Racial Differences in Kidney Function Among Individuals With Obesity and Metabolic Syndrome: Results From the Kidney Early Evaluation Program (KEEP)

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Background: Obesity and metabolic syndrome may differ by race. For participants in the National Kidney Foundation's Kidney Early Evaluation Program (KEEP), we examined whether African American and white participants with obesity and metabolic syndrome differ regarding albuminuria, estimated glomerular filtration rate (eGFR), anemia, and bone/mineral metabolism derangements in chronic kidney disease (CKD).

Methods: 3 study cohorts were assembled: (1) eligible African American and white KEEP participants with body mass index $\geq$ 30 kg/m^2, (2) a subgroup meeting criteria for metabolic syndrome, and (3) a subgroup with eGFR $<$ 60 mL/min/1.73 m^2 and laboratory measurements for hemoglobin, parathyroid hormone, calcium, and phosphorus. Patient characteristics and kidney function assessments were compared and tested using χ^2 (categorical variables) and *t* test (continuous variables). Univariate and multivariate logistic regression analyses were performed to evaluate associations of race with kidney disease measures.

Results: Of 37,107 obese participants, 48% were African American and 52% were white. Whites were more likely to have metabolic syndrome components (hypertension, 87.1% vs 84.8%; dyslipidemia, 81.6% vs 66.7%; diabetes, 42.7% vs 34.9%) and more profoundly decreased eGFR than African Americans (CKD stages 3-5 prevalence, 23.6% vs 13.0%; $P < 0.001$). African Americans were more likely to have abnormal urinary albumin excretion (microalbuminuria, 12.5% vs 10.2%; OR, 1.60 [95% CI, 1.45-1.76]; macroalbuminuria, 1.3% vs 1.2%; OR, 1.61 [95% CI, 1.23-2.12]) and CKD stages 1-2 (10.3% vs 7.1%; OR, 1.54 [95% CI, 1.38-1.72]). For participants with CKD stages 3-5, anemia prevalence was 32.4% in African Americans and 14.1% in whites; corresponding values for secondary hyperparathyroidism were 66.2% and 46.6%, respectively.

Conclusions: Obesity and metabolic syndrome may be heterogeneous disease states in African Americans and whites, possibly explaining differences in long-term kidney and cardiovascular outcomes.
Am J Kidney Dis 55(S2):S4-S14.

INDEX WORDS: Anemia; chronic kidney disease; metabolic syndrome; obesity; proteinuria.

During the last 3 decades, prevalence rates of obesity and metabolic syndrome have more than doubled in US adults. In the most recent National Health and Nutrition Examination Survey (NHANES), 32.2% of US adults met clinical criteria for obesity, with body mass index (BMI) $\geq$ 30 kg/m^2.[1] Metabolic syndrome, a clinical syndrome marked by abdominal obesity, dyslipidemia, increased blood pressure, and impaired insulin sensitivity, was detectable in approximately 1 of every 3 US adults.[2] Notably, increasing rates of obesity and metabolic syndrome have paralleled the increasing national burden of chronic kidney disease (CKD).[3]

To date, much of the attention given to obesity and metabolic syndrome as risk factors for CKD has aptly focused on their links to diabetes and

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Received August 5, 2009. Accepted in revised form October 26, 2009.

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0272-6386/10/5503-0102$36.00/0
doi:10.1053/j.ajkd.2009.10.045

hypertension, the 2 leading causes of kidney disease. In addition, a growing body of evidence has emerged suggesting that obesity by itself, independent of its association with hypertension or diabetes, is a key factor in kidney injuries.[4-13] Several mechanisms have been proposed for the obesity-CKD relationship, including altered mechanical forces, chronic inflammation, abnormal vascular remodeling, renal lipotoxicity, and a disordered relationship between volume status and aldosterone secretion.[4,7,14-16] This pathophysiologic process may be more pronounced in African Americans, who have high rates of hypertension, obesity, and aggressive CKD.[17-20]

We hypothesized that obesity and metabolic syndrome may be different disease entities in African Americans and whites. Using data from the National Kidney Foundation's Kidney Early Evaluation Program (KEEP), we examined whether obese African Americans with metabolic syndrome had greater odds of albuminuria and impaired kidney function than whites with the same conditions. In obese participants with CKD stages 3-5, we then examined whether rates of anemia and bone/mineral metabolism derangements were higher for African Americans than whites.

