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Goal-Striving Stress Is Associated with Chronic Kidney Disease Among Participants in the Jackson Heart Study

Loretta R. Cain[1], **LáShauntá Glover**[2], **Bessie Young**[3,4], **Mario Sims**[2]

[1]Department of Data Science, University of Mississippi Medical Center, Jackson, MS, USA

[2]Department of Medicine, University of Mississippi Medical Center, Jackson, MS, USA

[3]Division of Nephrology and Kidney Research Institute, University of Washington, Seattle, WA, USA

[4]Veterans Affairs, Hospital and Specialty Medicine and Center for Innovation, Seattle, WA, USA

Abstract

Objective—Research that assesses the relationship between psychosocial factors and chronic kidney disease (CKD) among African Americans (AAs) is limited. Using the Jackson Heart Study (JHS) cohort data, we investigated the association of goal-striving stress (GSS)—the stress experienced from not reaching goals—with prevalent CKD among AAs.

Design—This was a cross-sectional analysis of JHS exam 1 data that assessed the relationship between GSS and CKD.

Setting and Participants—We utilized a sample from the JHS (n = 4967), an AA sample of women and men, 35–84 years old from the Jackson, MS metro area.

Main Outcome Measures—The baseline relationship between GSS levels (low, moderate, and high) and CKD (eGFR < 60 mL/ min/1.73m^2) was evaluated using a logistic regression model to estimate odds ratios (OR) on a 95% confidence interval (CI). The final model was adjusted for sex, age, socioeconomic status, health behaviors, risk factors, and total stress.

Results—After full adjustment, the odds of prevalent CKD increased by 52% (OR 1.52; 95% CI 1.04, 2.24) for those reporting high (versus low) GSS.

Conclusions—Deficiencies between goal aspiration and achievement were associated with prevalent CKD. Potential interventions might consider the impact GSS contributes to prevalent CKD.

Loretta R. Cain, lcain@umc.edu.

Compliance with Ethical Standards

Informed Consent Informed consent was obtained from all individual participants included in the study.

DisclosuresThe authors declare that they have no conflicts of interest.

Disclaimer The Veterans Affairs does not endorse any of the statements or opinions advocated by this manuscript. The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the U.S. Department of Health and Human Services. The funders had no role in the study design, collection, analysis, interpretation of data, writing the report, or the decision to submit the report for publication.

Keywords

Goal-striving stress; Stress; Kidney disease; Psychonephrology; African Americans; Blacks; Jackson Heart Study (JHS)

Introduction

Thirty million Americans are affected by chronic kidney disease (CKD), which has many underlying causes [1]. Key risk factors for CKD include a history of cardiovascular disease (CVD), diabetes, and hypertension [2]. The prevalence of CKD for the US population is approximately 15%; 13% for Caucasians, 15% for Hispanics, and 18.0% for African Americans (AAs) [1]. Also in 2014, end-stage renal disease (ESRD) prevalence was three times greater in AAs than in Caucasians [1]. Clearly, AAs are disproportionately affected by kidney-related diseases compared to other racial and ethnic groups. Health behaviors including alcohol use, tobacco use, and drug use are mechanisms by which persons (particularly lower socioeconomic-status minorities) cope with stress. These behaviors have implications for CKD development and progression [3, 4]. However, the relationship between psychosocial factors and CKD prevalence has not been thoroughly explored [5]. Therefore, exploring traditional as well as non-traditional risk factors for CKD is important for preventing and treating CKD in all populations, particularly among AAs [6].

The interest in the association of psychosocial factors with CKD has grown [7, 8], terming this area of research psychonephrology [9]. Prolonged exposure to chronic stress is the mechanism by which negative physiological changes occur and cause disease. Goal-striving stress, the difference between aspiration and achievement [10], is one neglected dimension of stress that may be important in the etiology of CKD. AAs, in particular, experience substantial barriers in achieving goals and economic success. For example, AAs report higher discrimination in a variety of social settings [11] and earn less income despite having the same education as their White counterparts [12]. Although there are a few studies that have shown significant associations between stressors and CKD and related risk factors [4, 13, 14], no study has examined the association between goal-striving stress (GSS) and CKD.

