Chronic Kidney Disease Awareness Among Individuals with Clinical Markers of Kidney Dysfunction

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Summary

Background and objectives Awareness of chronic kidney disease (CKD) among providers and patients is low. Whether clinical cues prompt recognition of CKD is unknown. We examined whether markers of kidney disease that should trigger CKD recognition among providers are associated with higher individual CKD awareness.

Design, setting, participants, & measurements CKD awareness was assessed in 1852 adults with an estimated GFR <60 ml/min per 1.73 m^2 using 1999 to 2008 National Health and Nutrition Examination Survey data. CKD awareness was a "yes" answer to "Have you ever been told you have weak or failing kidneys?" Participants were grouped by distribution of the following abnormal markers of CKD: hyperkalemia, acidosis, hyperphosphatemia, elevated blood urea nitrogen, anemia, albuminuria, and uncontrolled hypertension. Odds of CKD awareness associated with each abnormal marker and groupings of markers were estimated by multivariable logistic regression.

Results Among individuals with kidney disease, only those with albuminuria had greater odds of CKD awareness (adjusted odds ratio, 4.0, $P < 0.01$) than those without. Odds of CKD awareness increased with each additional manifested clinical marker of CKD (adjusted odds ratio, 1.3, $P = 0.05$). Nonetheless, 90% of individuals with two to four markers of CKD and 84% of individuals with ≥5 markers of CKD were unaware of their disease.

Conclusions Although individuals who manifest many markers of kidney dysfunction are more likely to be aware of their CKD, their CKD awareness remains low. A better understanding of mechanisms of awareness is required to facilitate earlier detection of CKD and implement therapy to minimize associated complications.

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Introduction

Chronic kidney disease (CKD) is a public health concern, affecting an estimated 13% of the US population (1). Better management of CKD can slow progression of renal dysfunction, prevent metabolic complications, and reduce cardiovascular-related outcomes (2). Physician awareness of disease is critical for implementation of evidence-based therapies, and patient awareness is a major determinant of adherence to those therapies.

Despite national efforts to heighten public concern surrounding kidney disease (3), individual awareness of CKD and its risk factors remains low (1,4–6). In the 1999 to 2004 National Health and Nutrition Examination Surveys (NHANES), only 8% and 41% of persons with CKD stages III and IV, respectively, self-reported their CKD (1). Similarly, only 9% of patients with CKD and diabetes in a screening study were aware of their CKD status (7), and only 5% of those with CKD and coronary heart disease self-reported CKD awareness in a cohort study (8).

CKD awareness may be particularly important among persons who exhibit clinical markers possibly directly resulting from their renal dysfunction, because they would benefit from lifestyle and medical interventions to enhance well-being. Wagner's Chronic Care Model (9), which posits an informed patient and a prepared practice team produce productive interactions that lead to improved outcomes, offers one theoretical framework for how CKD awareness could arise. Thus, clinical markers of CKD should trigger provider recognition of CKD and, through patient-provider communication, increase individual awareness. Provider recognition has been shown to be low (10), but prior studies have not assessed whether providers are sensitive to other clinical cues that might help them recognize CKD.

We examined whether well-known manifestations

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of kidney disease were associated with greater individual CKD awareness. We hypothesized that participants who exhibited markers of kidney dysfunction for any given level of estimated GFR (eGFR) were more likely to have a provider who detected CKD and communicated the individual's CKD status to the participant, resulting in greater individual awareness of CKD.

Materials and Methods

Study Design

The NHANES is a continuous survey conducted by the National Center for Health Statistics to examine disease prevalence and trends in cross-sectional representative samples of noninstitutionalized US civilian residents. The survey consists of a standardized in-home interview and a physical examination/specimen collection at a mobile examination center. All of the participants gave informed consent. The protocol was approved by an institutional review board.

We examined data from the 1999 to 2008 NHANES (11). The total number of adult nonpregnant NHANES study participants with an eGFR of 15 to 59 ml/min per 1.73 m^2 was 2375. Our sample included individuals who self-reported awareness or unawareness of CKD (n = 2365), had complete laboratory data (n = 1932), and had seen a health-care provider within the previous year (final n = 1852). This ensured that participants had the opportunity to develop CKD awareness.

