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ORIGINAL ARTICLE

Geographic difference in the prevalence of chronic kidney disease among Japanese screened subjects: Ibaraki versus Okinawa

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Abstract
Background In Japan, there is a geographic difference in the prevalence of end-stage renal disease (ESRD). Few epidemiologic studies, however, have compared the prevalence of chronic kidney disease (CKD) among different geographic areas. Other than genetic factors, socioeconomic conditions and lifestyle are targets for modification.
Methods We examined the prevalence of CKD among two large community-based screened populations, 40 years of age and older, in Japan: Ibaraki ($N = 187{,}863$) and Okinawa ($N = 83{,}150$). Prevalence of CKD was defined as an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m^2 using the coefficient modified abbreviated Modification of Diet in Renal Disease (aMDRD) study equation using a standardized serum creatinine value. CKD prevalence was compared among screenees with (+) or without (−) hypertension (systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg) and hyperglycemia (plasma glucose ≥ 126 mg/dl).
Results Both male and female participants in Okinawa had a significantly lower prevalence of hypertension (−)/hyperglycemia (−) than did patients in Ibaraki. The prevalence of CKD in Okinawa was higher than that in Ibaraki among screenees with hypertension (−)/hyperglycemia (−), and highest among screenees with hypertension (+)/hyperglycemia (−).
Conclusion The regional difference in CKD prevalence may underlie the variation in ESRD prevalence observed in Japan.

Keywords Chronic kidney disease · Glomerular filtration rate · Prevalence · Screening

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Introduction

The prevalence of end-stage renal disease (ESRD) is linearly increasing and is as high as 2,000 per million people in Japan [1]. The geographic difference in the prevalence of ESRD in Japan is well known; Okinawa has the highest ESRD population, whereas the ESRD population in Ibaraki is smaller than the National average [1]. This trend might be explained by either a high prevalence of chronic kidney disease (CKD), a faster progression of CKD, or both. The north-south gradient in the incidence and prevalence of certain diseases, such as stroke and hypertension are also well known in Japan [2]. Populations in northern Japan have a higher salt intake and other dietary habits also vary [3]. People in Okinawa tend to be more obese and have a

higher prevalence of metabolic syndrome, which causes CKD [4, 5]. The prevalence of CKD may reflect the health and functional status of the community, such as the proportion of the population with diabetes and hypertension, as well as differences in muscle mass, diet, and lifestyle.

We compared the prevalence of CKD between two large community-based screening registries available in two target prefectures (Ibaraki and Okinawa). To define CKD, we applied the newly developed and modified abbreviated Modification of Diet in Renal Disease (MDRD) study equation as it provides the most accurate formula for this purpose [6]. Determining the factors related to the regional difference in CKD prevalence might be useful for preventing ESRD. The present study is the first to demonstrate a regional difference in CKD prevalence in Japan.

Methods

The Japanese Society of Nephrology has organized an epidemiology work group and has collected data to estimate CKD population in Japan [7, 8]. The authors are participating with the epidemiology work group. Among the community-based screening programs, we selected two cohorts because the details of these subjects were previously reported and the method of serum creatinine measurement was verified. Okinawa, 128°E 27°N, is in the southern-most part of Japan, and Ibaraki, 140°E 36°N, is in northern Japan. Screening was performed during April 2005 to March 2006. Hypertension was defined as 140/90 mmHg and over and hyperglycemia was defined as fasting plasma glucose 126 mg/dl and over.

Community-based screening registry

(Okinawa) Details of the screening in Okinawa were published previously [9, 10]. For this study, we used the 2005 Okinawa General Health Maintenance Association (OGHMA) registry, and analyzed data for those aged 40 years and over at the time of screening. There were 83,150 screenees, 13.0% of the target population of 0.64 million in 2005 (Total 1.36 million).

(Ibaraki) Details of the screening in Ibaraki were published previously [11–13]. For this study, we used the 2005 registry, and analyzed data for those aged 40 years and over at the time of screening. There were 187,863 screenees, 11.6% of the target population of 1.62 million in 2005 (Total 2.98 million). The central laboratory measured creatinine using an autoanalyzer (Hitachi 7170). Data were provided after written agreement by the research committee for each registry.

