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# Epidemiologic and clinical factors associated with Chronic Kidney Disease among Asian Americans and Native Hawaiians

Marjorie K. Mau, Margaret R. West,  
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**Objective.** *To examine the association between key susceptibility factors and measures of chronic kidney disease in Asian American and Native Hawaiian participants enrolled in the Hawai'i site of the national Kidney Early Evaluation Program (KEEP-2) study community screening program.*

**Design.** *In 2001–2003, 793 participants from five ethnic groups (Japanese, Native Hawaiian, Chinese, Filipino and Caucasian) were enrolled in the Hawai'i KEEP-2 program. Odds ratios were used as the measure of association and were computed using unconditional logistic regression. Renal susceptibility factors for chronic kidney disease were included in a multivariable model if found to be statistically significant in univariate analysis. The proportion of Hawai'i KEEP-2 study participants manifesting various clinical characteristics were compared by ethnicity with Japanese as the referent group.*

**Results.** *Significant ethnic differences in the occurrence of chronic kidney disease were found, with Japanese having the lowest occurrence of chronic kidney disease (18%) and Native Hawaiians the highest (40%). Within each ethnic group, the occurrence of chronic kidney disease was associated with a different ethnic-specific clustering of susceptibility factors. Hypertension was associated with chronic kidney disease among four of the five ethnic groups: Japanese, Caucasian, Native Hawaiian and Filipino. Overweight was*

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associated with a decreased occurrence of chronic kidney disease among Caucasians, while diabetes and lower educational attainment were associated with increased occurrence of chronic kidney disease among Native Hawaiians. For Filipinos, diabetes and age 65 years and older were both associated with an increased occurrence for chronic kidney disease while lower educational attainment was associated with a reduced occurrence of chronic kidney disease. Among Chinese, no factors were significantly associated with chronic kidney disease, although trends for all factors paralleled those of the overall study group.

**Conclusions.** The occurrence of chronic kidney disease in the Hawai'i KEEP-2 study was nearly fourfold greater compared with the general US population. The clustering of susceptibility factors for chronic kidney disease occurrence was found to differ for all five ethnic groups.

**Keywords:** Chronic kidney disease (CKD); Kidney Early Evaluation Program (KEEP-2); Asian American and Native Hawaiian; Ethnic/minority; Early intervention; Community-based Screening; Estimated glomerular filtration rate (EGFR); Diabetes; Hypertension; Microalbumin

## Introduction

The issue of health disparities among racial and ethnic minorities is a topic of major public health interest, especially since prognosis and treatment may differ (Earle *et al.* 2001; Powe 2003; Bloche 2004; Lakkis & Weir 2004; Taylor *et al.* 2004). Health disparities especially are evident in the end stage renal disease program in which the incidence of end stage renal disease for African Americans is fourfold greater compared with Caucasians (US Renal Data System 1999, 2001). The sharpest rise in the rate of new cases of end stage renal disease in the USA was found among Asian Americans and Pacific Islanders (including Native Hawaiians) (US Renal Data System 1999, 2001). Since 1980 the prevalence of end stage renal disease in the USA has increased fivefold from 271 to ~1,400 cases per million population (US Renal Data System 2003). During this same time period, the Asian American/Pacific Islander population has seen a 12-fold increase (US Renal Data System 2003).

The disparity in end stage renal disease among Asian Americans and Pacific Islanders also extends into earlier stages of chronic kidney disease as the precursor of end stage renal disease (Coresh *et al.* 2003; El Nahas & Bello 2005; Hall *et al.* 2005a). Specific ethnic health disparities are difficult to assess as longitudinal cohort data available from the National Health and Nutrition Examination Survey does not adequately include all ethnic minority populations at highest susceptibility for end stage renal disease (Coresh *et al.* 2003; Nickolas *et al.* 2004). Thus, little is known about chronic kidney disease and its disease course among ethnic minority populations and in particular among Asian Americans, Native Hawaiians and Pacific Islanders.

This gap in our understanding of chronic kidney disease among susceptible populations also confounds efforts to develop appropriate interventions aimed at reducing the increasing occurrence of end stage renal disease in these populations. In part to address this gap in renal disparities, the National Kidney Foundation undertook a national screening program, entitled the Kidney Early Evaluation Program (KEEP) which identifies early stages of chronic kidney disease especially among susceptible populations in the USA (Brown *et al.* 2003). The national KEEP report for 2005 included African Americans (40%), Caucasians (39%), Hispanics (10%) and Other ethnicity/race (11%) for a total population of 24,048 participants (National Kidney Foundation 2005). A subgroup analysis of the Asian American and Pacific Islander cohort was not included in the original KEEP report and forms the basis for the current paper.

The Hawai'i KEEP study is one of the national KEEP program sites and has participated in the national KEEP screening program since the late 1990s. Unlike other KEEP sites, the Hawai'i KEEP-2 study has collected ethnic-specific self-identification for Asian American and Pacific Islander subgroups since 2001. In August 2000, the national KEEP protocol was revised in an attempt to improve screening tools and the new protocol referred to as KEEP-2 also was implemented at the Hawai'i KEEP site. The KEEP-2 program is nationally recognized and is conducted by local affiliates of the National Kidney Foundation to screen for chronic kidney disease in susceptible individuals throughout the USA (National Kidney Foundation 2005). The goals of KEEP-2 are to provide assessment of factors important in disease occurrence, early detection of asymptomatic disease, individual counseling for follow-up recommendations and education about kidney disease (Brown *et al.* 2003). Since chronic kidney disease is a chronic progressive health problem, early diagnosis can lead to earlier interventions that may delay the progression to, and/or ultimately prevent, end stage renal disease.

