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Abstract

Objective The objective of this study was to further examine the relationship of associated cardiovascular risk factors and chronic kidney disease (CKD) with a large cross-sectional sample of Native Hawaiians, Japanese, Chinese, Filipino, and White participants who were enrolled in the National Kidney Foundation of Hawai'i Kidney Early Detection Screening (KEDS) program.

Methods Data for this cross-sectional study was collected between 2006 and 2009 from the National Kidney Foundation of Hawaii (NKFH). Nine hundred and fifteen participants who attended the NKFH KEDS program were 18 years and older, and residents of the State of Hawaii. Data included demographic information, clinical risk factors, anthropometric measurements, and lab values. Microalbuminuria was used as an indicator for CKD. Descriptive analysis using frequencies, means, and standard deviations, chi-square tests, and ANOVA were conducted to examine the differences in cardiovascular disease (CVD) risk factors and normal and abnormal microalbuminuria groups. A multivariate hierarchical logistic regression model was used to identify the CV risk factors associated with abnormal microalbuminuria. The Hosmer and Lemeshow Goodness of Fit test and R-2-type indices examined the fit of the regression model to the data. *Results* Significant results related to microalbuminuria included BMI (p=0.004), glucose (p=.004), and Japanese ethnicity (p=.008).

Conclusion The findings support the need to address CVD risk factors in NKFH KEDS program.

Keywords: chronic kidney disease, CVD risk factors, microalbuminuria, Asians, Native Hawaiians Pacific Islanders

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ABSTRACT

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INTRODUCTION

Approximately 11% of U.S. adults (26 million) have CKD (Chronic Kidney Disease) (Centers for Disease Control & Prevention, 2014) and 1 in 3 American adults are at risk for developing kidney disease (CDC, 2015). In 2010, the World Health Organization (WHO) recognized that CKD was common in people with Cardiovascular Disease (CVD) and associated CVD risk factors (i e. diabetes, hypertension, smoking, obesity, dyslipidemia) (Levey et al., 2007). CVD is the leading cause of morbidity and mortality in patients with CKD followed by associated CVD risk factors (Ardhamari, Alpert, & Aggarwal, 2014; Kazancioglu, 2013). Both CVD and CKD are closely inter-related to each other (Liu, Li, Lu, Cao et al., 2014). It is also known that patients with CKD are at risk of developing CVD and CVD risk factors. These studies suggest that the relationship between CKD and CVD is bi-directional (Nashar & Egan, 2014).

Both CVD and CKD share common risk factors such as diabetes, hypertension, obesity, dyslipidemia, and smoking which are often under-diagnosed and untreated if not screened early (Said & Hernandez, 2014). Diabetes and hypertension are the two major associated CVD risk factors of CKD worldwide (Zhang & Rothenbacher, 2008) and are listed as the primary cause for 7 of 10 new cases of end-stage-renal disease in the U.S. (CDC, 2014). Diabetes is a leading CVD risk factor in the U.S. which leads to CKD (CDC, 2014; Saran, Li, Robinson, Avanian et al., 2015). High blood pressure is the second leading CVD risk factor of CKD. Obesity is associated with increased risk of development CKD and may be mediated through CVD risk factors, including hypertension, diabetes, and low HDL cholesterol levels (Foster, Hwang, Larson, Lichtman et al., 2008). High cholesterol and triglyceride levels have been shown to be independent risk factors for progression of CKD (Trevisan, Dodesini, & Lepore, 2006). Smoking is also a risk factor for progression of CKD and CV morbidity and mortality in CKD patients (Orth & Hallan, 2008).

Microalbuminuria is a primary determinant of CKD (Rosansky, 2012; Amin,Whaley-Connell, Li, Chen et al., 2013) and a major risk factor for the development and progression of CKD and CVD (Glassock, 2010; Koroshi, 2007; Tillin, Forouhi, McKeigue, & Chaturvedi, 2005; Bakris & Molitch, 2014; Jarraya, Lakhdar, Kammoun, Mahfoudh et al, 2013). Studies also indicate that microalbuminuria is the most important correlate of systolic hypertension among patients with CKD (Agarwal, 2010), is an indicator of insulin resistance and increased renal and cardiovascular risk associated with metabolic syndrome (Koroshi, 2007), and suggest that it may be a better marker of kidney disease progression than of cardiovascular risk for diabetes, obesity, and hypertension (Bentata & Abougal, 2014).