GFR estimation

GFR was estimated using the coefficient modified MDRD study equation after obtaining the standardized serum creatinine (SCr) from the Cleveland Clinic. Serum creatinine (C-SCr) was calibrated using the following formula: for Okinawa, C-SCr = 1.03557343 × SCr + 0.00736639; for Ibaraki, C-SCr = 1.01758277 × SCr − 0.0643799. Both laboratories measure SCr using an enzymatic method. We confirmed the accuracy of creatinine measurement using a calibration panel composed of 42 serum samples, whose values were determined by the Cleveland Clinic (kindly provided by Dr. Van Lente at the Cleveland Clinic). eGFR (ml/min/1.73 m^2) = 175 × $Age^{-0.203}$ × $S\text{-}Cr^{-1.154}$ × (if female × 0.742) × (if Japanese × 0.741). Performance of the IDMS aMDRD equation for evaluating Japanese CKD patients was recently published [6].

Statistical analyses

Data are expressed as means ± standard deviation (SD). The st CKD was defined as eGFR <60 ml/min/1.73 m^2 [6]. A statistical significance of differences in the characteristics among participants was examined using non-paired *t* test, the Wald chi-square test, and Wilcoxson test (categorical variables). Multivariate logistic analyses were performed using SAS (Version 8.2, SAS Institute Inc., Cary, NC). A *P* value of less than 0.05 was considered statistically significant.

Results

The demographics of the screened cohorts were different between the two community-based registries: 35.6% of the participants in Ibaraki and 42.6% of those in Okinawa were men. Therefore, the mean (SD) glomerular filtration rate (GFR) levels are summarized for each age-class for both men and women among the total number of screenees (Table 1). The mean GFR levels were significantly higher in Okinawa than in Ibaraki, except in those age 80 and over among both sexes. Prevalence of CKD in Ibaraki (Okinawa) was 18.1% (15.3%) in men and 16.0% (13.9%) in women, respectively. However, the fraction of screenees were different between the two cohorts. In Ibaraki (Okinawa), it was 8.9% (23.3%) in age 40–49, 18.7% (24.9%) in age 50–59, 35.1% (23.9%) in age 60–69, 30.6% (21.9%) in age 70–79, and 6.7% (6.0%) in age 80 and over in men. In women, that was 14.4% (21.2%) in age 40–49, 27.1% (25.1%) in age 50–59, 31.7% (23.9%) in age 60–69, 22.3% (22.1%) in age 70–79, and 4.5% (7.8%) in age 80 and over.

The proportion of screenees without either hypertension or high plasma glucose was significantly smaller in

Table 1 Comparison of GFR among screened subjects in Okinawa and Ibaraki: total screened

	Ibaraki	Okinawa	*P* value
Men			
40–49	76.8 (13.3), $N = 5{,}961$	78.4 (14.7), $N = 8{,}238$	<0.0001
50–59	74.8 (14.4), $N = 12{,}485$	75.6 (15.4), $N = 8{,}810$	<0.001
60–69	69.6 (14.3), $N = 23{,}515$	70.4 (15.1), $N = 8{,}476$	<0.0001
70–79	65.8 (14.8), $N = 20{,}513$	66.5 (15.5), $N = 7{,}757$	<0.001
80 and over	61.6 (15.6), $N = 4{,}463$	60.6 (15.9), $N = 2{,}112$	<0.05
Women			
40–49	80.7 (15.6), $N = 17{,}388$	86.1 (16.5), $N = 10{,}120$	<0.0001
50–59	77.1 (15.5), $N = 32{,}798$	80.8 (16.5), $N = 11{,}991$	<0.0001
60–69	72.8 (15.4), $N = 38{,}309$	74.7 (15.7), $N = 11{,}401$	<0.0001
70–79	67.8 (15.3), $N = 27{,}008$	68.7 (16.2), $N = 10{,}541$	<0.0001
80 and over	62.1 (15.7), $N = 5{,}423$	62.1 (19.3), $N = 3{,}704$	NS