Hawai'i is an ideal location to recruit Asian Americans and Pacific Islander populations because of its stable, ethnically diverse population of Asian Americans, Pacific Islanders and Caucasian racial/ethnic groups (Mau *et al.* 2003). The five major ethnic groups in Hawai'i include Japanese (20.4%), Caucasian (24.3%), Native Hawaiian (19.8%), Filipino (14.1%) and Chinese (4.7%). Collectively these five groups comprise 80% of the state's 1.2 million residents (US Census Bureau 2000, 2001; US Renal Data System 2001). Native Hawaiians, the indigenous people of Hawai'i, are the single largest group of Pacific Islanders in the USA and the largest concentration of Native Hawaiians reside in Hawai'i (US Census Bureau 2001).

The purpose of this study is to examine the etiologic association between key epidemiologic/clinical factors and specific measures of chronic kidney disease in a multi-ethnic group of Asian American and Native Hawaiian participants enrolled in the Hawai'i KEEP-2 community screening program. We hypothesized that differences in the occurrence of chronic kidney disease between ethnic/racial groups in this program will be associated with a clustering of different factors leading to a common clinical endpoint of chronic kidney disease.

## Methods

### *Participant Recruitment*

The local affiliate of the National Kidney Foundation, the National Kidney Foundation Hawai'i, conducted KEEP-2 screening programs at 10 sites (6 on Oahu and 4 on neighbor islands) between September 2001 and September 2003. Recruitment methods included use of flyers, posters and advertisements (radio and newspaper). Diverse recruitment venues were used with the intent of increasing the yield for enrolling ethnic minority groups at higher susceptibility for chronic kidney disease. The sites included community recreational centers, worksites, churches, and Native Hawaiian Healthcare Systems and community health centers that service primarily ethnic minority groups such as Filipino, Japanese, Native Hawaiians and other Pacific Islanders.

Before undergoing testing, all participants were pre-screened for the presence of one or more of the following factors: (1) prior history of diabetes mellitus; (2) prior history of hypertension; or (3) positive family history for diabetes mellitus, hypertension or kidney disease (dialysis or transplant). All participants had to be 18 years or older to enroll. Individuals with pre-existing kidney disease or end stage renal disease were excluded. A total of 885 volunteer participants were screened. For purposes of this study, only 793 participants with complete data on the following variables: (1) serum creatinine; (2) urine microalbumin; (3) ethnicity; and (4) screening site were included.

### *Screening Protocol and Renal Susceptibility Factors*

The KEEP 2.0 protocol included a standardized self-administered questionnaire and clinical measurements according to the National Kidney Foundation KEEP-2 protocol (National Kidney Foundation 2005). Hawai'i KEEP-2 screenings were conducted by National Kidney Foundation Hawai'i trained and certified staff as well as volunteers from the health professional and lay community. Informed consent was obtained from all participants prior to undergoing interview and blood draw. Questionnaire data included demographics, medical history, health behavior factors and health access. Ethnicity was self-reported with participants asked to identify the largest proportion of their ethnic background by identifying one of the following: Japanese, Native Hawaiian, Filipino, Chinese, Caucasian or Other ethnic groups. Participants who were equally bi-ethnic were allowed to self-identify the ethnic group they most closely associate with. Individuals identified as 'Other' were excluded from this study because of heterogeneity and small sample size.

Capillary blood samples were tested for a non-fasting glucose level (Accu-Check Advantage<sup>®</sup>, Roche Pharmaceuticals, Mannheim, Germany) at the time of the interview. Venous blood samples also were collected and sent to a single central laboratory (Satellite Laboratory Services, Redwood City, CA, USA) for batch measurement of serum creatinine and non-fasting lipid levels (total cholesterol and

high-density lipoprotein cholesterol). Non-fasting lipid levels were not measured at two of the screening sites due to a logistical error. Thus, only a subset of 625 participants had lipid levels available for analysis in this study.

Comparison of participants with missing vs non-missing lipid levels indicated that participants with missing data differed significantly according to their ethnic distribution ( $p=0.002$ ) with a greater percentage of Japanese and Chinese participants having missing lipid levels (data not shown). However, there was no difference in the prevalence of chronic kidney disease in the missing vs the non-missing groups ( $p=0.83$ ).

Body weight was measured in pounds using a digital scale (Tanita® BWB-800, Arlington Heights, IL, USA) and self-reported height was recorded. Body mass index (BMI) was calculated by weight converted to kilograms divided by height in meters squared. Overweight and obese were defined using the Asia-Pacific World Health Organization–Western Pacific Region definitions (Inoue *et al.* 2000). Based upon these criteria, the following BMI definitions for overweight and obese individuals were used: overweight  $\geq 23 \text{ kg/m}^2$  and obese  $\geq 25 \text{ kg/m}^2$  for adult Asians (Japanese, Chinese and Filipino); overweight  $\geq 26 \text{ kg/m}^2$  and obese  $\geq 32 \text{ kg/m}^2$  for Native Hawaiians (Inoue *et al.* 2000). Caucasian participants were defined as overweight if their BMI was  $\geq 25 \text{ kg/m}^2$  and obese if  $\geq 30 \text{ kg/m}^2$  (Flegal *et al.* 2002).