Measurements

Self-reported sociodemographics (age, gender, race/ethnicity, marital status, social support, primary language, education, and income), access to care (insurance and routine site for medical care), and diagnoses (CKD and diabetes) were obtained during interviews. BP was measured during the examination; the mean of all measurements was used. Serum potassium, serum bicarbonate, serum phosphate, blood urea nitrogen, and hemoglobin were measured using a Beckman Synchron LX20 analyzer from 1999 to 2007 and the Beckman Coulter UniCel DxC800 in 2008. Serum creatinine was measured by the modified kinetic method of Jaffe, and levels were corrected for different analyzers (12,13). Random spot urine albumin and creatinine levels were measured using frozen specimens. Urine albumin was measured using a solid-phase fluorescence immunoassay; urine creatinine was measured using the modified Jaffe kinetic method. Albuminuria and creatinine were corrected according to NHANES documentation to allow for comparison across all 10 years (13). Serum hemoglobin A1C was measured by an automatic high performance liquid chromatography system.

Definitions

The outcome variable was awareness of CKD. As in prior studies, participants who responded "yes" to "Have you ever been told by a doctor or other health professional that you have weak or failing kidneys (excluding kidney stones, bladder infections, or incontinence)?" during the interview were defined as being aware of their CKD (1,7).

Predictors included common clinical markers of CKD: hyperkalemia, metabolic acidosis, hyperphosphatemia, elevated blood urea nitrogen (BUN), anemia, albuminuria, and uncontrolled hypertension. Abnormal values were defined *a priori* as: serum potassium, >5 mEq/L; serum bicarbonate, < 22 mEq/L; serum phosphate, >4.5 mEq/L; and BUN, >15 mmol/L. Anemia was defined as a hemoglobin of <12.5 g/dl in women and <13.5 g/dl in men; albuminuria was considered present at urinary albumin-to-creatinine ratios of >17 mg/g for men and >25 mg/g for women (14). Hypertension was considered uncontrolled if the average measurement of systolic or diastolic BP was >140 or >90 mmHg, respectively. We created a composite variable describing the number of manifest clinical markers of CKD, ranging from 0 to 7, consisting of equally weighted binary indicators of the aforementioned abnormal values. Categorization of this number was determined by distribution of clinical markers (zero to one markers, two to four markers, and five to seven markers). Diabetes was defined by self-report or a glycosylated hemoglobin of ≥6.5% (15).

Kidney disease was defined using single assessments of eGFR, according to the Kidney Disease Outcomes Quality Initiative staging guidelines (16). Estimated GFR was calculated according to the modified Modification of Diet in Renal Disease Study equation for calibrated serum creatinine level (17).

Statistical Methods

Participant characteristics were compared by number of abnormal clinical makers of CKD. Chi-squared and Wilcoxon rank-sum tests were used to evaluate associations between number of abnormal markers and demographic variables. Variance of proportions was estimated with Taylor series linearization. Multivariable logistic regression was used to estimate the independent association between CKD awareness and individual markers of CKD as well as the overall burden of clinical markers of CKD. We adjusted for characteristics that were shown or thought *a priori* to be associated with clinical markers of CKD: age, gender, race/ethnicity, education, income, eGFR, and presence of diabetes. To more closely mirror clinical practice, when clinical markers of CKD may be obtained simultaneously with eGFR (*i.e.* acidosis, hyperkalemia, and elevated BUN), we also examined the association between each clinical marker and CKD awareness without adjustment for eGFR.

Two sensitivity analyses were conducted. In the first, percentiles of continuous predictor variables (rather than binary indicators) were summed and equally weighted to create a continuous composite variable, ranging from 0 to 100. This analysis ensured that any excess in odds of CKD awareness was not due to inappropriate binary cutoff points for the abnormal markers of CKD. In the second analysis, eGFR was calculated according to the Chronic Kidney Disease Epidemiology Collaboration equation (18), which may more accurately estimate renal function at higher levels of GFR. This was performed to ensure that results were robust to the choice of eGFR estimating equation. All of the analyses were weighted to reflect the US population, using STATA version 11 (StataCorp., College Station, TX).