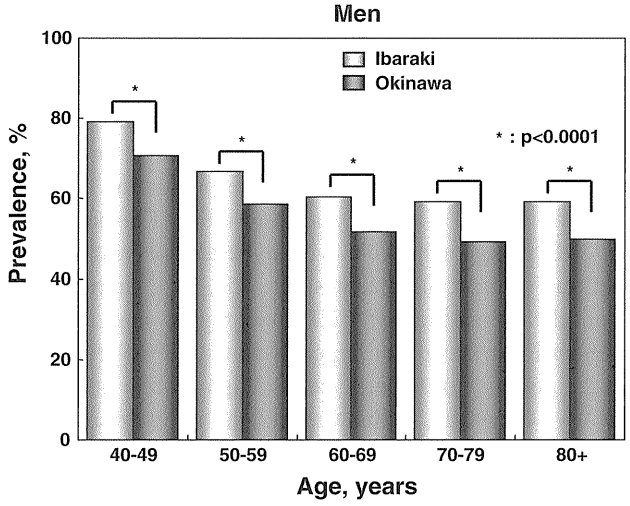

Fig. 1 Prevalence of screenees without hypertension or hyperglycemia in Okinawa and Ibaraki (men)

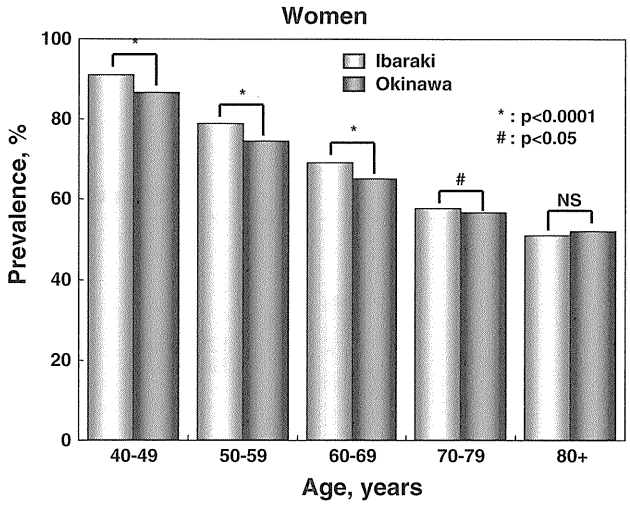

Fig. 2 Prevalence of screenees without hypertension or hyperglycemia in Okinawa and Ibaraki (women). *NS* not significant

Okinawa than in Ibaraki among men (Fig. 1) and women (Fig. 2) of all age-groups. Overall prevalence of hypertension and hyperglycemia in Okinawa was 29.9% and 10.4%: 35.5% and 14.2% in men, 26.2% and 7.6% in women, and that of Ibaraki was 27.9% and 5.1%: 31.9% and 8.4% in men, 25.9% and 3.4% in women. Among those 40–79 years of age, the prevalence of CKD of eGFR <45 ml/min/1.73 m^2, was higher in Okinawa than in Ibaraki in those with normal blood pressure and normal glucose levels, high plasma glucose, hypertension, and the total screened populations in men (Fig. 3). In each sex, the prevalence of CKD of eGFR <45 ml/min/1.73 m^2, was compared with Okinawa and Ibaraki (Fig. 4). The prevalence of CKD of eGFR <45 ml/min/1.73 m^2 among those with age 80 years and over in Okinawa (Ibaraki) was 12.6% (10.1%) in men ($P < 0.05$) and 13.0% (11.4%) in women ($P < 0.001$), respectively.

Similarly, mean GFR levels were high in Okinawa among those without either hypertension or high plasma glucose (Table 2). Compared to Ibaraki, the prevalence of low GFR (<45 ml/min/1.73 m^2) was significantly higher in Okinawa, particularly in those under 60 years of age (Table 3). Similar trends were observed among screenees without either hypertension or high plasma glucose (Table 4).