Blood pressure was measured twice according to guidelines in the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII) (National High Blood Pressure Education Committee 2003). We report the mean value of the two blood pressure measurements.

Presence of hypertension was defined by (1) prior history of hypertension and/or taking blood pressure medication or (2) for persons without a history of hypertension or diabetes mellitus, a systolic blood pressure  $\geq 140 \text{ mmHg}$  and/or diastolic blood pressure  $\geq 90 \text{ mmHg}$  (National High Blood Pressure Education Committee 2003). Individuals with diabetes mellitus were defined as hypertensive if systolic blood pressure was  $\geq 130 \text{ mmHg}$  and/or diastolic blood pressure  $\geq 80 \text{ mmHg}$  (National High Blood Pressure Education Committee 2003; National Kidney Foundation 2005).

Diabetes mellitus was defined by prior history or a random blood glucose value  $\geq 200 \text{ mg/dl}$ . Of the 172 individuals classified as having diabetes mellitus by this definition, only 6 individuals identified as having diabetes mellitus by the random glucose value of  $\geq 200 \text{ mg/dl}$ .

Cardiovascular disease was ascertained by self-report of prior history of heart attack or stroke. Abnormal serum creatinine was defined as  $\geq 1.4 \text{ mg/dl}$  for men and  $\geq 1.2 \text{ mg/dl}$  for women of Japanese, Chinese and Filipino ethnic background (Iseki *et al.* 1997). For Caucasian and Native Hawaiian participants abnormal serum creatinine was defined as  $\geq 1.6 \text{ mg/dl}$  in men and  $\geq 1.4 \text{ mg/dl}$  in women (Coresh *et al.* 2001). Abnormal lipid levels were defined by: (1) total cholesterol  $\geq 200 \text{ mg/dl}$  or (2) high-density lipoprotein cholesterol  $< 40 \text{ mg/dl}$  (Cleeman 2001).

*Outcome Measurement: EGFR and Urine AC Ratio*

The primary outcome of interest was chronic kidney disease, defined as estimated glomerular filtration rate (EGFR) of less than 60 ml/min/1.73 m<sup>2</sup> or random urine albumin-to-creatinine (AC) ratio greater than or equal to 30 mg/g Cr. Estimated glomerular filtration rates were computed using the abbreviated Modification of Diet in Renal Disease (MDRD) Study Equation (Levey *et al.* 1999; National Kidney Foundation 2002). A random urine sample was assayed for urine AC ratio using the Clinitek<sup>®</sup> method (Bayer Diagnostics, Tarrytown, PA, USA).

*Statistical Analysis*

Statistical analyses were generated using SAS V9. Descriptive analyses were performed for key study factors including sociodemographic data (age, sex, ethnicity, education, primary care doctor, doctor visits, health insurance status), clinical indicators (hypertension, diabetes mellitus, cardiovascular disease, serum creatinine, EGFR, microalbuminuria, BMI, non-fasting lipid levels) and lifestyle behaviors (smoking). Ethnic-specific univariate analyses of sociodemographic and clinical characteristics also were performed with a focus on the chronic kidney disease endpoints. Descriptive statistics of key study factors were stratified by ethnicity. Due to missing data in some cases, analyses including these variables are indicated by a reduced number of participants. Continuous variables such as BMI, creatinine and EGFR were dichotomized and overall ethnic differences, as well as pair-wise ethnic differences were tested using chi-square test. Distributional differences of key study factors across the different ethnicities were assessed and pair-wise comparisons were conducted using Japanese as the referent group. Japanese showed the lowest chronic kidney disease occurrence in the Hawai'i KEEP-2 cohort and hence was chosen as the referent group for pair-wise comparisons.

Multivariable logistic regression models were used to quantify associations between individual study factors and chronic kidney disease in each ethnic group. The present study was largely exploratory in nature and based upon a community screening sample; thus no adjustments were made to the analysis for multiple comparisons. All statistical tests were two-sided and considered significant at  $p \leq 0.05$ . Only variables that were statistically significant in univariate analysis were included in the multivariable model. The resulting multivariable model included age, smoking habits, education, number of doctor visits, BMI, diabetes mellitus, hypertension and history of cardiovascular disease. The maximum likelihood method was used to obtain adjusted odds ratios (OR),  $p$ -values and confidence intervals (CI) for the association between each study factor and the dichotomous chronic kidney disease outcomes.