METHODS

Study and Participants

KEEP is a free community-based health screening program that targets populations aged ≥ 18 years at high risk of kidney disease, defined as history of diabetes or hypertension or a first-order relative with diabetes, hypertension, or kidney disease, as has been described previously.[21] Since August 2000, the program has screened > 128,000 participants from 49 states and the District of Colombia. In this study, we included 107,309 eligible KEEP participants from August 2000 through December 31, 2008, from 47 National Kidney Foundation affiliates and 2,336 screening programs in 49 states and the District of Columbia.

This study included 3 study cohorts. The first cohort included eligible KEEP participants with BMI ≥ 30 kg/m^2, excluding participants who reported Hispanic or Latino origin, race other than white or African American, or being on dialysis therapy or undergoing transplant. The second cohort included participants from the first cohort who participated in KEEP after May 1, 2005, when laboratory measurements for cholesterol and triglycerides became available, allowing evaluation of metabolic syndrome. The third cohort included participants from the first cohort with estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 and who participated in KEEP after November 1, 2005, when laboratory measurements for parathyroid hormone (PTH), calcium, and phosphorus became available. Details of laboratory value measurements (eg, serum creatinine, urinary albumin excretion, and intact PTH) have been reported elsewhere.[22-24]

Definitions

eGFR was calculated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation,[25] and serum creatinine was calibrated by the Cleveland Clinic Research Laboratory. In a sensitivity analysis, GFR also was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[26] Albumin-creatinine ratios (ACRs) were calculated from urine samples and recorded as <30, 30-300, or >300 mg/g. Microalbuminuria was defined as ACR of 30-300 mg/g, and macroalbuminuria, as ACR > 300 mg/g. eGFR values were grouped by stages: stage 1, ≥ 90 mL/min/1.73 m^2 with ACR ≥ 30 mg/g; stage 2, 60-89 mL/min/1.73 m^2 with ≥ ACR 30 mg/g; stage 3, 30-59 mL/min/1.73 m^2; and stages 4-5, <30 mL/min/1.73 m^2. Anemia was defined as hemoglobin level < 11 g/dL in premenopausal women and < 12 g/dL in men and postmenopausal women. Secondary hyperparathyroidism was defined as PTH level > 70 pmol/L for participants with CKD stage 3, >110 pmol/L for stage 4, and >300 pmol/L for stage 5.

Metabolic syndrome was defined as BMI ≥ 30 kg/m^2 and at least 2 of the following conditions: (1) dyslipidemia, defined as triglyceride level > 150 mg/dL or cholesterol level > 200 mg/dL (Adult Treatment Panel [ATP] III criteria); (2) diabetes mellitus, defined as fasting blood glucose level > 109 mg/dL (ATP III criteria), self-reported history, or use of glucose-lowering medications; and (3) hypertension, defined as average systolic blood pressure > 129 mm Hg or diastolic blood pressure > 84 mm Hg (ATP III criteria), self-reported history, or use of

blood pressure–lowering medication. Other measures, including education level, tobacco and alcohol use, and family history of diseases, were self-reported. Blood pressure, height, weight, and waist circumference were directly measured for all participants.

Statistical Analysis

Patient characteristics and assessment of kidney function between African Americans and whites were compared and tested using χ^2 for categorical variables and *t* test for continuous variables. In addition to univariate logistic regression analyses of microalbuminuria, macroalbuminuria, and CKD prevalence, we also performed polytomous logistic regression (multinomial logit) analyses controlling for age, sex, BMI, smoking, alcohol use, hypertension, diabetes, dyslipidemia, family history of kidney disease, and eGFR (for the outcome of albuminuria). In examining the association of race with anemia and secondary hyperparathyroidism in KEEP participants with BMI $\geq$ 30 kg/m^2 and eGFR $<$ 60 mL/min/1.73 m^2, we also performed both univariate and multivariate logistic regression analyses controlling for age, sex, smoking, alcohol use, and eGFR for the outcome of anemia and additionally controlling for calcium and phosphorus levels for the outcome of secondary hyperparathyroidism. Participants with missing covariate data were not