Sellers et al. found that GSS was associated with a greater odds of hypertension, a higher count of physical health problems, and a decreased odds of reporting optimal health after adjustment for stressors (personal problems, lifetime and everyday racial discrimination) [15]. Other studies have assessed the relationship between mental health and GSS [10], but published literature suggests that no studies have assessed GSS's association with chronic diseases.

In light of this gap, the purpose of our study was to assess the relationship between GSS and prevalent CKD. Our guiding hypothesis is that GSS will be positively associated with prevalent CKD and inversely associated with estimated glomerular filtration rate (eGFR).

Methods

This study was a cross-sectional analysis of the JHS cohort data at baseline (2000–2004). At the baseline assessment, there were 5306 AA participants enrolled in the study, age ranging from 21 to 94 years from Hinds, Madison, and Rankin counties, the greater Jackson, MS metropolitan area. Thirty percent of the participants were recruited from the Atherosclerosis Risk (ARIC) study, 25% from family members of participants, 17% from random selection, and 25% from community volunteers. The primary purpose of the JHS is to examine risk factors for the development of CVD and the etiology of CVD development in AA men and women. Two subsequent follow-up visits were completed with the JHS participants between 2005 and 2008 and between 2009 and 2013. Details regarding the study have been previously published [16, 17].

Goal-Striving Stress

GSS was defined in the JHS as the difference between "where one would like to be next year" using a 10-point scale and "where one was 10 years ago" using a 10-pointscale,weighted by one's "disappointment score" if the goal was not achieved by next year, using a 4-point scale. Participants were asked to imagine a ladder consisting often possible steps, where step 10 represented the best possible way of life and step 1 represented the worst possible way of life for the participant. Then, participants were asked to describe the step number where they were 10 years ago (achievement) and the step they would like to be by the following year (aspirations). Participants were then asked how disappointed they would be if they found out they could never reach their aspiration step (very disappointed, fairly disappointed, slightly disappointed, not at all disappointed). GSS scores ranged from 0 to 20 and were categorized into increasing tertiles: low GSS (0–1), moderate GSS (2–4), and high GSS stress (5–20). GSS was also measured as a continuous variable in standard deviation (SD) units.

Chronic Kidney Disease

Glomerular filtration rate is a measure of kidney function, with an eGFR < 60 mL/min/1.73 m^2 indicative of CKD [18, 19]. Serum creatinine has been commonly used to calculate eGFR [18]. However, GFR estimates can remain imprecise due to variations in serum creatinine [18]. Such imprecisions can result in the misclassification of patients whose eGFR is < 60 mL/min/1.73 m^2 but who actually have no CKD, resulting in unnecessary therapeutic interventions. Cystatin C is considered to be a more stable marker than serum creatinine and eGFR and could be used as a confirmatory test in patients diagnosed with CKD [20–22]. Therefore, we used the CKD-epidemiology creatinine-cystatin C equation for analysis [19].

At baseline, a multipoint enzymatic spectrophotometric assay [Vitros Ortho-Clinical Diagnostics Analyzer (Raritan, NJ)] was used to measure serum creatinine [23]. Serum creatinine was re-measured in 2006 for 206 participants using the enzymatic method on a Roche Chemistry analyzer (Roche Diagnostics Corp, Indianapolis, IN). In order to harmonize serum creatinine measurements across study visits, we calibrated all exam 1 serum creatinine measurements to those at exam 3, using the isotope dilution mass spectrometry(IDMS)traceable method [24]. Serum creatinine measurements at exam 1 were

additionally calibrated using a Deming regression model [24]. eGFR was then calculated from the serum creatinine and serum cystatin c using the five-variable CKD-EPI equation [19]. CKD was defined as eGFR < 60 mL/min/1.73 m^2 [18, 19].