**Results**

No single ethnic group comprised the majority of the 793 participants included in this study (Table 1). Sex, screening site, education, smoking, insurance and having a

**Table 1** Sociodemographic Characteristics of Hawai'i KEEP-2 Study Participants by Ethnicity<sup>a</sup> (N = 793)

	Japanese <sup>a</sup> N = 236 (%)	Native Hawaiian N = 196 (%)	Chinese N = 81 (%)	Filipino N = 134 (%)	Caucasian N = 146 (%)	Total N = 793 (%)	Overall p-value
<b>Sex</b>							
Women	170 (72)	137 (70)	50 (62)	92 (69)	83 (57)	532 (67)	0.02*
<b>Age (years)</b>							
18–34	26 (11)	27 (14)	11 (14)	31 (23)	19 (13)	114 (14)	0.32
35–44	51 (22)	39 (20)	18 (22)	23 (17)	27 (18)	158 (20)	
45–54	62 (26)	45 (23)	17 (21)	29 (22)	40 (27)	193 (24)	
55–64	47 (20)	47 (24)	19 (23)	30 (22)	40 (27)	183 (23)	
65+	50 (21)	38 (19)	16 (20)	21 (16)	20 (14)	145 (18)	
<b>Screening sites</b>							
1	27 (11)	4 (2)***	19 (23)*	12 (9)**	8 (6)***	70 (9)	<0.0001***
2	13 (6)	32 (16)	2 (3)	6 (4)	5 (3)	58 (7)	
3	33 (14)	6 (3)	3 (4)	29 (22)	10 (7)	81 (10)	
4	46 (20)	9 (5)	12 (15)	25 (19)	29 (20)	121 (15)	
5	5 (2)	42 (21)	3 (4)	8 (6)	19 (13)	77 (10)	
6	8 (3)	56 (29)	1 (1)	13 (10)	10 (7)	88 (11)	
7	32 (14)	1 (1)	10 (12)	6 (4)	18 (12)	67 (9)	
8	37 (16)	5 (3)	14 (17)	21 (16)	19 (13)	96 (12)	
9	1 (0)	32 (16)	0 (0)	1 (1)	16 (11)	50 (6)	
10	34 (14)	9 (5)	17 (21)	13 (10)	12 (8)	85 (11)	
<b>Education</b>							
High school or less	56 (24)	116 (59)***	20 (25)	42 (31)*	35 (24)	269 (34)	<0.0001***
Some college	68 (29)	46 (24)	17 (21)	50 (38)	53 (36)	234 (29)	
College graduate	112 (47)	34 (17)	44 (54)	42 (31)	58 (40)	290 (37)	
<b>Smoking habits<sup>b</sup></b>							
Never smoked	137 (59)	87 (45)*	55 (69)	88 (68)	65 (45)*	432 (55)	<0.0001***
Former smoker	76 (33)	77 (40)	22 (27)	30 (23)	66 (45)	271 (35)	
Current smoker	19 (8)	28 (15)	3 (4)	12 (9)	14 (10)	76 (10)	
<b>Insurance</b>							
None	15 (6)	30 (15)**	4 (5)	14 (11)	17 (12)	80 (10)	0.01*
Single coverage	174 (74)	132 (67)	67 (83)	105 (78)	110 (75)	588 (74)	
Dual coverage	47 (20)	34 (17)	10 (12)	15 (11)	19 (13)	125 (16)	
<b>Have a primary care doctor<sup>b</sup></b>							
Yes	222 (95)	179 (92)	74 (94)	123 (94)	123 (86)**	721 (92)	0.03*
<b>Last doctor visit<sup>b</sup></b>							
Less than 6 months	173 (74)	141 (72)	58 (73)	101 (75)	99 (69)	572 (73)	0.63

**Table 1** (Continued)

	Japanese <sup>a</sup> N = 236 (%)	Native Hawaiian N = 196 (%)	Chinese N = 81 (%)	Filipino N = 134 (%)	Caucasian N = 146 (%)	Total N = 793 (%)	Overall p-value
6 months–1 year	35 (15)	35 (18)	11 (14)	25 (18)	28 (19)	134 (17)	
More than 1 year	26 (11)	19 (10)	11 (14)	7 (5)	17 (12)	80 (10)	

<sup>a</sup>For pair-wise comparisons using Japanese as the reference group, levels of significance are indicated as \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

<sup>b</sup>Change in number of participants for the following variables: *Smoking habits*: Japanese = 232; Native Hawaiian = 192; Chinese = 80; Filipino = 130; Caucasian = 145; Total = 779. *Have a primary care doctor*: Japanese = 234; Native Hawaiian = 195; Chinese = 79; Filipino = 131; Caucasian = 143; Total = 782. *Last doctor visit*: Japanese = 235; Native Hawaiian = 195; Chinese = 80; Filipino = 134; Caucasian = 144; Total = 788.

primary care doctor were significantly different between ethnic groups. Compared with Japanese, several ethnic-specific differences were observed for the above factors. Screening site was significantly different for each of the other four ethnic groups, indicating that at each of the screening sites, enrollment of Hawai'i KEEP-2 participants included a different distribution of ethnic groups. Fewer Native Hawaiians and Filipinos had a college degree. A significantly greater proportion of Native Hawaiians reported having no insurance. Native Hawaiians and Caucasians more frequently stated being a former or current smoker. Having a primary care doctor was indicated less often among Caucasians.

