} \times (0.85 \text{ if female})$
Children
Schwartz equation
$Ccr (ml/min) = \frac{0.55 \times length}{Scr}$
Counahan-Barratt equation
$GFR (ml/min/1.73m^2) = \frac{0.43 \times length}{Scr}$

GFR: Glomerular filtration rate; MDRD: Modification of diet in renal disease; Ccr: Creatinine clearance; Scr: Serum creatinine

Screening for Chronic Kidney Disease

Chronic kidney disease (CKD) detected early can be managed to prevent or slow down the rate of progression to ESRD.^{8, 10, 12} Failure to recognize

CKD early is a missed opportunity to improve patient outcome. While blood pressure is checked at almost every visit to the doctor, dipstick urinalysis is seldom considered even though it is cheap, available even in the rural areas and very valuable.¹²

Whole population based programs to promote screening for CKD should increase the rate that persons with previously undetected renal injury are identified and linked to further evaluation and disease modifying interventions.^{7, 8, 10} Whole population surveys provide an opportunity for health education and counseling by health care providers to promote awareness about the risk of CKD and the benefits of early diagnosis and treatment. Despite the appeal and potential benefits of whole population based screening programs, it is clear from cost effective analysis that high risk population screening is more practicable, more cost effective and more readily acceptable to policy makers.⁹

The international society of nephrology (ISN) consensus workshop on the prevention of progression of renal disease held in Hong Kong in June 2004 came out with a consensus on screening for chronic kidney disease; who to screen, how to screen and how to evaluate the result (Table 5).

Persons with increased risk of developing chronic kidney disease should be tested for markers of kidney damage and estimate the GFR. A risk factor is an attribute that is associated with increased risk of an outcome. The relationship may be causal, determining the out come or may be non causal. Interventions that reduce exposure to causal factors would improve outcome. Non causal factors are associated with outcome through confounding relationship and intervention to reduce exposure may not necessarily improve outcome.

The risk of occurrence or progression of CKD can be predicted from the existence of certain risk factors (Table 3) and this enables the clinician to identify individuals who may benefit from a limited screening program which is cost effective. Such individuals will benefit from a more closely supervised care and follow up and more intensive disease modifying interventions. Some of the risk factors have been tested in randomized clinical trials and found to be suitable targets for intervention.^{7, 8, 10}

If health care providers integrate the needed CKD screening within the existing health care system, the population at high risk will be identified and targeted for screening and intervention. The K/DOQI guidelines identify certain demographic groups characterized by high incidence or prevalence of CKD as populations that should be targeted for screening and prevention.¹⁰ The progression of CKD is affected by interplay of multiple risk factors with wide variability in the rate of progression among individuals even when similar risk factors are identified.^{8, 10}

Who should be screened?

If everyone were to be screened, hardly will anyone with chronic kidney go undetected. Whole population screening is desirable but not practicable because of logistics and huge financial burden. Representative sampling of the community is recommended for establishing the burden of disease in the community. Screening for chronic kidney disease should be part of routine examination for all persons presenting to any

health facility for any kind of service. Special attention should be paid on persons at high risk of chronic kidney disease (Tables 3 and 4) if found negative, should be re screened at regular intervals every one to three years depending on the underlying risk factors.

What to look for

1. Urine abnormalities

Proteinuria

Dipstick urine test on spot urine sample is a very valuable screening test. It is simple, quick, cheap and easy to perform.^{15 - 18} Abnormal urinary excretion of albumin is a highly sensitive indicator of glomerular disease.^{8, 10, 19, 20} Normal individuals excrete small amounts of albumin less than 30mg/day or proteins 80±24mg/day. Standard urine dipsticks are acceptable for detecting increased total urine protein while albumin specific dipsticks are acceptable for detecting albuminuria and will detect albumin levels in urine when excretion is 300mg/day or more. Excretion between 30mg and 299mg/day are detected as microalbuminuria. The dipstick test does not detect paraproteins and is recommended for detecting CKD in adults and post pubertal children because of its high sensitivity as a marker of CKD in hypertension, diabetes and glomerular disease.¹⁰ These are the three leading causes of CKD in Nigeria.^{21, 22}

The National Kidney foundation K/DOQI clinical practice guidelines the following for the assessment of proteinuria:¹⁰

- a. Under most circumstances, untimed (spot) urine samples should be used to detect and monitor proteinuria in children and adults.
- b. It is usually not necessary to obtain a timed urine collection (24 hours or overnight) for these evaluations in either children or adults.
- c. First morning specimens are preferred, but random specimens are acceptable if first morning specimens are not available.
- d. In most cases, screening with the urine dipsticks is acceptable for detecting proteinuria:
 - i. Standard urine dipsticks are acceptable for detecting increased total urine protein.
 - ii. Albumin specific dipsticks are acceptable for detecting albuminuria
- e. Patients with a positive dipstick test ($\geq 1^+$) should undergo confirmation of proteinuria by a quantitative measurement (protein-to-creatinine ratio or albumin-to-creatinine ratio) within 3 months.
- f. Patients with two or more positive quantitative tests temporarily spaced by 1 to 2 weeks should be diagnosed as having persistent proteinuria and undergo further
- g. Monitoring proteinuria in patients with chronic kidney disease should be performed using quantitative measurements.

Patients with diabetes and/or hypertension, who

have negative dipstick test for proteinuria, should be tested for microalbuminuria as it predicts the later occurrence of overt proteinuria and also a marker of increased cardiovascular complications in diabetes and hypertension.^{10, 23-26} Orthostatic proteinuria must be excluded especially in children by repeat measurements on first morning specimen if the initial proteinuria was obtained on a random specimen.

2. Other urine abnormalities

The presence of red blood cells and/or white blood cells in the urine may indicate renal damage. Microscopic analysis of the urine sediment is recommended in patients with chronic kidney disease and those at increased risk of developing chronic kidney disease.¹⁰ A significant number of cellular casts highly suggest significant renal damage.

Imaging studies of the kidney should be performed in patients with chronic kidney disease and those at increased risk of developing the disease.

Estimate glomerular filtration rate

The glomerular filtration rate should be the parameter used to evaluate the level of kidney function because it is the best overall index of renal function.^{10, 27-28} This should be estimated from prediction equations that take into account serum creatinine concentration and some or all of the following variables: age, gender, race and body size.²⁹⁻³¹ The following equations provide useful estimates of GFR (Table 6):

- i. The MDRD (Modification of diet in renal disease) study group and Cockcroft-Gault equations for adults
- ii. Schwartz and Counahan-Barratt equations for children

The Cockcroft-Gault equation estimates the creatinine clearance which over estimates GFR in the obese, however it is a simple useful tool in estimating the level of renal function and very valuable in adjusting drug dosages.²⁹⁻³² It has been validated in adult Africans and shown to be reliable in screening for CKD in the African adults.³³⁻³⁴ The MDRD study equation estimates the glomerular filtration rate more accurately and reflects the level of renal function better especially in the obese and those with glomerular filtration rate less than 90mls/min,³⁰ but it is more cumbersome to calculate. The prediction equations are less reliable in screening for CKD in the African children³⁵ and should be applied with caution while more reliable methods are being sought. The serum creatinine alone should not be used to assess the level of renal function because it is affected by factors such as the muscle mass of the individual, diet, secretion, generation and extra renal excretion.³⁶⁻³⁸

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