Discussion

We compared the CKD prevalence between two community-based screened cohorts using the standardized serum creatinine measurements and adopted a new, accurate GFR estimation formula for the screened Japanese populations. The strengths of the study include the large study population containing a comparable number of men and women

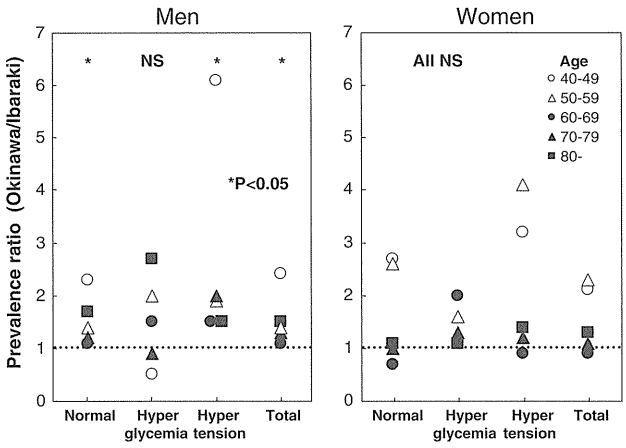

Fig. 3 Prevalence ratio of CKD, GFR <45 ml/min/1.73 m^2, in Okinawa and Ibaraki among screenees aged 40–79 years and those with age 80 years. Age-groups are 40–49 (*open circle*), 50–59 (*open triangle*), 60–69 (*filled circle*), 70–79 (*filled triangle*), and 80 and over (*open square*). In women, there was none with GFR <45 ml/min/1.73 m^2 among those with hyperglycemia age 40–49 years. $P < 0.05$ by the Wilcoxson test

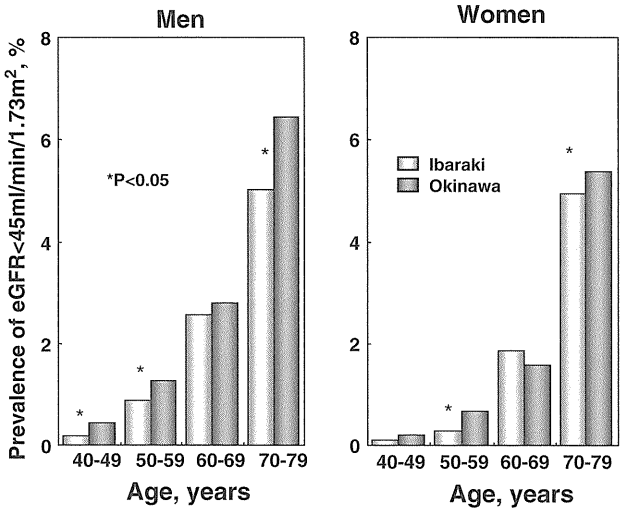

Fig. 4 Prevalence ratio of CKD, GFR <45 ml/min/1.73 m^2, by age in Okinawa and Ibaraki among screenees aged 40–79 years

and comparable age-groups, and the creatinine assays in each population were calibrated to standardized values. The key finding of the present study was that CKD prevalence was higher in Okinawa than in Ibaraki, even among groups of similar age and sex. As shown in Fig. 3, prevalence rate of GFR<45 ml/min/1.73 m^2 was higher in Okinawa, in particular age-class less than 60 years in both sexes. This may reflect the increase in obesity and metabolic syndrome in Okinawa. As a whole, mean levels of eGFR was higher in Okinawa (Table 1). This could be explained the two peaks of eGFR levels or wider distribution due to hyperfiltration related to obesity or hyperglycemia.

The findings of the present study may explain the high prevalence of ESRD in Okinawa [14]. According to the registry data of the Japanese Society for Dialysis Therapy, the prevalence of ESRD was 2,055 (Ibaraki), 2,704 (Okinawa), and 2,070 (Total) per million population in Japan in 2006 [1]. This number increased from the 2001 values of 1584 (Ibaraki), 2330 (Okinawa), and 1722 (Japan) per million population, respectively. The trend might also be explained by a rapid progression of CKD, insufficient therapy for CKD, or both.