Table 1. Characteristics of African American and White KEEP Participants With Body Mass Index $\geq$ 30 kg/m^2

Characteristics	African American (n = 17,929)	White (n = 19,178)	*P*
Age (y)	52.4 ± 13.4	56.9 ± 13.8	<0.001
Women[a]	76.5 (13,709)	67.6 (12,963)	<0.001
Body mass index (kg/m^2)	36.6 ± 5.7	35.9 ± 5.4	<0.001
Waist circumference[a] (inches)	43.9 ± 5.4	44.8 ± 5.5	<0.001
Systolic blood pressure[a] (mm Hg)	138.0 ± 20.2	137.2 ± 18.6	<0.001
Diastolic blood pressure[a] (mm Hg)	83.2 ± 11.9	80.8 ± 11.1	<0.001
Hypertension	84.8 (15,204)	87.1 (16,705)	<0.001
Total cholesterol[a] (mg/dL)	198.4 ± 40.3	197.9 ± 43.4	0.3
Triglycerides[a] (mg/dL)	130.2 ± 87.6	203.2 ± 138.4	<0.001
Dyslipidemia[a]	66.7 (6,534)	81.6 (9,759)	<0.001
Fasting blood glucose[a] (mg/dL)	112.3 ± 45.2	115.1 ± 46.3	0.009
Diabetes[a]	34.9 (6,256)	42.7 (8,189)	<0.001
Highest level of education[a]			<0.001
<High school	13.6 (2,406)	11.0 (2,094)	
High school graduate	25.0 (4,410)	30.8 (5,857)	
College graduate	48.9 (8,639)	47.2 (8,958)	
Professional degree	12.5 (2,210)	11.0 (2,080)	
Current tobacco use[a]	10.4 (1,751)	9.5 (1,740)	0.003
Alcohol use[a]	57.8 (5,428)	59.2 (6,892)	0.04
Family history			
Kidney disease[a]	22.7 (3,930)	17.8 (3,286)	<0.001
Diabetes[a]	66.3 (11,446)	60.6 (11,177)	<0.001
Hypertension[a]	86.1 (15,092)	77.7 (14,419)	<0.001

Note: Values expressed as mean ± standard deviation or percentage (number). Conversion factors for units: waist circumference in inches to cm, ×2.54; total cholesterol in mg/dL to mmol/L, ×0.02586; triglycerides in mg/dL to mmol/L, ×0.01129; fasting blood glucose in mg/dL to mmol/L, ×0.05551.

Abbreviation: KEEP, Kidney Early Evaluation Program.

[a]Excludes missing values.

included in multivariate models, but were included in univariate analyses. Comparing the included populations in the univariate and multivariate models showed no major differences in demographic data, such as age, race, sex, and comorbid conditions.

RESULTS

A total of 46,725 KEEP participants were found to have BMI $\geq$ 30 kg/m^2. After excluding participants who reported Hispanic or Latino origin, race other than African American or white, or history of dialysis or kidney transplant, 37,107 obese KEEP participants remained, of whom 48% were African American and 52% were white (Table 1). African American participants in this cohort were more likely to be younger and women and to have family histories of diabetes, hypertension, and kidney disease.

The prevalence of the components of metabolic syndrome was higher in white than African American participants. Despite lower mean BMI values, white participants had higher mean waist circumferences (44.8 vs 43.9 inches) and were more likely to have hypertension (87.1% vs 84.8%), dyslipidemia (81.6% vs 66.7%), diabetes (42.7% vs 34.9%), and higher fasting blood glucose levels (115.1 vs 112.3 mg/dL).