The prevalence of kidney failure in Hawaii is 30% higher than the national level (Western Pacific Renal Network, 2006) and a larger proportion (88%) of patients on dialysis are of Asian and/or Native Hawaiian Pacific Islander (NHPI) ancestry with major ethnic groups being Japanese (26.7%), Filipino (24.7%), and Native Hawaiian (17%) (U.S. Renal Data System, 2013). The percentage breakdown of the State of Hawaii population based on Japanese, Filipino, and Native Hawaiians is 16.7%, 14.1%, and 6.6 %, respectively (U.S. Bureau of Census, 2014). In Hawaii, it is estimated that over 156,000 individuals have CKD and another 100,000 are at risk (almost 20% of the population) (CDC, 2007). Studies of large national data on Asian and NHPI populations and CKD are sparse and often data is aggregated or placed in the "other"

category. The prevalence of CKD in Hawaii has continued to rise due in part to rates of diabetes, hypertension, obesity, and CKD reported in this population (Mau, West, Sugihara, Kamaka et al., 2003; Mau, West, Shara, Efird et al., 2007). King, McNeely, Thorpe, Mau et al. (2012) examined the National Health Interview Survey prevalence of type 2 diabetes in Asian American NHPI populations and found the odds of prevalence of diabetes adjusting for age and sex was 40% higher in Asian Americans relative to Whites. More specifically, there was a significant association between diabetes and CKD among Filipinos and Native Hawaiians (Mau, West, Shara, Efird et al., 2007). Native Hawaiians have a fourfold greater age-adjusted prevalence rate for type 2 diabetes (Grandinetti, Chang, Mau, Curb et al., 1998). Almost 1 in 5 of Asians and NHPIs also have hypertension (American Kidney Fund, 2015) and hypertension has been associated with CKD among four of the five ethnic groups (Japanese, Native Hawaiian, Filipino, and Whites) (Mau, West, Shara, Efird et al., 2007). Native Hawaiian/Part Hawaiian ethnicity have the highest mean BMI for men and women in comparison to other ethnic groups in Hawaii (Moy, Sallis, & David, 2010; Mau, West, Shara, Efird et al., 2007).

In 2005, the National Kidney Foundation of Hawaii (NKFH) developed the Kidney Early Detection Screening (KEDS) program to raise awareness about individual risk for kidney disease and conducted early screenings in the rural and urban communities in the State. The KEDS program was adapted from a national program called Kidney Early Evaluation Program (KEEP). A formative program evaluation of the NKFH KEDS program was completed in 2012 and over 1,000 participant data was collected and descriptive results were reported (Kataoka-Yahiro, Wong, Page, Tamashiro et al., 2012).

The unique contribution of KEDS was the use of disaggregated Asian and NHPI data not reported in the Kidney Early Evaluation Program (KEEP) (National Kidney Foundation, 2009). The majority of KEDS participants were between the ages of 46 and 75 years of age, primarily women. White, Japanese, Chinese, Filipino, and Hawaiian/Part Hawaiian were most represented. Participants had an average of one or two risk factors out of the seven total risk factors. The three most identified individual risk factors included: (1) blood relative with diabetes, (2) blood relative with cardiovascular disease, and (3) self-reported high blood pressure. Ethnicity was significantly associated with BMI and Hawaiian/Part Hawaiian ethnicity had a higher value of BMI than other ethnicities.

Objective

The objective of this study was to further examine the relationship of associated cardiovascular risk factors and CKD with a large cross-sectional sample of Native Hawaiians, Japanese, Chinese, Filipino, and White participants who were enrolled in the National Kidney Foundation of Hawai'i Kidney Early Detection Screening (KEDS) program.