Covariates

For covariates, we used age (continuous), sex (men/women (referent)), income (poor (referent), lower-middle income, upper-middle income, affluent), education [< high school graduate, high graduate or greater (referent)], and body mass index (BMI),calculated as weight (kg)divided by height (m^2). Blood pressure ≥ 140/90 mmHg or use of blood pressure-lowering medication was used to defined hypertension prevalence, and a fasting glucose ≥ 126 mg/dL or hemoglobin A1c ≥ 6.5% or use of diabetic mediation within 2 weeks prior to the clinic visit was the criteria for diabetes diagnosis [23]. CVD history was defined asself-reported physician diagnosed cardiovascular history (CVD/no CVD (referent)). Smoking status was defined as smoking cigarettes within the last year [yes/no (referent)]. Alcohol status was defined as alcohol use within the last year (yes/no (referent)). Global Perceived Stress Scale, an eight-item questionnaire that measures the severity of chronic stress experienced over the last year, was used as our stress measure [25]. Global stress, different from GSS, measures eight dimensions: stress on the job, stress from relationships, stress in neighborhood, stress from caring for others, stress from legal problems, stress from medical problems, stress due to discrimination, and stress meeting basic needs. In this sample, GSS and global stress were only 38% correlated. Global stress is a potential confounder in the association between GSS and CKD. Adjusting for global stress would eliminate the question of whether social and environmental stressors impact the GSS-CKD association.

Statistics

At baseline, we excluded participants who had missing GSS values (n = 113), those with outlying GSS values (n = 60) (for a better fit in the linear regression model), and those missing serum creatinine and cystatin C values (n = 166), leaving a sample of 4967 participants.

Differences in baseline characteristics were examined across GSS tertiles using Kruskal-Wallis tests for non-normal continuous variables and chi-square test for categorical variables. Linear regression analyses were used to examine the baseline association of GSS levels and SD units with mean differences (standard errors—SE) in eGFR. Multivariable logistic regression analyses estimated associations of GSS levels and SD units with prevalent CKD using odds ratios (OR) on a 95% confidence interval (CI). Model 1 was unadjusted. Model 2 included age, sex, income, and education. Model 3 included model 2 plus smoking status, alcohol use, and global stress. Model 4 included model 3 plus hypertension, BMI, diabetes mellitus, and history of CVD.

Statistical Analysis Software (SAS) 9.3 (SAS Institute Inc., Cary, NC) was used to perform all analyses. A two-sided $p < 0.05$ was considered statistically significant.

Results

There were 4967 participants in the sample categorized into categorized into GSS tertiles: low GSS (n = 2052), moderate GSS (n = 1662), and high GSS (n = 1253). Because of the high frequencies in some of the discrete responses of the GSS scale, the tertiles were not equal. Those in the highest GSS tertile were more likely to be younger, current smokers, have higher BMI, and have higher overall global stress levels. They were also less likely to be female, hypertensive, diabetic, and a high school graduate, use alcohol, have a history of CVD, and have CKD compared those in the lowest GSS tertile (Table 1).

The association between eGFR and GSS was statistically significant after adjusting for age, sex, income, education, smoking status, alcohol use, stress, hypertension, BMI, diabetes, and history of CVD when calculating eGFR using the creatinine-cystatin C equation [$\beta = -0.71$ (0.31); $p < 0.05$], respectively (Table 2). In other words, for every 1 SD unit (5.05 units) increase in GSS, we would expect a 0.71 unit decrease in eGFR.

When adjusting for age, sex, income, education, smoking status, alcohol use, stress, hypertension, BMI, diabetes, and history of CVD, participants who reported high GSS were 1.52 times more likely to have prevalent CKD than those who reported low GSS (Table 3). There was also a 25% increase in GSS SD in those participants with prevalent CKD versus those without prevalent CKD. Overall, increasing levels of GSS were positively associated with prevalent CKD.