Table 2. Assessment of Kidney Function in African American and White KEEP Participants with BMI $\geq$ 30 kg/m^2 and Metabolic Syndrome

	African American	White	*P*
BMI $\geq$ 30 kg/m^2			
No. of participants	17,929	19,178	
Albumin-creatinine ratio[a]			<0.001
Normal (<30 mg/g)	86.3 (13,575)	88.6 (15,734)	
Microalbuminuria (30-300 mg/g)	12.5 (1,959)	10.2 (1,807)	
Macroalbuminuria (>300 mg/g)	1.3 (205)	1.2 (222)	
Serum creatinine[a] (mg/dL)	0.97 $\pm$ 0.38	0.93 $\pm$ 0.29	<0.001
eGFR[a]	86.3 $\pm$ 24.4	75.5 $\pm$ 21.0	<0.001
eGFR < 60 mL/min/1.73 m^{2,a}	11.7 (2,011)	22.3 (4,145)	<0.001
CKD stage[a]	n = 15,380	n = 17,540	<0.001
No CKD	76.6 (11,780)	69.3 (12,149)	
1	4.6 (710)	2.0 (357)	
2	5.7 (879)	5.1 (889)	
3	12.3 (1,897)	22.5 (3,947)	
4-5	0.7 (117)	1.1 (198)	
Metabolic syndrome[b]			
No. of participants	6,931	10,065	
Albumin-creatinine ratio[a]			<0.001
Normal (<30 mg/g)	84.4 (5,744)	88.0 (8,703)	
Microalbuminuria (30-300 mg/g)	14.0 (956)	10.5 (1,041)	
Macroalbuminuria (300 mg/g)	1.6 (107)	1.4 (142)	
Serum creatinine[a] (mg/dL)	0.99 $\pm$ 0.35	0.94 $\pm$ 0.29	<0.001
eGFR[a] (mL/min/1.73 m^2)	83.1 $\pm$ 22.3	74.2 $\pm$ 20.3	<0.001
eGFR < 60 mL/min/1.73 m^{2,a}	13.8 (929)	23.8 (2,364)	<0.001
CKD stage[a]	n = 6,662	n = 9,807	<0.001
No CKD	74.4 (4,959)	68.7 (6,737)	
1	4.7 (310)	2.0 (195)	
2	7.0 (464)	5.2 (511)	
3	13.2 (876)	22.9 (2,246)	
4-5	0.8 (53)	1.2 (118)	

Note: Values expressed as mean $\pm$ standard deviation or percentage (number). Conversion factors for eGFR in mL/min/1.73 m^2 to mL/s/1.73 m^2, $\times$0.0166.

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program.

[a]Excludes missing values.

[b]Includes cohort from May 1, 2005, when laboratory measurements for cholesterol and triglycerides became available.

We examined racial differences in kidney function by serum creatinine measurement (with subsequent GFR estimation and CKD stage classification) and urine testing for albuminuria. Obese African American participants were more likely to have abnormal urinary albumin excretion than obese white participants (Table 2; Fig 1); this difference was slightly more pronounced in participants who met criteria for metabolic syndrome. In multivariate analyses (Table 3), obese African American participants compared with obese white participants had ~1.6 times the odds of having microalbuminuria (odds ratio [OR], 1.60; 95% confidence interval [CI], 1.45-1.76), macroalbuminuria (OR, 1.61; 95% CI, 1.23-2.12), and CKD stages 1-2 (OR, 1.54; 95% CI, 1.38-1.72). These odds for disease were virtually identical in a smaller cohort of African American and white participants with metabolic syndrome (Table 4).

Obese African American participants with and without metabolic syndrome, despite slightly higher mean serum creatinine levels, had significantly higher eGFRs (Table 2). Thus, in obese African American participants, regardless of the presence or absence of metabolic syndrome, prevalence rates of CKD stages 1-2 were significantly higher and rates of CKD stages 3-5 were lower than in their white counterparts. In multivariate analyses, lower odds of CKD stages 3-5 persisted in obese African American participants with and without metabolic syndrome (Tables 3 and 4).

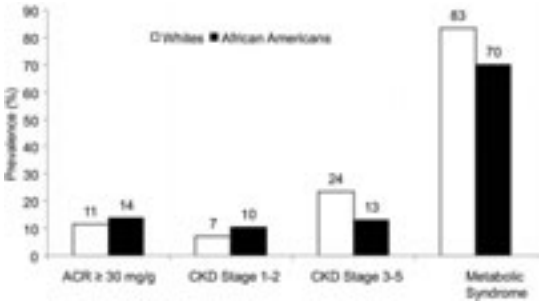

Figure 1. Prevalence of kidney function and metabolic syndrome in obese Kidney Early Evaluation Program participants by race. All differences between whites and African Americans were significant at $P < 0.001$. Total n for calculating kidney function = 37,107; total n for calculating metabolic syndrome = 21,996, including cohort from May 1, 2005, when laboratory measurements for cholesterol and triglycerides became available. Abbreviations: ACR, albumin-creatinine ratio; CKD, chronic kidney disease.