METHODS

Design

This was a cross-sectional study on National Kidney of Foundation of Hawaii (NKFH) (KEDS) data collected between 2006 and 2009. The study was approved by the University of Hawaii at Manoa, Human Studies Program. CHS # is 19344.

Sample

This study included 915 participants who were enrolled in a KEDS screening program, were 18 years and older, and residents of the State of Hawaii. This was a free screening program

offered by the National Kidney Foundation of Hawaii to cast a "wider net" by reaching those possibly at risk for CKD who may not have seen a primary care provider. The participants attended one of the 14 KEDS events held in the State in both urban and rural areas of the State. The KEDS sites included shopping malls, community colleges, community health centers, hospitals, community centers, and the Hawaii State Capitol.

Measures

Demographic information included gender, age, ethnicity, zipcode, and individual/total risk factors. Clinical risk factors included a medical history of diabetes, hypertension, hypercholesterolemia, a family history of diabetes, cardiovascular disease, or kidney disease, or a social history of cigarette smoking. Anthropometric measurements included blood pressure (BP), height, weight, body mass index (BMI) and lab values (ie. glomerular filtration rate, fasting and non-fasting glucose, levels, total cholesterol, urine microalbuminuria, and albumin to creatinine ratio (A:C ratio) were obtained. Microalbuminuria was used as an indicator for CKD with 30 mg/L or greater being the cut off for reporting possible kidney damage.

Data collection

Approximately 25 to 45 volunteers were trained and participated at each event. Every volunteer participated in an orientation which included: (a) screening purpose and program procedures, (b) paperwork and documentation, (c) interviewing techniques, (d) equipment protocols for blood testing, (e) physical measurements, (f) urinalysis, and (g) screening follow-up recommendations..

A typical KEDS event consisted of five stations - Registration, Physical Measurements, Urinalysis, Blood Draw, and Exit Interview. Participants signed a consent form and then completed the assessment form. Professional volunteers or students performed blood pressure readings and height and weight measurements. Blood pressure readings were measured using Welch-Allyn Spot Vital Signs (420 Series) BP monitor, and a Tanita BWB-800 digital weight scale. BP cuffs were fitted for proper arm size and clothing was removed on the left or right upper arm. Volunteers provided participants with a specimen cup and instructions to provide a "clean-catch" urine sample. Specimens were processed utilizing either a Clinitek 50 or Clinitek Status Analyzer and Bayer/Siemens Diagnostics Microalbumin Reagent test strips were used. Capillary blood specimens were completed using Accu-Check Aviva blood glucose meters and test strips by Roche. Venous or capillary blood specimens were collected by professionals skilled in phlebotomy and specimens were transported by couriers to local laboratories for processing. Health professionals (Registered Nurse, Advanced Practice Nurse) conducted brief 5 to 10 minute interviews with participants and reviewed screening results. General recommendations and education regarding risk factors for CKD were also provided. Participants with abnormal results were advised to follow-up with their primary care providers. Venous blood specimen results were mailed to the participants' homes seven to ten days after the screening.

Participant demographic data collected included gender, age, ethnicity, zipcode, and risk factors. Clinical risk factors were collected medical history of diabetes, hypertension, hypercholesterolemia, family history of diabetes, cardiovascular disease, or kidney disease, or social history of cigarette smoking. Anthropometric measures including measurements of blood pressure (BP), height, weight, body mass index (BMI), and lab values (i e. glomerular filtration rate (GFR), fasting and non-fasting glucose levels, total cholesterol, urine microalbuminuria, and albumin to creatinine ratio [A:C ratio] were obtained.

Data analysis

Frequency distributions and summary statistics were used to describe the characteristics of participants. Chi-square tests and one-way ANOVA were used to examine the differences in CVD risk factors for normal and abnormal microalbuminuria groups. A hierarchical logistic regression model was applied to the KEDS screening data to identify the risk factors associated with abnormal microalbuminuria. The effects of demographic characteristics (age, gender, ethnicity (Hawaiian/Part-Hawaiian, Japanese, Chinese, Filipinos, White), history of diabetes, hypertension, high cholesterol, smoking) were analyzed first to describe the study group. Then the basic biometrical measurements (glucose, upper and lower blood pressure, BMI) were added to the model to examine their effects on microalbuminuria after adjusting the effects of demographic variables. All statistical analyses were conducted in IBM SPSS Statistics for Windows (SPSS Statistics for Windows, Version, 20.0, 2011). The significance level for all tests was set at 5%. The Hosmer and Lemeshow goodness of fit test and R2-type indices were used to examine the fit of the hierarchical logistic regression model to the data.