Discussion

This study assessed the relationship between GSS and CKD in a large cohort of AAs. Higher levels of GSS were significantly associated with lower eGFR and greater CKD prevalence, which suggest that stressors such as GSS may contribute to kidney disease in AAs.

There are limited studies that explore the association between psychosocial stress and kidney function; however, some studies have found depression and anxiety to be prevalent among CKD patients [26, 27]. Even fewer studies have investigated the association of psychosocial stress with kidney function among AAs, who are disproportionately affected by CKD. One study, among 129 healthy (non-diabetic and non-hypertensive) AAs, found that symptoms of depression, perceived stress, and hostility did not predict kidney dysfunction [28]. The current study extends their findings by including a larger sample of AAs and a measurement of a different psychosocial stressor. We found that after adjustment for health behaviors and risk factors, higher GSS was associated with a significant decrease in eGFR and greater odds of CKD.

We expect that the pathway by which GSS was predictive of CKD is similar to the pathway by which stress is thought to cause CKD [5]. Overall, stress is multifaceted and generally is defined as an environmental or internal demand that results in a physiological, psychological, or behavioral response [5]. If stress is experienced over long periods of time, the subsequent physiological and psychological response may cause the body to be at risk for diseases [29]. For example, allostatic load, which accumulates after repeated exposure to stressors, activates stress resistance responses [30]. These responses result in

damaging alterations to metabolic pathways (e.g., persistent oxidative stress, tissue damage, elevated inflammatory gene expression in leukocytes, and autonomic imbalance), which can eventually progress to muscular wasting, vascular calcification, and premature aging [31].

Although studies that examine psychosocial stress and CKD are limited, our study should be evaluated in the context of the limitations. For instance, measurement error in GSS is a possibility due to self-reported data. Additionally, the cross-sectional design of this study limits the ability to infer causation, as we were unable to determine whether kidney function decline influences GSS or vice versa. Residual confounding variables are also a potential limitation as there may be poorly measured or unmeasured covariates that were not accounted for in the analyses. Because the current research is derived from a single-site study of AAs in Jackson, MS, our results may not be generalizable to other AA populations in other regions. However, important strengths of our research include that this is one of the largest studies of AAs, for which the GSS is available with standardized measurements of kidney function.

In conclusion, our study expands the literature by examining the association of a psychosocial factor, particularly GSS, with eGFR and prevalent CKD in an AA cohort. We found that higher levels of GSS were associated with lower eGFR and prevalent CKD. This novel predictor may have potential important health implications for AAs and renal health. Specifically, GSS may be a point of interest in preventing and treating CKD in AAs. Future studies should assess longitudinal associations of GSS with kidney function decline and incident CKD development.

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References

1. Centers for Disease Control and Prevention. National Chronic Disease Fact Sheet, 2017. https://www.cdc.gov/diabetes/pubs/pdf/kidney_factsheet.pdf. Accessed December 6, 2017.
2. Mozaffarian D, Benjamin E, Go A, et al. Heart Disease and Stroke Statistics—2016 update: a report From the American Heart Association. Circulation. 2016;133(4):e38–360. [PubMed: 26673558]
3. Seeman T, Mcewan B. Impact of social environment characteristics on neuroendocrine regulation. Psychosom Med. 1996;58(5):459–71. [PubMed: 8902897]
4. Cohen S, Herbert T. Health psychology: psychological factors and physical disease from the perspective of human psychoneuroimmunology. Annu Rev. Psychol. 1996;47:113–42. [PubMed: 8624135]
5. Bruce M, Griffith D, Thorpe RJ. Stress and the kidney. Adv Chronic Kidney Dis. 2015;1:46–53.