Of 2,030 obese KEEP participants with CKD stages 3-5 (ie, eGFR $<$ 60 mL/min/1.73 m^2), African Americans again on average were younger than their white counterparts (Table 5). Despite nearly identical mean eGFRs, African Americans were more likely than whites to have microalbuminuria (24.8% vs 17.6%; $P < 0.001$) and macroalbuminuria (5.6% vs 3.6%; $P = 0.04$). Mean hemoglobin concentrations were lower (12.5 vs 13.5 g/dL; $P < 0.001$) and mean intact PTH levels were higher (108.0 vs 81.9 pmol/L; $P < 0.001$) in African Americans. Using the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for diagnoses of anemia and secondary hyperparathyroidism, anemia prevalence was more than twice as high in obese African Americans (32.4%) than in obese whites (14.1%) with CKD; secondary hyperparathyroidism prevalence was almost 1.5 times higher in African Americans than in whites (66.2% vs 46.6%). In multivariate analyses comparing obese African Americans with CKD stages 3-5 with whites with the same characteristics (Table 6), ORs were 3.85 (95% CI, 2.94-5.03) for anemia and 2.63 (95% CI, 2.09-3.31) for secondary hyperparathyroidism.

DISCUSSION

In this cross-sectional study of $>$ 37,000 obese African American and white participants who presented for KEEP screening activities, we report that components of metabolic syndrome, such as increased waist circumference, diabetes, hypertension, and dyslipidemia, were more prevalent in white participants. White participants also were more likely to have lower eGFRs and more severe stages of CKD (stages 3-5) than their African American counterparts. However, obese African Americans with and without metabolic syndrome had significantly higher rates of abnormal urinary albumin excretion than their white counterparts and consequently showed a significantly higher prevalence of earlier stage CKD (stages 1-2; Fig 1).

These results support the hypothesis that obesity and metabolic syndrome may be distinct disease states with differing manifestations of kidney disease in Africans Americans and whites. Obese whites were at higher risk of full-blown metabolic syndrome and decreased eGFR (ie,

Table 3. Association of Race With Prevalent Microalbuminuria, Macroalbuminuria, CKD Stages 1-2, and CKD Stages 3-5 in KEEP Participants With BMI ≥ 30 kg/m^2

Condition	OR (95% CI) for African American Participants
Microalbuminuria vs normal	
Univariate analysis (n = 33,502)	1.26 (1.17-1.35)
Multivariate analysis[a,b] (n = 18,709)	1.60 (1.45-1.76)
Macroalbuminuria vs normal	
Univariate analysis (n = 33,502)	1.07 (0.88-1.30)
Multivariate analysis[a,b] (n = 18,709)	1.61 (1.23-2.12)
Macroalbuminuria vs microalbuminuria	
Univariate analysis (n = 33,502)	0.85 (0.70-1.04)
Multivariate analysis[a,b] (n = 18,709)	1.01 (0.76-1.34)
CKD stages 1-2 vs no CKD	
Univariate analysis (n = 32,920)	1.32 (1.22-1.42)
Multivariate analysis[a,c] (n = 18,775)	1.54 (1.38-1.72)
CKD stages 3-5 vs no CKD	
Univariate analysis (n = 32,920)	0.50 (0.47-0.53)
Multivariate analysis[a,c] (n = 18,775)	0.58 (0.53-0.64)
CKD stages 3-5 vs stages 1-2	
Univariate analysis (n = 32,920)	0.38 (0.35-0.42)
Multivariate analysis[a,c] (n = 18,775)	0.38 (0.33-0.43)

For each category, the reference group (odds ratio of 1.00) is white participants.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; KEEP, Kidney Early Evaluation Program; OR, odds ratio.

[a]Results from multinomial logit regression analyses.

[b]Adjusted for age, sex, BMI, current smoking, alcohol use, hypertension, diabetes, dyslipidemia, estimated glomerular filtration rate, and family history of kidney disease.