RESULTS

The majority of the participants in the screening program were females (62.4%) with the mean age of around 55 years old. Almost half of the participants were Asian-American (Japanese-American (23.3), Filipino-American) (18.1%), Chinese-American (7.2%)), followed by Hawaiian/Part Hawaiian/Mixed (26.0%) and White (25.4%). The sample of African-American and Native American were not included in this study due to a very small sample size < .01%. About 39.2% of the participants had hypertension with a mean systolic blood pressure of 127 and mean diastolic blood pressure of 76. Twenty percent of the participants had diabetes with a mean glucose level at 113. The mean BMI for participants attending the screening was 27.3 (see Table 1).

Table 1: Demographics of participants (n=915)

Variable		n
Gender	Male	336 (37.6%)
	Female	558 (62.4%)
Ethnicity	White	198 (25.4%)
	Hawaiian/Part Hawaiian	203 (26.0%)
	Japanese	182 (23.3%)
	Filipino	141 (18.1%)
	Chinese	56 (7.2%)
	Missing	135(14.8%)
Hypertension*	Yes	359 (39.2%)
	No	556 (60.8%)
Diabetes**	Yes	185 (20.2%)
	No	730 (70.8%)
Cholesterol***	Yes	265 (29.9%)
	No	650 (71.0%)
Smoking#	Yes	5.1 (5.1%)

No		868 (94.9%)
	Mean	SD
Age (Years, n=847)	55.3	16.4
Systolic BP (n=893)****	127.3	17.8
Diastolic BP (n=893)^	76.2	10.0
BMI (n=893)++	27.3	6.5
Glucose (n=794)+++	113.00	44.5

*Hypertension: USDHHS NIH. (2004). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: Complete Report.

**Diabetes: National Kidney Foundation. (2003). KEEP Results Explanation Sheet for screening participants.

***Cholesterol: National Kidney Foundation.(2010). About KEEP, Understanding Test Values

#Smoking: Social History of Cigarette Smoking

****Systolic BP: Chobanian A., Bakris, G.L., Black, H.R., Cushman, W.C., Green, L.A., Izzo, J.L., Jr., Jones, D.W., Materson, B.J., Oparil, S., Wright, J.T., Jr., Roccella, E.J. (2003). National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. JAMA, 289 (19), 2560-2572.

****Systolic BP: USDHHS NIH. (2004). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure-Complete Report.

^ Diastolic BP: change reference to Martinson, M.L., Teitler, J.O., & Reichman, N.E. (2011). Health across the lifespan in the U.S. & England. American Journal of Epidemiology, 173 (3), 858-865

++BMI: CDC. About BMI for Adults. (2010). www.cdc.gov.healthyweight/assessing/bmi/adult_bmi/index

+++Glucose: National Kidney Foundation. (2003). KEEP results explanation sheet for screening participants.

Microalbuminuria was used as an indicator for CKD. A 30mg/L or greater microalbuminuria indicates possible CKD. Pearson chi-square tests were performed to compare the differences between the group with normal microalbuminuria (n=426) and those with abnormal microalbuminuria (30 mg/L or greater) (n=438). Forty-nine percent of the sample had normal microalbuminurea results and 51% had abnormal results.