6. Norton J, Moxey-Mims M, Eggers P, et al. Social determinants of racial disparities in CKD. J Am Soc Nephrol. 2016;27(9):2576–95. [PubMed: 27178804]
7. Kimmel P, Cohen S, Peterson R. Depression in patients with chronic renal disease: where are we going? J Ren Nutr. 2008;18(1):99–103. [PubMed: 18089453]
8. Cukor D, Coplan J, Brown C, et al. Anxiety disorders in adults treated by hemodialysis: a single-center study. Am J Kidney Dis. 2008;52(1):128–36. [PubMed: 18440682]
9. Levy NPsychonephrology 2: Psychological problems in kidney failure and their treatment. New York: Plenum Medical Book Company; 1983.
10. Neighbors H, Sellers S, Zhang R, et al. Goal-striving stress and racial differences in mental health. Race Social Problems. 2011;3(1):51–62.
11. Mendez D, Hogan V, Culhane J. Institutional racism and pregnancy health: using Home Mortgage Disclosure Act data to develop an index for mortgage discrimination at the community level. Publ Health Rep. 2011;126(Suppl 3):102–14.
12. Isaacs J, Sawhil l, Haskins R Getting ahead or losing ground: economic mobility in America. 2008. https://www.brookings.edu/research/getting-ahead-or-losing-ground-economic-mobility-inamerica/. Accessed December 6, 2017.
13. Bruce M, Beech B, Sims M, et al. Social environmental stressors, psychological factors, and kidney disease. J Investig Med. 2009;57(4):583–9.
14. Everson-Rose S, Lewis T. Psychosocial factors and cardiovascular diseases. Annu Rev. Public Health. 2005;26:469–500. [PubMed: 15760298]
15. Sellers SL, Neighbors HW, Zhang R, Jackson JS. The impact of goal-striving stress on physical health of white Americans, African Americans, and Caribbean blacks. Ethn Dis. 2012 Winter;22(1): 21–8. [PubMed: 22774305]
16. Fuqua S, Wyatt S, Andrew M, et al. Recruiting African-American research participation in the Jackson Heart Study: methods, response rates, and sample description. Ethn Dis. 2005;15(4 Suppl 6):S6. –18–29
17. Taylor HJ, Wilson J, Jones D, et al. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. Ethn Dis. 2005;15(4 Suppl 6):S6):4–17.
18. Levey A, Stevens L, Schmid C, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–12. [PubMed: 19414839]
19. Inker L, Schmid C, Tighiouart H, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. N Engl J Med. 2012;367(1):20–9. [PubMed: 22762315]
20. Tangri N, Stevens L, Schmid C, et al. Changes in dietary protein intake has no effect on serum cystatin C levels independent of the glomerular filtration rate. Kidney Int. 2011;79(4):471–7. [PubMed: 20980977]
21. Stevens L, Schmid C, Greene T, et al. Factors other than glomerular filtration rate affect serum cystatin C levels. Kidney Int. 2009;75(6): 652–60. [PubMed: 19119287]
22. Shlipak M, Sarnak M, Katz R, et al. Cystatin C and the risk of death and cardiovascular events among elderly persons. N Engl J Med. 2005;352(20):2049–60. [PubMed: 15901858]
23. Carpenter M, Crow R, Steffes M, et al. Laboratory, reading center, and coordinating center data management methods in the Jackson Heart Study. Am J Med Sci. 2004;328(3):131–44. [PubMed: 15367870]
24. Wang W, Young B, Fülöp T, et al. Effects of serum creatinine calibration on estimated renal function in African Americans: the Jackson Heart Study. Am J Med Sci. 2015;349(5):379–84. [PubMed: 25806862]
25. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24(4):385–96. [PubMed: 6668417]
26. Hedayati S, Minhajuddin A, Toto R, et al. Validation of depression screening scales in patients with CKD. Am J Kidney Dis. 2009;54(3):433–9. [PubMed: 19493600]
27. Kessler R, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095–105. [PubMed: 12813115]

28. Gholson G, Mwendwa D, Wright R, et al. The combined influence of psychological factors on biomarkers of renal functioning in African Americans. Ethn Dis. 2015;25(2):117–22. [PubMed: 26118136]

29. Crews D, Pfaff T, Powe N. Socioeconomic factors and racial disparities in kidney disease outcomes. Seminars in Nephrology. 2013;33(5):468–75. [PubMed: 24119852]