Results

Participant Characteristics and Burden of Abnormal Clinical Markers of CKD

Among study participants, 40% had zero or one abnormal clinical markers of CKD, whereas only 2% displayed at least five markers. Individuals with a greater number of clinical markers were more likely than those with fewer markers to be male, older than 60 years of age, and of race/ethnicity other than non-Hispanic white (Table 1). In addition, a greater number of clinical markers was significantly associated with lower yearly income (P trend $<$ 0.0001) and less social support (P trend $<$ 0.03).

Included individuals were similar to those excluded because of no provider visit in the previous year, with respect to age, race/ethnicity, social support, yearly income, and access to health care ($P > 0.05$ for all). Additionally, compared with individuals who were excluded from the analysis because of missing awareness information, the study population had a similar racial/ethnic minority distribution ($P = 0.75$). A broader definition of CKD including albuminuria, however, would have included higher proportions of racial/ethnic minorities relative to the study population (35% *versus* 15% nonwhite, $P < 0.001$).

In general, a greater burden of CKD markers was associated with lower eGFR ($P < 0.001$) (Figure 1). Among study participants with an eGFR of 45 to 59 ml/min per 1.73 m^2, 57% had zero to one clinical markers of CKD, and 1% had at least five markers. By contrast, among those with an eGFR 15 to 29 ml/min per 1.73 m^2, only 8% had zero to one clinical markers of CKD, and 12% exhibited at least five abnormal markers.

Association of Participant Awareness of CKD with Clinical Markers of CKD

Among individuals with kidney disease, the majority of whom had an eGFR between 30 and 59 ml/min per 1.73 m^2, only 9% were aware of their renal dysfunction. Examination of the association between individual clinical markers of CKD and awareness of CKD revealed that albuminuria and hyperkalemia were both associated with greater odds of CKD awareness (Table 2). However, independent of eGFR, only albuminuria remained associated with increased odds of CKD awareness. Other common manifestations of CKD were not significantly associated with patient awareness of kidney dysfunction (Table 2).

Individuals who displayed a greater number of markers of renal dysfunction had higher odds of being aware of their kidney disease than individuals with kidney dysfunction who did not exhibit clinical markers. Individuals with

Table 1. Characteristics associated with abnormal clinical markers of CKD in the US population, NHANES 1999 to 2008

	All	Number of Abnormal Clinical Markers of CKD			
		Zero to One	Two to Four	Five to Seven	*P*
Total, *n* (%)	1852	772 (41.68%)	1048 (56.58%)	32 (1.73%)	
Mean estimated GFR ml/min per 1.73 m^2 (SD)	49.70 (8.41)	52.70 (6.60)	47.20 (10.12)	33.38 (0)	
Demographics, %					
Male gender	38.22	31.13	44.98	45.51	<0.01
Age					<0.01
20 to 39 years	4.13	5.70	2.60	3.52	
40 to 59 years	20.95	27.39	14.70	18.40	
60 to 69 years	18.81	19.52	18.29	12.57	
≥70 years	56.11	47.40	64.41	65.51	
Race/ethnicity[a]					<0.01
non-Hispanic white	85.68	90.68	80.84	83.31	
non-Hispanic black	6.55	3.19	9.70	12.33	
Mexican American	1.93	1.22	2.56	4.35	
Greater than high school education	74.37	81.54	67.38	72.55	<0.01
Has social support	94.61	95.27	92.27	77.57	0.04
Currently married	61.82	67.48	56.69	45.69	0.03
Non-English language	2.76	1.99	3.54	1.85	0.14
Yearly family income					<0.01
<$19,999	27.76	21.37	33.42	52.06	
$20,000 to 44,999	33.65	30.20	36.83	32.97	
$45,000 to 74,999	21.81	26.91	17.23	4.63	
>$75,000	16.92	21.52	12.52	10.34	
Access to health care, %					
Has health insurance	96.28	95.34	97.14	98.21	0.14
Has a routine site for care	97.49	97.25	97.66	100.00	0.70
Comorbid conditions, %					
Diabetes	22.09	13.01	30.26	49.82	<0.01