Statistically significant ethnic differences were found for the clinical characteristics of BMI, history of cardiovascular disease, hypertension, diabetes mellitus and for specific measures of chronic kidney disease, such as microalbuminuria, abnormal EGFR and the presence of chronic kidney disease (Table 2). The occurrence of chronic kidney disease was found to be the lowest among Japanese (18%) and highest among Native Hawaiians (40%). Compared with Japanese, Native Hawaiians were significantly different for microalbuminuria, EGFR, BMI, hypertension, diabetes mellitus and chronic kidney disease. Chinese were significantly different from Japanese only for diabetes mellitus. Body mass index and abnormal EGFR also were found to differ significantly between Caucasians and Japanese. Filipinos were significantly different from Japanese only for microalbuminuria.

Several sociodemographic and clinical factors were found to be significantly associated with chronic kidney disease using the total Hawai'i KEEP-2 sample (Table 3). Increasing age, lower educational attainment and being a former smoker were associated with an increased occurrence for chronic kidney disease. A significant inverse relationship was found between occurrence of chronic kidney disease and seeing a physician more than one year ago. Significant associations also were found between chronic kidney disease occurrence and the presence of diabetes mellitus, hypertension, cardiovascular disease and overweight/obesity.

**Table 2** Clinical Characteristics of Hawai'i KEEP-2 Study Participants by Ethnicity<sup>a</sup> (N = 793)

	Japanese N = 236 (%)	Native Hawaiian N = 196 (%)	Chinese N = 81 (%)	Filipino N = 134 (%)	Caucasian N = 146 (%)	Total N = 793 (%)	Overall p-value
<b>Abnormal serum creatinine<sup>b</sup></b>	7 (3)	13 (7)	6 (7)	10 (8)	3 (2)	39 (5)	0.07
<b>Microalbuminuria</b> ( > 30 mg/g Cr)	79 (34)	124 (63)***	36 (44)	75 (56)***	62 (43)	376 (47)	<0.0001***
<b>Abnormal EGFR</b> ( < 60 ml/min/1.73 m <sup>2</sup> )	18 (8)	34 (17)**	12 (15)	16 (12)	23 (16)*	103 (13)	0.03*
<b>BMI<sup>b</sup></b>							
Overweight	42 (18)	69 (35)***	12 (15)	20 (15)	56 (38)***	199 (25)	
Obese	120 (51)	105 (54)	38 (47)	79 (59)	52 (36)	394 (49)	<0.0001***
<b>Hypercholesterolemia<sup>c</sup></b> ( ≥ 200 mg/dl)	82 (52)	68 (44)	28 (54)	45 (41)	46 (41)	269 (46)	0.21
<b>Low HDL-cholesterol<sup>c</sup></b> ( ≤ 40 mg/dl)	22 (14)	51 (33)	10 (19)	19 (17)	29 (26)	131 (22)	0.12
<b>History of cardiovascular disease</b>	12 (5)	17 (9)	5 (6)	3 (2)	6 (4)	43 (5)	<0.0001***
<b>Hypertension</b>	130 (55)	149 (76)***	48 (59)	76 (57)	72 (49)	475 (59)	0.0007**
<b>Diabetes</b>	33 (14)	63 (32)***	23 (28)**	27 (20)	26 (18)	172 (19)	<0.0001***
<b>Chronic kidney disease</b>	42 (18)	78 (40)***	22 (27)	30 (22)	35 (24)	207 (27)	<0.0001***

<sup>a</sup>For pair-wise comparisons using Japanese as the reference group, levels of significance are indicated as \**p* < 0.05; \*\**p* < 0.01; \*\*\**p* < 0.001.

<sup>b</sup>Ethnic-specific definition of clinical cut-points: *Abnormal creatinine*: for Asians (Japanese, Chinese and Filipino) = ≥ 1.2 mg/dl women and ≥ 1.4 mg/dl men; for Native Hawaiians and Caucasians defined as ≥ 1.4 mg/dl women and ≥ 1.6 mg/dl men. *BMI (body mass index)*: for Asians (Japanese, Chinese and Filipino) = overweight if BMI is ≥ 23 kg/m<sup>2</sup> and < 25 kg/m<sup>2</sup> or obese ≥ 25 kg/m<sup>2</sup>; for Native Hawaiians = overweight if BMI is ≥ 26 kg/m<sup>2</sup> and < 32 kg/m<sup>2</sup> or obese ≥ 32 kg/m<sup>2</sup>; for Caucasians = overweight if BMI is ≥ 25 kg/m<sup>2</sup> and < 30 kg/m<sup>2</sup> or obese ≥ 30 kg/m<sup>2</sup>.

<sup>c</sup>Change in number of participants for the following variables: *Hypercholesterolemia and Low HDL-cholesterol*: Japanese = 157; Native Hawaiian = 154; Chinese = 52; Filipino = 109; Caucasian = 111; Total = 583.