Pearson chi-square test and one-way ANOVA were used to test the differences in CVD risk factors for normal and abnormal microalbuminuria groups. There was no gender or ethnic differences in the proportion of abnormal microalbuminuria. Participants with diabetes had a significantly higher proportion of abnormal microalbuminuria (p =0.00) and participants with high blood pressure, high cholesterol, and history of smoking were not significant when compared with abnormal microalbuminuria. The mean age and diastolic blood pressure were not

significantly different between participants with normal microalbuminuria and participants with abnormal microalbuminuria. Participants with abnormal microalbuminuria were significantly higher in systolic blood pressure (p=0.00), BMI (p=0.00), and glucose level (p=0.00) compared to participants with normal microalbuminuria (see Table 2).

Table 2: Difference in CKD and CVD risk factors for normal and abnormal microalbuminuria groups (n=915)

Variable		Normal Microalbuminuria <30mg/L (n=426)	Abnormal Microalbuminuria ≥30mg/L (n=438)	Chi-Square test	p-value
Gender	Male	159	167	0.05	0.83
	Female	261	266		
Ethnicity	White	108	78	7.68	0.10
	Hawaiian/ Part Hawaiian	87	104		
	Japanese	83	94		
	Chinese	24	30		
	Filipino	67	69		
Hypertension	Yes	155	183	2.64	0.10
	No	271	255		
Diabetes	Yes	62	113	16.91	0.00*
	No	364	325		
Cholesterol	Yes	112	138	2.85	0.09
	No	314	300		
Smoking	Yes	29	18	3.05	0.08
	No	397	420		
	N	n	n	One-way ANOVA	p-value
Age (Years)	811	398 (49.1%)	413 (50.9%)	3.31	0.07
Systolic BP	856	425 (49.6%)	431 (50.4%)	8.78	0.00*
Diastolic BP	856	425 (49.6%)	431 (50.4%)	0.13	0.71
BMI	854	422 (49.4%)	432 (50.6%)	16.15	0.00*
Glucose	753	360 (47.8%)	393 (52.2%)	22.64	0.00*

Multivariate logistic regression model (n=594) was used to fit the data to identify CVD risk factors for CKD. BMI (p=0.004), Glucose (p=0.004), and Japanese ethnicity (p=0.008) compared to other racial/ethnic groups were significantly associated with abnormal microalbuminuia after adjusting the effects of all other variables in the model. Participants with

higher BMI and higher glucose levels were more likely to have abnormal microalbuminuria. No significant interactions were found between all these risk factors (see Table 3).

Table 3: Logistic Regression Model on Factors Related to CKD (n=594)

Predictor	B	S.E. of B	Wald's χ^2	df	p-value
Age	.003	.006	.191	1	.662
Gender	.098	.181	.297	1	.586
Ethnicity-White			7.664	4	.105
Hawaiian/Part Hawaiian	.409	.253	2.605	1	.107
Japanese	.673	.254	7.022	1	.008*
Chinese	.546	.371	2.174	1	.140
Filipino	.313	.271	1.341	1	.247
Hypertension	.033	.204	.026	1	.872
Diabetes	-.140	.251	.311	1	.577
Cholesterol	.022	.202	.012	1	.914
Smoking	.548	.381	2.067	1	.150
Systolic BP	.010	.007	2.246	1	.134
Diastolic BP	-.014	.012	1.511	1	.219
BMI	.046	.016	8.395	1	.004*
Glucose	.007	.002	8.311	1	.004*

The Hosmer and Lemeshow tests showed a reasonable goodness of fit of the hierarchical model. The Cox and Snell R Square indicated 7.5% of variability of the data could be explained by the hierarchical logistic regression model (see Table 4).

Table 4: Logistic Regression Model Evaluation and Goodness of Fit Statistics (n=594)

Test	R-Square	χ^2	df	p-value
Overall model evaluation				
Cox & Snell R Square	.075			
Nagelkerke R Square	.100			
Goodness of Fit				
Hosmer and Lemeshow Test		7.400	8	.494