Analyses have been weighted to reflect the US population. Total $n = 1852$ for all rows except education ($n = 1847$), social support ($n = 1726$), marital status ($n = 1813$), language ($n = 1813$), income ($n = 1681$), insurance ($n = 1839$), and diabetes ($n = 1851$).
CKD, chronic kidney disease.
[a]Individuals of "other" race/ethnicity not shown because of small sample size but are included in all analyses.

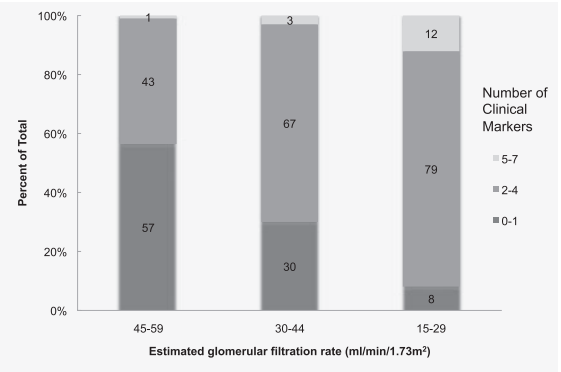

Figure 1. | Percentage of individuals with clinical markers of chronic kidney disease (CKD) by estimated GFR and number of abnormal markers of CKD.

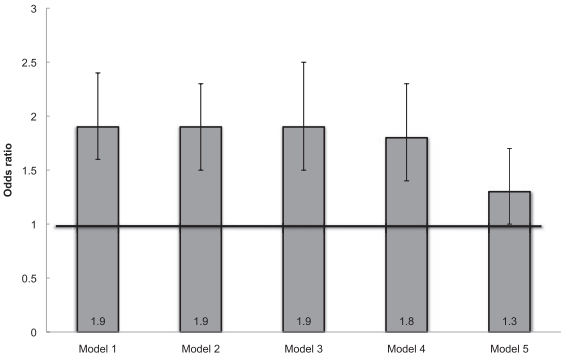

Figure 2. | Adjusted odds ratios and 95% confidence intervals of CKD awareness associated with each additional clinical marker of CKD. (Model 1) unadjusted. (Model 2) Model 1 + demographics (age, gender, race/ethnicity, education). (Model 3) Model 2 + socioeconomic status (income). (Model 4) Model 3 + diabetes. (Model 5) Model 4 + estimated GFR.

two to four clinical markers of CKD demonstrated 90% greater odds of CKD awareness compared with those with zero to one markers (adjusted odds ratio [AOR], 1.9; $P = 0.04$). Participants who displayed at least five markers of CKD demonstrated nonstatistically significant greater odds of awareness (AOR, 3.6; $P = 0.06$) relative to participants with zero to one clinical markers of CKD. There was a graded association between each additionally manifested clinical marker and awareness of CKD; this remained significant after adjustment for demographic and socioeconomic factors and diabetes (Figure 2). Adjusting for eGFR mitigated the association.

Despite the positive association between an increasing number of CKD clinical markers and individual awareness of CKD, awareness of CKD among participants was very low (Figure 3). Our model indicated that nearly 90% of individuals with two to four markers of kidney disease were unaware of their renal dysfunction, and among those with at at least five markers of kidney disease, 84% were unaware. These results remained consistent across all NHANES study periods.

Sensitivity analyses using continuous predictor variables rather than binary indicators and expanding the study population to all individuals with an eGFR <60 ml/min per 1.73 m^2 regardless of whether they had seen a provider within the previous year produced similar results (data not shown). When the Chronic Kidney Disease Epidemiology Collaboration estimating equation was used to determine whether participants had kidney disease, no substantial differences in association estimates were found (data not shown).