[c]Adjusted for age, sex, BMI, current smoking, alcohol use, hypertension, diabetes, dyslipidemia, and family history of kidney disease.

CKD stages 3-5). Some of the increased prevalence of CKD stages 3-5 may be caused by racial differences in GFR estimation using the MDRD Study formula.[27] However, in sensitivity analysis, the newer CKD-EPI equation[26] only slightly attenuated the marked differential in rates of CKD stages 3-5 (22.3% for whites vs 11.7% for African Americans using MDRD Study estimation, 17.5% vs 11.1% using CKD-EPI estimation). Given that obese whites were more likely to have diabetes, hypertension, and dyslipidemia, all traditional risk factors for kidney injury, it should not be altogether surprising that obese whites showed higher rates of advanced kidney dysfunction.

However, obese African Americans were more likely to have CKD stages 1-2 (abnormal urinary albumin excretion with preserved GFR), suggesting early kidney injury and enhanced cardiovascular risk. Microalbuminuria is a marker of endothelial insult and an independent risk factor for cardiovascular events.[28-30] Because increased urinary albumin excretion may solely reflect generalized endothelial dysfunction, microalbuminuria suggests, but does not definitively indicate, kidney disease.[31-35] Macroalbuminuria or overt proteinuria, sustained albumin excretion > 300 mg/d (or urinary ACR > 300 mg/g), is associated with much higher cardiovascular risk and clearly indicates the presence of kidney disease.[36,37] There is a direct relationship between degree of proteinuria and risk of progression to end-stage kidney disease. Post hoc analyses of 3 CKD outcomes trials (Irbesartan in Diabetic Nephropathy Trial [IDNT],[38] Reduction of Endpoints in Non-insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan [RENAAL],[39] and African American Study of

Table 4. Association of Race With Prevalent Microalbuminuria, Macroalbuminuria, CKD Stages 1-2, and CKD Stages 3-5 in KEEP Participants With Metabolic Syndrome

Condition	OR (95% CI) for African American Participants
Microalbuminuria vs normal	
Univariate analysis (n = 16,693)	1.39 (1.27-1.53)
Multivariate analysis[a,b] (n = 14,548)	1.64 (1.47-1.82)
Macroalbuminuria vs normal	
Univariate analysis (n = 16,693)	1.14 (0.89-1.47)
Multivariate analysis[a,b] (n = 14,548)	1.62 (1.22-2.16)
Macroalbuminuria vs microalbuminuria	
Univariate analysis (n = 16,693)	0.82 (0.63-1.07)
Multivariate analysis[a,b] (n = 14,548)	0.99 (0.74-1.33)
CKD stages 1-2 vs no CKD	
Univariate analysis (n = 32,920)	1.49 (1.34-1.66)
Multivariate analysis[a,c] (n = 18,775)	1.55 (1.38-1.75)
CKD stages 3-5 vs no CKD	
Univariate analysis (n = 32,920)	0.53 (0.49-0.58)
Multivariate analysis[a,c] (n = 18,775)	0.59 (0.54-0.65)
CKD stages 3-5 vs stages 1-2	
Univariate analysis (n = 32,920)	0.36 (0.32-0.41)
Multivariate analysis[a,c] (n = 18,775)	0.38 (0.33-0.44)

For each category, the reference group (odds ratio of 1.00) is white participants.

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; KEEP, Kidney Early Evaluation Program; OR, odds ratio.

[a]Results from multinomial logit regression analyses.

[b]Adjusted for age, sex, body mass index, current smoking, alcohol use, hypertension, diabetes, dyslipidemia, estimated glomerular filtration rate, and family history of kidney disease.

[c]Adjusted for age, sex, body mass index, current smoking, alcohol use, hypertension, diabetes, dyslipidemia, and family history of kidney disease.

Kidney Disease and Hypertension [AASK][40]) show that a decrease in proteinuria, independent of blood pressure, delays progression of kidney disease.