**Table 3** Univariate Association between Chronic Kidney Disease and Renal Susceptibility Factors in the Total Hawai'i KEEP-2 Study, 2001–2003<sup>a</sup> (*N* = 793)

	OR	95% CI
<b>Sex</b>		
Men	<b>1.26</b>	0.90–1.75
<b>Age (years)</b>		
35–44	<b>1.15</b>	0.56–2.37
45–54	<b>2.36**</b>	1.24–4.52
55–64	<b>3.40**</b>	1.79–6.44
65+	<b>5.64***</b>	2.95–10.79
<b>Education</b>		
High school or less	<b>2.03**</b>	1.39–2.96
Some college	<b>1.15</b>	0.76–1.74
<b>Smoking habits</b>		
Former smoker	<b>1.41*</b>	1.01–1.98
Current smoker	<b>1.14</b>	0.65–1.99
<b>Insurance</b>		
No insurance	<b>1.24</b>	0.75–2.06
<b>Have a primary care doctor</b>		
No	<b>1.65</b>	0.95–2.85
<b>Last doctor visit</b>		
6 months–1 year	<b>0.77</b>	0.49–1.19
More than 1 year/never	<b>0.48*</b>	0.26–0.89
<b>BMI</b>		
Overweight	<b>2.01**</b>	1.24–3.24
Obese	<b>1.92**</b>	1.25–2.94
<b>Presence of diabetes</b>		
Yes	<b>3.86***</b>	2.70–5.53
<b>Presence of hypertension</b>		
Yes	<b>6.58***</b>	4.25–10.17
<b>History of CVD</b>		
Yes	<b>4.33***</b>	2.31–8.13

<sup>a</sup>Reference groups for the following variables include: *Age*: 18–34 years; *Sex*: women; *Education*: college graduate; *Smoking habits*: never smoked; *Insurance*: yes; *Have primary care doctor*: yes; *Doctor visits*: less than six months ago; *Presence of diabetes mellitus*: no; *Presence of hypertension*: no; *BMI*: normal weight; *History of CVD*: no. Levels of significance are indicated as \**p* < 0.05; \*\**p* < 0.01; \*\*\**p* < 0.001. Total study participant analysis includes all ethnicities (Japanese, Native Hawaiian, Chinese, Filipino and Caucasian).

Multivariable logistic regression models were used to adjust for all statistically significant univariate factors and chronic kidney disease for the overall study group and then within each ethnic group (Table 4). For the overall study group (all ethnic groups), only diabetes mellitus (OR 2.57, CI 1.71–3.86) and hypertension (OR 4.28, CI 2.62–6.98) were independently associated with chronic kidney disease. Among the Japanese group, only hypertension was significantly associated with chronic kidney

**Table 4** Multivariable Association between Chronic Kidney Disease and Renal Susceptibility Factors Within Hawai'i KEEP-2 Study Ethnic Groups<sup>a</sup>

	Japanese N = 229 OR (95% CI)	Native Hawaiian N = 190 OR (95% CI)	Chinese N = 79 OR (95% CI)	Filipino N = 129 OR (95% CI)	Caucasian N = 143 OR (95% CI)	Total N = 770 OR (95% CI)
<b>Age</b>						
35–44	0.22 (0.03, 1.36)	0.51 (0.13, 1.91)	0.48 (0.03, 8.06)	2.33 (0.16, 34.08)	1.90 (0.28, 13.02)	0.70 (0.33, 1.52)
45–54	0.60 (0.12, 3.05)	0.44 (0.11, 1.69)	0.62 (0.04, 10.11)	5.63 (0.49, 64.19)	2.48 (0.45, 13.61)	1.20 (0.59, 2.43)
55–64	0.42 (0.07, 2.45)	1.02 (0.28, 3.70)	0.94 (0.06, 15.46)	5.23 (0.47, 58.17)	1.07 (0.17, 6.61)	1.16 (0.56, 2.40)
65 and older	0.67 (0.12, 3.87)	1.51 (0.39, 5.80)	2.46 (0.16, 38.65)	21.53 (1.73, 267.68)*	2.25 (0.33, 15.38)	2.08 (0.99, 4.36)
<b>Smoking habits</b>						
Former smoker	1.36 (0.60, 3.11)	1.07 (0.50, 2.32)	0.48 (0.10, 2.36)	1.72 (0.44, 6.65)	1.0 (0.40, 2.52)	1.13 (0.76, 1.67)
Current smoker	0.76 (0.15, 3.94)	0.96 (0.34, 2.74)	11.70 (0.39, 348.49)	3.88 (0.44, 34.09)	0.64 (0.10, 4.27)	1.33 (0.71, 2.49)
<b>Presence of diabetes</b>						
Yes	1.35 (0.50, 3.60)	3.12 (1.49, 6.55)**	4.13 (0.93, 18.38)	5.82 (1.52, 22.25)*	1.90 (0.60, 6.0)	2.57 (1.71, 3.86)***
<b>Presence of hypertension</b>						
Yes	5.15 (1.63, 16.32)**	4.59 (1.57, 13.43)**	2.03 (0.35, 11.77)	14.09 (2.50, 79.42)**	3.93 (1.35, 11.40)*	4.28 (2.62, 6.98)***
<b>BMI</b>						
Overweight	2.08 (0.63, 6.89)	1.46 (0.43, 5.02)	2.79 (0.34, 23.67)	1.22 (0.17, 8.77)	0.28 (0.08, 0.96)*	1.18 (0.69, 2.02)
Obese	1.43 (0.52, 3.99)	1.38 (0.40, 4.74)	1.55 (0.34, 7.07)	0.89 (0.21, 3.85)	0.50 (0.14, 1.76)	1.03 (0.63, 1.69)
<b>History of CVD</b>						
Yes	2.16 (0.52, 8.95)	0.96 (0.29, 3.18)	5.88 (0.37, 94.42)	0.62 (0.02, 20.49)	3.96 (0.56, 28.14)	1.84 (0.91, 3.71)
<b>Education</b>						
High school or less	1.01 (0.39, 2.61)	2.78 (1.01, 7.74)*	2.13 (0.32, 13.93)	0.17 (0.03, 0.87)*	0.44 (0.12, 1.56)	1.08 (0.70, 1.69)
Some college	0.58 (0.21, 1.56)	1.81 (0.56, 5.86)	0.73 (0.10, 5.36)	1.12 (0.26, 4.81)	0.85 (0.30, 2.36)	0.87 (0.54, 1.38)
<b>Doctor visits</b>						
6 months–1 year ago	1.21 (0.35, 4.17)	1.21 (0.49, 3.01)	1.16 (0.08, 17.57)	0.69 (0.12, 4.05)	1.70 (0.60, 4.92)	1.36 (0.82, 2.26)
More than 1 year ago/never	0.74 (0.18, 3.00)	0.95 (0.25, 3.69)	0.46 (0.03, 5.88)	1.81 (0.25, 13.22)	0.67 (0.14, 3.13)	0.92 (0.47, 1.81)