Usami et al. [15] reported that the intake of angiotensin-converting enzyme inhibitors in Okinawa was lower than that in other parts of Japan, suggesting the insufficiency of CKD therapy in Okinawa. Because the income levels in Okinawa are the lowest in Japan, cheaper drugs are preferred. Other socioeconomically related conditions, such as a high smoking rate, a high motorization rate, and use of erythropoietin [16] may also be involved in the high prevalence of CKD.

The prevalence of CKD stages 3–5 differs among various ethnic groups. The CKD prevalence in Japan is one of the highest in the world [17–19]. The CKD prevalence might be explained by the age of the population in Japan, as more than 20% are 60 years and older. The prevalence of CKD is higher in those with hypertension and diabetes mellitus in the United States [20, 21]. In Okinawa, however, the prevalence of CKD was higher even in those without hypertension or hyperglycemia. GFR varies based on the presence of hyperglycemia, high protein intake, and obesity. Generally, Okinawan people are short in stature and have a higher prevalence of low birth weight than the national average [22]. A lower birth weight is associated with a lower nephron number and a significant risk of developing ESRD [23]. A low nephron number may result in the future development of hypertension and diabetes mellitus-related nephropathy [24]. Lifestyles have changed rapidly after the return of Okinawa to Japan in 1972, including a rapid increase in obesity.

In the present study, we applied the Japanese coefficient to improve the accuracy of the abbreviated MDRD equation to identify patients with stage 3 and 4 CKD. We used a coefficient of 0.741 obtained from the data of patients with a Cin <90 ml/min/1.73 m^2 as the Japanese coefficient with the IDMS traceable abbreviated MDRD (aMDRD) study equation. The equation provided a reasonably accurate GFR estimation in the range of less than 90 ml/min/1.73 m^2 [25]. This equation can be easily used by Japanese clinicians because the equation does not require that serum creatinine values be calibrated to the 1990 Cleveland Clinic values, where creatinine was measured using the non-compensated Jaffe method [26]. An accurate measurement of serum creatinine, however, is critical for use of IDMS aMDRD equation. In Japan, almost all clinical laboratories use the

Table 2 Comparison of GFR among screened subjects in Okinawa and Ibaraki: normal blood pressure and normal fasting plasma glucose

	Ibaraki	Okinawa	*P* value
Men			
40–49	76.5 (12.9), *N* = 4,416	77.9 (13.8), *N* = 5,812	<0.0001
50–59	74.4 (13.5), *N* = 7,356	74.9 (14.3), *N* = 5,155	NS
60–69	69.3 (13.6), *N* = 12,093	70.1 (14.2), *N* = 4,364	<0.01
70–79	65.7 (14.4), *N* = 10,095	66.7 (15.0), *N* = 3,807	<0.001
80 and over	61.4 (15.2), *N* = 2,174	61.2 (16.2), *N* = 1,037	NS
Women			
40–49	80.5 (15.3), *N* = 15,428	85.9 (16.1), *N* = 8,765	<0.0001
50–59	76.6 (15.0), *N* = 24,392	80.5 (16.1), *N* = 8,921	<0.0001
60–69	72.5 (15.0), *N* = 24,103	74.7 (15.1), *N* = 7,419	<0.0001
70–79	67.4 (14.9), *N* = 13,801	68.6 (15.5), *N* = 5,946	<0.0001
80 and over	61.9 (15.6), *N* = 2,403	62.1 (19.2), *N* = 1,847	NS

Table 3 Comparison of the prevalence of low GFR, <45 ml/min/1.73 m^2 and <60 ml/min/1.73 m^2 among screened subjects in Okinawa to those in Ibaraki (reference): total screened

	GFR <45	*P* value	GFR <60	*P* value
Men				
40–49	2.37	<0.01	0.93	NS
50–59	1.44	<0.01	1.42	<0.0001
60–69	1.10	NS	0.84	<0.0001
70–79	1.29	<0.0001	0.85	<0.0001
80 and over	1.50	<0.0001	1.06	<0.05
Total	1.04	NS	0.76	<0.0001
Women				
40–49	2.1	<0.05	0.65	<0.0001
50–59	2.34	<0.0001	1.40	<0.0001
60–69	0.86	NS	0.56	<0.0001
70–79	1.11	<0.05	0.76	<0.0001
80 and over	1.26	<0.0001	0.95	<0.05
Total	1.27	<0.0001	0.75	<0.0001