Our results are consistent with recent clinical and epidemiologic studies suggesting that obesity itself, independent of its ties to diabetic and hypertensive disease risk, has an important role in CKD development.[12,41] These results should be viewed in the context of a recent report from the AASK showing that metabolic syndrome predicted a higher level of proteinuria in a high-risk group of African Americans with hypertensive kidney disease.[42] The association of metabolic syndrome and progression of established CKD in the AASK analysis was confounded by the degree of proteinuria, suggesting that abnormal urinary albumin excretion was the key influence on disease progression in these patients. Our findings of more micro- and macroalbuminuria in African American KEEP participants thus emphasize the importance of recognizing obesity and metabolic syndrome as key risk factors for kidney disease and its associated complications in this population. Although higher microalbuminuria prevalence could explain the larger cardiovascular disease burden in obese African Americans than obese whites,[43] the trend toward higher macroalbuminuria rates could translate to greater risk of CKD progression and complications of decreased kidney function, as in the anemia and secondary hyperparathyroidism discrepancies between African Americans and whites reported here.

Despite higher eGFRs and lower rates of comorbid conditions, such as diabetes, hypertension, dyslipidemia, and overt metabolic syndrome, obese African American KEEP participants manifested

Table 5. Characteristics of African American and White KEEP Participants With BMI ≥ 30 kg/m^2 and CKD Stages 3-5 (eGFR < 60 mL/min/1.73 m^2)

Characteristic	African American (n = 547)	White (n = 1,483)	*P*
Age (y)	64.5 ± 11.3	67.0 ± 10.5	<0.001
Women	79.0 (432)	71.2 (1,056)	<0.001
Serum creatinine (mg/dL)	1.50 ± 0.48	1.29 ± 0.36	<0.001
eGFR (mL/min/1.73 m^2)	48.3 ± 9.8	47.8 ± 9.4	0.3
Albumin-creatinine ratio			
Normal	69.6 (373)	78.8 (1,146)	<0.001
Microalbuminuria[a]	24.8 (133)	17.6 (256)	
Macroalbuminuria[a]	5.6 (30)	3.6 (52)	
Diabetes	65.5 (358)	63.0 (934)	0.3
Hypertension	98.0 (536)	95.4 (1,415)	0.008
Hemoglobin[a] (g/dL)	12.5 ± 1.4	13.5 ± 1.5	<0.001
Anemia[a]	32.4 (177)	14.1 (209)	<0.001
Parathyroid hormone (pmol/L)	108.0 ± 69.9	81.9 ± 55.5	<0.001
Secondary hyperparathyroidism	66.2 (362)	46.6 (691)	<0.001
Calcium[a] (mg/dL)	9.69 ± 0.50	9.63 ± 0.51	0.03
Phosphorus[a] (mg/dL)	3.75 ± 0.68	3.75 ± 0.60	0.9
Calcium-phosphorus product (mg^2/dL^2)[a]	36.3 ± 6.9	36.1 ± 6.3	0.6

Note: Values expressed as mean ± standard deviation or percentage (number). Conversion factors for units: GFR in mL/min/1.73^2 to mL/s/1.73 m^2, ×0.01667, serum creatinine in mg/dL to μmol/L, ×88.4; hemoglobin in g/dL to g/L, ×10; calcium in mg/dL to mmol/L, ×0.2495; phosphorus in mg/dL to mmol/L, ×0.3229.

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program.

[a]Excludes missing values.

more derangements in urinary albumin excretion than obese whites. Several factors may explain this. African Americans had significantly higher BMI levels than whites, and the glomerulopathy of obesity may precede the development of frank diabetic kidney disease.[44,45] In addition, differences in the weight gain time course (eg, gradual gain since childhood vs rapid gain during adult life) appear to be related to diabetes and hypertension development.[46] Adiposity in African Americans may induce earlier hormonal failure in the CKD state, evidenced here by higher rates of anemia and secondary hyperparathyroidism, with a resultant earlier development of parenchymal fibrosis. These explanations argue for diet, exercise, and, potentially, surgery as means to reduce weight and affect disease course.