Discussion

We demonstrated that individual awareness of CKD is positively associated with a greater number of manifestations of renal dysfunction, independent of eGFR. Although this association was expected, the high degree of CKD unawareness among individuals with at least five markers of their kidney disease and the persistence of unawareness over time were not. Our study is consistent with previous investigations demonstrating low levels of individual CKD awareness (1,4,6) but highlights the profound lack of awareness among individuals with an eGFR <60 ml/min per 1.73 m^2 who have already developed either late complications of kidney disease (hyperkalemia, acidosis, and hyperphosphatemia) or albuminuria, which are associated

Table 2. Odds ratios for awareness of CKD by abnormal levels of individual clinical markers of CKD in the US population, NHANES 1999 to 2008

	Odds Ratios for Awareness of CKD (95% CI)[a]	Odds Ratios for Awareness of CKD, Independent of estimated GFR (95% CI)[b]
Albuminuria[c]	5.46 (3.10 to 9.60)	4.00 (2.11 to 7.39)
Hyperkalemia (serum potassium, >5.0 mEq/L)	2.63 (1.32 to 5.18)	1.56 (0.86 to 2.83)
Hyperphosphatemia (serum phosphorus, >4.5 mEq/L)	1.41 (0.67 to 2.95)	1.10 (0.54 to 2.26)
Anemia (hemoglobin <12.5 g/dl in women, 13.5 g/dl in men)	1.56 (0.98 to 2.50)	1.03 (0.59 to 1.81)
Acidosis (serum bicarbonate, <22 mEq/L)	1.11 (0.72 to 1.72)	0.94 (0.60 to 1.45)
Elevated blood urea nitrogen (>15 mmol/L)	1.05 (0.58 to 1.90)	0.62 (0.30 to 1.23)
Uncontrolled hypertension (>140/>90 mmHg)	0.65 (0.26 to 1.67)	0.50 (0.14 to 1.78)

Analyses have been weighted to reflect the US population. CKD, chronic kidney disease; CI, confidence interval.
[a]Adjusted for other manifestations listed and age, gender, race/ethnicity, education, income, and diabetes.
[b]Adjusted for everything in previous model and estimated GFR.
[c]Albuminuria is defined as urinary albumin-to-creatinine ratio >17 mg/g in men and >25 mg/g for women.

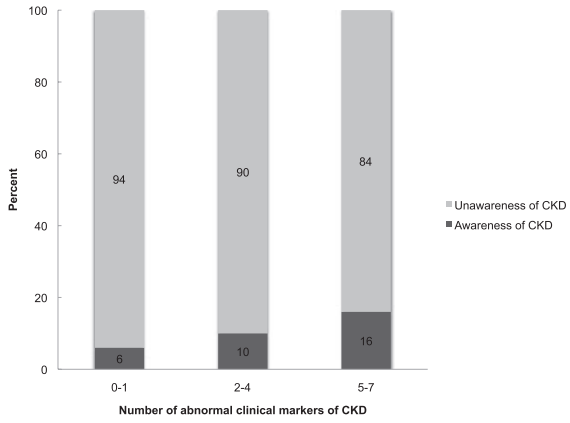

Figure 3. | Adjusted percentage of chronic kidney disease (CKD) awareness and unawareness by number of abnormal clinical markers of CKD. The values are adjusted for age, gender, race/ethnicity, education, income, diabetes, and estimated GFR.

with poor outcomes in this patient population (19,20). Unlike individuals who may never experience sequelae of their kidney disease, namely individuals with CKD defined solely by albuminuria and elderly patients with decreased eGFR from "natural aging" (21,22), patients who exhibit complications from their renal dysfunction may particularly benefit from being aware of their CKD. Awareness of CKD is a necessary first step toward adopting lifestyle and risk-factor modifications necessary to prevent progression of kidney disease and to minimize adverse sequelae (23).

The mechanism behind individual awareness of CKD is not understood. In this study, we illustrated that sociodemographic factors such as increased age, nonwhite race/ethnicity, low income, and low levels of formal education were independently associated with a greater burden of abnormal markers of CKD, in addition to low CKD awareness. However, in our study, these factors did not significantly affect the association between an increasing number of CKD markers and CKD awareness. The high percentage of individuals with a routine site for medical care in our study population may explain these results, because traditional demographic and socioeconomic factors associated with poor CKD awareness may not play as large a role in an established primary care provider relationship.