DISCUSSION

In this secondary data analysis, abnormal microalbuminuria was significant for having a high BMI, high glucose, and being of Japanese ethnicity, independent of each other. There are very few CVD risk factors and CKD U.S. studies in which only one ethnic Asian and NHPI group are studied and many of the studies have originated in Japan. Ogata, Yorioka, Gilbertson, Chen et al. (2009), a cross-cultural study, compared the U.S. Renal Data System data and the Japanese Society for Dialysis Therapy data from 1983 to 2002 and found survival rates were better for Japanese versus U.S. Japanese Americans. In this study, Japanese-Americans were older, male, and had a higher rate of diabetes and hypertension and died more often of heart failure than other U.S. groups. When compared to other Japanese groups, there were more Japanese-Americans in Hawaii with diabetes and hypertension. Mau, West, Shara, Efird et al. (2007) examined the association between key factors and measures of CKD in 793 Asian American and Native Hawaiian participants enrolled in KEEP-2 study (2001-2003). CKD was defined as the estimated glomerular filtration rate (EGFR) or random urine microalbuminuria. Disaggregated data on Japanese, Native Hawaiian, Chinese, Filipino, and Whites were analyzed and the overall independent associated CVD risk factors of CKD were diabetes and hypertension. In this study, Japanese had the lowest prevalence of CKD (18%) and Native Hawaiians had the highest (40%). The authors concluded that genetic and environmental factors may affect patient outcomes.

Our study results also indicated that participants are at risk for CKD if they have a higher BMI and higher glucose, independent of each other and are well-referenced indicators of obesity and or diabetes. Ohno, Ishimura, Naganuman, Kondo et al. (2012) found among their Japanese patients, diabetes and obesity were independently associated with CKD. Nagata, Ninomiya, Doi, Yonemoto et al. (2010) investigated further the trends in prevalence of risk factors and CKD in the general Japanese population. They found that diabetes, hypercholesterolemia, and obesity increased over three decades. The Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (2014) group investigated cardiometabolic risk factors in international countries from 1980 to 2010 and found that the mortality burden of high BMI and glucose nearly doubled from 1980 to 2010 and has shifted from high-income to low-income and middle-income countries. Matsushita, Yasuda, Shouda, Umemura et al. (2009) found obesity was an

independent risk factor for CKD and proteinuria even among healthy Japanese patients 40 years of age and younger.

The current study results add to the existing body of literature since Mau et al. (2007) by using a large kidney data set to disaggregate and examine the relationship CV risk factors and CKD. In comparison to the KEEP Program (2009), the authors in the KEDS program disaggregated the Asians and NHPIs by various subgroups such as Native Hawaiians, Japanese, Chinese, Filipino, and Whites versus categorizing and reporting the Asians and NHPI groups in the "Other" category. There is an imperative need to address health disparities by conducting disaggregated large population studies which target ethnic minority populations. This activity will capture the unique demographic and social characteristics and care needs related to individual subgroups of Asians and NHPI populations in CKD research and practice.

The limitations of this study was that it was a cross-sectional study utilizing a convenience sample in Hawaii. Participants self-selected to be in this study and the sample was situated in one geographic island state which may not be representative of the general population. The low R-square values from the logistic regression may indicate other factors related to CKD were not included such as specific lab work - fasting glucose, lipid levels - LDL, HDL, triglycerides, and eGFR. These lab values were not included in the logistic regression model due to a small n. The screening questionnaire did not include questions on diet and physical activity, which may be interesting to add in future KEDS screening. An R-square of 10% or less could still provide valuable information when looking for a relationship between predictor variables and outcome (Cox & Snell, 1989; Kvalseth, 1985). Finally, an investigation of the effects of CKD risk factors on different race/ethnic groups is also worthy to pursue in future studies.

CONCLUSION

Though there are limitations of this study, the findings were consistent with studies reported in the literature and supported the need for CVD risk factor screening in the NKFH KEDS program. Understanding the relationship between CVD risk factors and CKD is important in developing future public health policy to improve outcomes. It is important to continue to examine large sample disaggregate data of racial/ethnic minority populations in order to identify CVD risk factors targeted to culturally appropriate screening, detection, referral, and intervention. More specifically, targeted kidney programs should include screening, detection, referral, and education for associated CVD risk factors in routine kidney screening and distinguish CVD risk factors to different stages of CKD, taking into consideration age, race/ethnicities, and gender in efforts to improve health outcomes.

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