Table 4 Comparison of the prevalence of low GFR, <45 ml/min/1.73 m^2 and <60 ml/min/1.73 m^2 among screened subjects in Okinawa to those in Ibaraki (reference): normal blood pressure and normal fasting plasma glucose

	GFR < 45	*P* value	GFR < 60	*P* value
Men				
40–49	2.28	NS	0.86	<0.05
50–59	1.43	NS	1.47	<0.0001
60–69	1.08	NS	0.84	<0.0001
70–79	1.19	<0.05	0.84	<0.0001
80 and over	1.65	<0.0001	1.00	NS
Total	0.97	NS	0.73	<0.0001
Women				
40–49	2.72	<0.01	0.65	<0.0001
50–59	2.60	<0.0001	1.37	<0.0001
60–69	0.71	<0.01	0.53	<0.0001
70–79	1.01	NS	0.73	<0.0001
80 and over	1.14	NS	0.92	<0.05
Total	1.18	<0.001	0.72	<0.0001

enzymatic method to measure serum creatinine. The enzymatic method is more precise and accurate than the Jaffe method, which usually overestimates serum creatinine due to interference from the non-creatinine chromogen. Nevertheless, we further confirmed that the difference is still evident when using the original Japanese Society of Nephrology GFR estimation equation (S. Matsuo et al., personal observation).

The strengths of the present study were as follows: (1) eGFR was calculated using the serum creatinine value after calibration and standardization, (2) both cohorts were large enough to compare by age and sex, (3) CKD prevalence was also evaluated using the two equations currently available in Japan.

There were some limitations of the present study: (1) Serum creatinine was not measured at a single laboratory, although assay methods of the participating laboratories were evaluated by standard samples from the Cleveland Clinic and the inter-laboratory coefficient of variation was very small (0.88%), (2) The formula for estimating GFR was developed using CKD patients; therefore, it is not applicable to a healthy population. In particular, underestimation is possible in those with an eGFR of more than 60 ml/min/1.73 m^2 [6]. Serum creatinine concentration is affected not only by GFR, but by various other factors as well, such as muscle mass, sex, race, diet, drugs, and tubular function. Ideally, the clearance of exogenous GFR markers, such as inulin, should be measured for GFR estimation, but the method is time-consuming and difficult and is not feasible for community-based screening. The Kidney Disease Improving Global Outcomes (KDIGO) group has initiated an action to improve clinical practice by

introducing GFR estimating equations that were developed for a large cohort of a variety of racial and other groups for international comparisons [27–29]. Asian populations, including the Japanese, generally have low muscle mass and low protein intake, which could impair the performance of the MDRD study equation, (3) Clinical information, such as inflammation, nutritional status, or drug treatment, was not included in the registry data.

In conclusion, the findings of the present study revealed that there are significant regional differences in CKD prevalence among screened subjects in Japan. Although, our results may need to be confirmed in other parts of Japan. Reasons for the difference in CKD prevalence remain speculative. Generally, people in Okinawa are short in stature and have a larger body mass index. Lifestyle habits, such as smoking, drinking, and exercise among people in Okinawa also differ from those in Ibaraki. The observed differences in ESRD prevalence might be at least partly due to the difference in the CKD prevalence. Further studies on CKD progression and background demographics in the two cohorts are warranted.

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Conflict of interest statement We have no conflict of interest.