With regard to potential pharmacologic therapies, it is important to note that aldosterone secretion tends to be more pronounced in obese African Americans than obese whites.[15] The nonepithelial, proinflammatory, and profibrotic effects of aldosterone on the kidney first manifest clinically as abnormal urinary albumin excretion and occur in the presence of high sodium intake with expanded extracellular volume.[47] Obesity and metabolic syndrome frequently are associated with increased aldosterone levels[14,48-52] and impaired sodium excretion,[53] and this "double hit" of expanded volume and relative hyperaldosteronism may be particularly important in African Americans. Several studies have reported a "mild variant of primary aldosteronism" in hypertensive African Americans that is even more pronounced in the subgroup with obesity and metabolic syndrome.[17,19,20,54,55]

Therapeutic regimens consequently may differ for obese African American and white pa-

Table 6. Association of Race With Anemia and Secondary Hyperparathyroidism in KEEP Participants With BMI ≥ 30 kg/m^2 and CKD Stages 3-5 (eGFR < 60 mL/min/1.73 m^2)

Condition	OR (95% CI) for African American Participants
Anemia	
Univariate analysis (n = 2,025)	2.91 (2.31-3.66)
Multivariate analysis[a] (n = 1,809)	3.85 (2.94-5.03)
Secondary hyperparathyroidism	
Univariate analysis (n = 2,030)	2.24 (1.83-2.75)
Multivariate analysis[b] (n = 1,811)	2.63 (2.09-3.31)

For each category, the reference group (odds ratio of 1.00) is white participants.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program; OR, odds ratio.

[a]Adjusted for age, sex, current smoking, alcohol use, and eGFR.

[b]Adjusted for age, sex, smoking, alcohol use, eGFR, calcium level, and phosphorus level.

tients despite the same target goal of slowing or preventing kidney disease progression. White patients should benefit from heightened attention to the traditional risk factors of diabetes, hypertension, and dyslipidemia, along with weight loss. African American patients also should benefit from treating these traditional risk factors, and they may benefit further from addressing the disordered aldosterone-volume relationship with renin-angiotensin-aldosterone system blockade, diuretics, and salt restriction. Speculatively, obese African Americans with early urinary abnormalities might be ideal candidates for mineralocorticoid receptor blockade with spironolactone or eplerenone, which both antagonize aldosterone and have a diuretic effect.

This study has several limitations. First, because the analysis is cross-sectional, only prevalent data are presented. We were unable to assess the equally if not more important question of how obesity and metabolic syndrome affect the kidney during long-term follow-up. Additionally, because data collection was not repeated, we were forced to assume that abnormalities in serum creatinine levels and urinary albumin excretion were measured appropriately and represent chronic disease states. In clinical practice, such tests should be repeated and results should be shown to be persistent for at least 3 months.[56] Urinary albumin excretion was measured categorically (urinary ACR < 30, 30-300, and > 300 mg/g) and not continuously as in the AASK; continuous measurement may have afforded a more detailed look into the relationship between albuminuria and disease risk. Finally, we speculate that the racial differences observed here may be caused by a more profound state of relative hyperaldosteronism in African Americans than whites, yet neither serum nor urine aldosterone was measured in these participants. Other key data, such as vitamin D and iron levels in patients with CKD stages 3-5, were missing and likely would have further informed our results.

Nonetheless, the many KEEP participants with BMI ≥ 30 kg/m^2 make up a unique cohort of obese people with a fairly thorough one time assessment of kidney function. KEEP has started collecting follow-up data for some participants, and future longitudinal studies should further test the hypotheses presented here. We hope that our results will inform, but not necessarily guide, clinical decisions about how obesity and metabolic syndrome impact on the kidney.

In conclusion, in a national cohort of > 37,000 obese participants who presented voluntarily for KEEP kidney function screenings, whites were more likely than African Americans to present with components of metabolic syndrome and, perhaps as a consequence, more advanced CKD stages. However, African Americans showed significantly higher rates of early-stage CKD with preserved eGFR, but abnormal urinary albumin excretion. These differences may translate into disparate rates of kidney disease progression and cardiovascular disease burden between obese whites and African Americans.

ACKNOWLEDGEMENTS

The authors thank Shane Nygaard, BA, and Nan Booth, MSW, MPH, of the Chronic Disease Research Group for manuscript preparation and manuscript editing, respectively.

Support: The KEEP is a program of the National Kidney Foundation Inc and is supported by Amgen, Abbott, Novartis, Siemens, Genentech, Genzyme, Nephroceuticals, Pfizer, LifecSan, and Suplena.

Financial Disclosure: None.

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