The large percentage of CKD unawareness among individuals with a greater number of clinical markers of kidney disease can be interpreted in a variety of ways. It is possible that low individual awareness of CKD despite multiple markers of kidney dysfunction reflects a low level of provider testing for kidney disease or poor recognition of kidney disease by clinicians. Low levels of CKD awareness among primary care providers have been documented (10,24,25); however, it is unlikely that clinician unawareness of CKD could fully explain this degree of patient unawareness of kidney disease. Ineffective communication by providers who appropriately recognize CKD and its complications may also play a role. Provider time constraints, clinician/patient language discordance, patient cognitive disabilities, and low patient health literacy may all contribute to poor communication surrounding the diagnosis of CKD. Lastly, our results could reflect flaws in ascertainment of patient awareness of CKD.

Among the abnormal laboratory markers of CKD that are often obtained simultaneously with eGFR, only hyperkalemia was associated with greater odds of CKD awareness. This can be explained by the frequent, although not exclusive, presence of hyperkalemia in severe (rather than moderate) kidney dysfunction and its association with potential life-threatening cardiovascular events. This association did not hold true when tested independently of eGFR, however. Thus, it is possible that providers consider some of the markers of CKD, such as anemia or acidosis, as independent illnesses rather than markers of kidney disease. Interestingly, elevated BUN was not associated with increased odds of CKD awareness. Elevated BUN is not only a marker of CKD but also of dehydration and acute kidney injury. Thus, although not assessed in this study, it is plausible that elevated serum BUN levels are associated with greater awareness of acute kidney injury rather than CKD.

Among all of the common markers of CKD, only albuminuria was associated with greater odds of CKD awareness independent of eGFR. Educational efforts to increase CKD awareness among the general public, such as formation of the National Kidney Disease Education Program by the National Institutes of Health in 2001 (26) and dissemination of the Kidney Disease Outcomes Quality Initiative staging (16), have focused on recognition of albuminuria as a risk factor for CKD progression. Our results may reflect, in part, the success of these programs and suggest that educational programs should further emphasize other clinical manifestations of CKD as markers of advanced kidney disease, irrespective of eGFR.

This study has several limitations. First, the cross-sectional nature of NHANES may lead to misclassification of participants with CKD, because estimates of GFR and albuminuria were on the basis of single laboratory values. As in other research endeavors (27,28), lack of longitudinal data may have led to inclusion of individuals with acute kidney injury and not CKD. Second, awareness is self-reported and is subject to recall bias. Third, it is possible that the cutoffs used to define abnormal clinical markers of CKD were not extreme enough to trigger clinician recognition of kidney dysfunction. However, these definitions of abnormality were set *a priori*, and a sensitivity analysis using continuous predictors rather than binary predictors depicted similar associations between individual markers of CKD and CKD awareness. Fourth, neither provider factors associated with CKD awareness nor the communication process between providers and participants could be assessed using these data. Provider understanding and recognition of CKD, quality of provider-patient communication, and frequency of patient visits with the same health care provider are likely determinants of patient understanding of CKD and would help frame our results.

In summary, despite efforts to increase CKD awareness in the community, individuals with many complications of their kidney dysfunction remain unaware of their disease. Current educational efforts for primary care providers and the general public should reinforce not only recognition of CKD on the basis of eGFR and presence of albuminuria but

also recognition of other common manifestations of CKD. As a marker for increased risk of cardiovascular and all-cause mortality, routine incorporation of CKD into provider-patient communication and clinical decision-making for patients with clinical manifestations of CKD is warranted. In addition, future research should focus on better understanding the mechanisms of patient awareness of CKD and the best metrics by which CKD awareness can be measured. Examination of the effect of patient health literacy and patient-provider communication on CKD awareness is necessary to determine optimal points of intervention to facilitate earlier recognition of CKD, slow the progression of kidney disease, and minimize associated complications.

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Disclosures

None.

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