30. Brotman D, Golden S, Wittstein I. The cardiovascular toll of stress. Lancet. 2007;370(9592):1089–100. [PubMed: 17822755]

31. Kooman J, Kotanko P, Schols AM, et al. Chronic kidney disease and premature ageing. Nat Rev. Nephrol. 2014;10(12):732–42. [PubMed: 25287433]

Table 1

JHS characteristics by GSS tertiles (n = 4967)

	GSS (low) (n = 2052)	GSS (moderate) (n = 1662)	GSS (high) (n = 1253)	p value
	Mean ± standard deviation			
Age	60.37 ± 11.54	53.27 ± 11.98	49.68 ± 12.37	< 0.001
BMI	31.37 ± 6.63	31.81 ± 7.37	32.36 ± 7.84	0.03
Stress	3.50 ± 3.62	5.29± 4.08	7.48 ± 4.67	< 0.001
	N (%)			
Females	1294 (41.37%)	1011 (32.32%)	823 (26.31%)	0.03
High school graduate	1502 (37.70%)	1424 (35.74%)	1058 (26.56%)	< 0.001
Poor	229 (36.94%)	152 (24.52%)	239 (38.55%)	< 0.001
Current smoker	214 (33.44%)	197 (30.78%)	229 (35.78%)	< 0.001
Alcohol use	792 (32.72%)	805 (35.29%)	684 (29.99%)	< 0.001
Hypertension	1298 (46.09%)	904 (32.10%)	614 (21.80%)	< 0.001
Diabetes	507 (46.56%)	331 (30.39%)	251 (23.05%)	< 0.001
History of CVD	268 (50.0%)	146 (27.24%)	122 (22.76%)	< 0.001
CKD	135 (51.72%)	71 (27.20%)	55 (21.07%)	0.002

p values were obtained using chi-square and Kruskal-Wallis tests as appropriate

Because of the high frequencies in some of the discrete responses of the GSS scale, the tertiles were not equal

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Table 2

Mean differences (SE) of estimated glomerular filtration rate (eGFR) with GSS in JHS at baseline

	eGFR (*n* = 4967)
	Beta (SE)
Model 1 GSS SD	*3.87 (0.35)
Model 2 GSS SD	− 0.40 (0.30)
Model 3 GSS SD	*− 0.71 (0.32)
Model 4 GSS SD	*− 0.71 (0.31)

Model 1—unadjusted; model 2—adjusted for age, sex, income, and education; model 3—model 2 + smoking status, alcohol use status, and stress; model 4—model 3 + hypertension, BMI, diabetes, and history of cardiovascular disease

*p value < 0.05

Table 3

The Association of CKD status with levels and standard deviation of GSS among African Americans in the JHS at baseline

		Odds ratio (95% CI)
		Odds of CKD
Model 1	Low GSS	Referent
	Moderate GSS	*0.63 (0.47, 0.85)
	High GSS	*0.65 (0.47, 0.90)
	GSS SD	*0.83 (0.70, 0.99)
Model 2	Low GSS	Referent
	Moderate GSS	1.15 (0.84, 1.58)
	High GSS	*1.48 (1.04, 2.11)
	GSS SD	*1.28 (1.03, 1.43)
Model 3	Low GSS	Referent
	Moderate GSS	1.11 (0.80, 1.53)
	High GSS	*1.61 (1.10, 2.33)
	GSS SD	*1.28 (1.07, 1.52)
Model 4	Low GSS	Referent
	Moderate GSS	1.07 (0.77, 1.49)
	High GSS	*1.52 (1.04, 2.24)
	GSS SD	*1.25 (1.04, 1.50)

Model 1—unadjusted; model 2—adjusted for age, sex, income, and education; model 3—model 2 + smoking status, alcohol use status, and stress; model 4—model 3 + hypertension, BMI, diabetes, and history of cardiovascular disease

* p value < 0.05