<sup>a</sup>Reference groups for the following variables include: *Age*: 18–34 years; *Education*: college graduate; *Smoking habits*: never smoked; *Doctor visits*: less than six months ago; *Presence of diabetes mellitus*: no; *Presence of hypertension*: no; *BMI*: normal weight; *History of CVD*: no. Levels of significance are indicated as \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.0001$ .

disease (Japanese OR 5.15, CI 1.63–16.32). Among Caucasians, hypertension was also significantly associated with chronic kidney disease (OR 3.93, CI 1.35–11.40) and overweight was found to reduce the odds ratio for chronic kidney disease (OR 0.28, CI 0.08–0.96). By contrast, in Native Hawaiians, diabetes mellitus (OR 3.12, CI 1.49–5.55), hypertension (OR 4.59, CI 1.57–13.43) and lower educational attainment (OR 2.78, CI 1.01–7.74) were all significantly associated with increased occurrence for chronic kidney disease. Among Filipinos, diabetes mellitus (OR 5.82, CI 1.52–22.25), hypertension (OR 14.09, CI 2.50–79.42), age 65 years and older (OR 21.53, CI 1.73–267.68) were all associated with increased occurrence for chronic kidney disease, while high school education or less was found to be associated with a reduced occurrence for chronic kidney disease. Among the Chinese group, no factors were found to be statistically associated with chronic kidney disease, although trends for all examined factors paralleled those of the total study group. Sex, smoking, history of cardiovascular disease and doctor visits were not independently associated with chronic kidney disease for any of the individual ethnic groups.

## Discussion

The occurrence of chronic kidney disease in the Hawai'i KEEP-2 study sample was 27% and considerable variability for chronic kidney disease was found among the five ethnic groups studied. The Japanese group was found to have the lowest occurrence of chronic kidney disease (18%) and Native Hawaiians were found to have the highest occurrence (40%) more than twofold greater ( $p < 0.0001$ ). When compared to the national KEEP-2 study, which used similar study methodology, the proportion of individuals in the Hawai'i KEEP-2 study at Kidney Disease Outcomes Quality Initiative (K/DOQI) stage 3 or greater (13%) was slightly less than the national KEEP-2 study of 17%. Compared to prevalence estimates of moderate to severe chronic kidney disease in the general US population of 4.5%, the increased occurrence of chronic kidney disease found in both the national KEEP-2 study (17%) and the Hawai'i KEEP-2 study (13%) is not unexpected given the program's overarching goal to identify and screen individuals from high risk chronic kidney disease populations (Coresh *et al.* 2003).

Although this study is not a population-based study, the findings from the Hawai'i KEEP-2 study provide preliminary results from a screening program for chronic kidney disease on ethnic differences of renal susceptibility factors in three major Asian American groups (Japanese, Chinese and Filipino) and a relatively large number of Native Hawaiians. Few studies are available on chronic kidney disease risk factors in Asian Americans and Pacific Islanders (including Native Hawaiians) (El Nahas & Bello 2005). Yet, recognizing these ethnic differences and capitalizing on the unique characteristics of this diverse population offers the potential for improving interventions for reducing the rising occurrence of chronic kidney disease and end stage renal disease in these high risk populations (Louie 2001; Lopes 2004).

A recent study by Hall *et al.*, found that the risk for end stage renal disease in Asians compared with whites increased after adjustment for risk factors, while adjusting for the same set of risk factors decreased the risk for chronic kidney disease in blacks compared to whites (Hall *et al.* 2005a). The authors concluded that the excess risk for end stage renal disease in Asians may extend beyond the usual demographic and co-morbidity factors for end stage renal disease (Hall *et al.* 2005a). Our study also suggests that the impact of susceptibility factors for chronic kidney disease may have a differential impact on ethnic minority groups at high risk for chronic kidney disease or end stage renal disease. For example, lower educational attainment in this study was significantly associated with increased occurrence for chronic kidney disease in Native Hawaiians but had an opposite effect in the Filipino group. Similarly, overweight/obese in the Caucasian group was found to be associated with a reduced occurrence for chronic kidney disease but in all other ethnic groups overweight/obese was associated with an increased occurrence for chronic kidney disease.

Thus, a better understanding of the epidemiologic and clinical factors associated with end stage renal disease and chronic kidney disease in Asian American and Pacific Islander subgroups has the potential for improving future treatment or prevention programs aimed at reducing health disparities in these ethnically diverse groups. Few studies have adequately characterized the health profiles for chronic kidney disease and end stage renal disease in the major Asian American groups in the USA even though worldwide the number of patients on end stage renal disease therapy in Asian nations such as Taiwan and Japan has now eclipsed the USA (National Kidney Foundation 2005).

Our study also found an independent relationship between low educational attainment and chronic kidney disease among Native Hawaiians and this is consistent with published studies among other indigenous populations (Cass *et al.* 2004). Studies among other indigenous populations and developing countries around the world also have found that geographic isolation and other socio-economic disadvantages in addition to clinical factors such as underlying diabetes mellitus and hypertension to be associated with chronic kidney disease and end stage renal disease (Cass *et al.* 2004; El Nahas & Bello 2005). In our study, we found that in the Filipino group, lower educational attainment was associated with a reduced occurrence for chronic kidney disease. One possible explanation for this paradoxical association may be that Filipino individuals with lower educational attainment may be recent immigrants to the USA and may not have been exposed to other environmental factors that may predispose them to chronic kidney disease, such as diabetes mellitus or hypertension (Cass *et al.* 2004; Lopes 2004).

Ethnic differences for other sociodemographic factors were noted when compared with Japanese as the reference in sex, smoking, insurance and having a primary care doctor. Significant differences between the Japanese reference group and other ethnic groups for BMI, history of cardiovascular disease, hypertension and diabetes mellitus also were noted. However, when all ethnicities were combined in the KEEP-2 study

group, only age, education, smoking, doctor visits, BMI, history of cardiovascular disease, hypertension and diabetes mellitus remained significant as susceptibility factors for chronic kidney disease (Cass *et al.* 2004).

In Caucasians enrolled in the Hawai'i KEEP-2 program, hypertension was identified as a significant etiologic factor but unlike other ethnic groups, overweight was found to reduce the occurrence for chronic kidney disease. The association of chronic kidney disease or end stage renal disease and BMI in prior studies has shown mixed results. For example, Leavey *et al.* found that increasing BMI in end stage renal disease patients was associated with improved survival except in Asian Americans (Leavey *et al.* 2001). However, a study examining the reported survival advantage experienced by Japanese patients with a higher BMI on dialysis found that ethnic differences with the white comparison group was largely due to background death rates in Japan and the USA and not apparently due to treatment differences (Wong *et al.* 1999). Finally, two recent studies found that increasing BMI increased the risk for developing chronic kidney disease (Gelber *et al.* 2005; Hsu *et al.* 2006). Thus further investigations are needed to fully understand the relationship between body weight and chronic kidney disease or end stage renal disease in Asian Americans and Pacific Islanders.

It is important to recognize the limitations of this study: first, participants in this analysis only included those enrolled in the Hawai'i KEEP-2 study and may not be representative of the general population. Results were compared with the larger national KEEP-2 study, in which a similar study design and sampling methodology were used and thus provides the most suitable comparison of study results. The Hawai'i KEEP-2 study, however, provides additional data to the national KEEP-2 report by including ethnic-specific Asian American and Native Hawaiian assessment of renal susceptibility factors for chronic kidney disease. Another limitation of this study is its cross-sectional nature which does not allow for determination of cause and effect relationships. The study also was limited by missing data and a small sample size for some ethnic groups when performing subgroup analyses. However, despite the study's limitations, the overall group finding of hypertension and diabetes mellitus being independently associated with chronic kidney disease does provide face validity to the study results.

In summary, the findings from this study provide preliminary data on ethnic-specific characteristics associated with chronic kidney disease and end stage renal disease among the growing group of Asians and Pacific Islanders, and suggest that further research is needed to better understand the potential for differential effects of renal susceptibility factors or groups of factors that impact the occurrence of chronic kidney disease in these high risk and ethnically diverse Asian American and Pacific Islander groups. Other potentially important factors such as cultural influences, language and years since emigration may influence the effectiveness of public health programs to prevent end stage renal disease are needed (Srinivasan & Guillermo 2000; Mau *et al.* 2003). Few studies have included a significant number of Asian American, Native Hawaiians or other Pacific Islanders and even fewer studies have

been able to distinguish between the various Asian American ethnic groups to further delineate appropriate intervention or prevention programs (Lopes 2004; El Nahas & Bello 2005; Hall *et al.* 2005a,b). This study helps to address this gap by providing preliminary data on individual ethnic group differences related to the occurrence of chronic kidney disease in a nationally recognized community-based screening program. The rising tide of new cases of kidney failure in the heterogeneous groups of Asian Americans and Pacific Islanders (including Native Hawaiians) suggests that future investigations are needed to better inform programs aimed at reducing the occurrence of end stage renal disease based on ethnic-specific profiles of chronic kidney disease factors in these distinct populations.

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