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ORIGINAL ARTICLE

Prevalence of anemia according to stage of chronic kidney disease in a large screening cohort of Japanese

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Abstract
Background The prevalence of chronic kidney disease (CKD) is high in developed countries, including Japan. However, little is known about the prevalence of anemia according to the estimated glomerular filtration rate (eGFR) among Japanese.
Methods We studied screenees on the Okinawa General Health Maintenance Association (OGHMA) registry in 1993 ($N = 94,602$; 54,848 women and 39,754 men) who had both serum creatinine and hematocrit data. Anemia was defined as follows: hematocrit level <40% in men, <32% in women aged <50 years, and <35% in women aged ≥50 years. GFR was estimated using a new Japanese equation: eGFR (ml/min per 1.73 m^2) = 194 × serum creatinine$^{1.094}$ × age$^{0.287}$ × 0.739 (if female).
Results The prevalence of anemia clearly increased as CKD progressed below an eGFR of 60 ml/min per 1.73 m^2 in both genders. Logistic analysis adjusted with body mass index and older age (≥70 years) revealed that the odds ratio for complications of anemia was significantly increased below an eGFR of 45 ml/min per 1.73 m^2 in women and 90 ml/min per 1.73 m^2 in men. The association of lower kidney function with anemia was found to be more prevalent: adjusted odds ratio ≥2.0, from approximately 50 ml/min per 1.73 m^2.
Conclusion The present study suggested that there might be as many as 1,000,000 people with CKD stage 3–5 complicated with anemia in Japan.

Keywords Chronic kidney disease · Anemia

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Introduction

Accumulating evidence has shown that even early-stage chronic kidney disease (CKD) is a risk factor for developing cardiovascular disease (CVD) [1–3]. In addition to traditional risk factors such as hypertension, anemia may be associated with CVD among general subjects [4]. Similarly, it has been reported that low hemoglobin, especially together with CKD, increases the risk of coronary heart disease (CHD), CHD-related death, and stroke [5–8]. Since anemia accelerates the progression of CKD and advanced CKD is likely to be complicated with anemia, the combination of anemia and CKD, which promote each other in a vicious circle, could result in an increased risk of CVD and vice versa, that is, cardio-renal anemia syndrome [9]. Therefore, it is critical to identify CKD patients complicated with anemia.

Recent studies have estimated that the incidence of mild kidney dysfunction is substantially high in the general population worldwide, though it varies across countries [10–13]. In the advanced stages of kidney failure, anemia is a common complication due to an inappropriately reduced endogenous erythropoietin production [14]. However, previous studies performed in the USA have found that even mild kidney dysfunction, with an estimated glomerular filtration rate (eGFR) of 60 ml/min per 1.73 m^2, had a

significant impact on the occurrence of anemia [15, 16]. The study by Astor et al. [16] also demonstrated that there was a significant racial difference in the relationship between kidney function and anemia, with Japanese reported to have a much higher prevalence of CKD than US subjects [12, 17]. However, it is not yet known whether Japanese have a much higher prevalence of CKD complicated with anemia.

In this study, we investigated the prevalence of anemia according to CKD stage in a large community-based screening of Japanese subjects.

Methods

About OGHMA

Screening program: The Okinawa General Health Maintenance Association (OGHMA), a nonprofit organization founded in 1972 and currently under the direction of Drs. Ikemiya and Kinjo, conducts a large community-based annual health examination. Once each year, the staff, doctors, and nurses visit residences and workplaces throughout the prefecture to carry out health examinations. All subjects participate voluntarily in the screening. The OGHMA personnel provide mass screening, inform the participants of their results, and when necessary, recommend further evaluation or treatment. This process includes an interview concerning health status, a physical examination, and urine and blood tests. A nurse or doctor measures blood pressure using a standard mercury sphygmomanometer with the subject in sitting position. Dipstick testing for proteinuria, hematuria, and glucosuria (Ames Dipstick, Tokyo, Japan) is performed in spontaneously voided fresh urine. Proteinuria is defined as a dipstick urinalysis score of 1+ or more. Body mass index (BMI) is calculated as weight (kg) divided by the square of height (m). Computer-based data were available from April 1, 1993 through March 31, 1994 ($n = 143{,}948$) for the 1993 screening.

Participants

For the purposes of the present study, we examined OGHMA 1993 screenees who had both serum creatinine (SCr) and hematocrit data ($N = 94{,}602$; 54,848 women and 39,754 men). SCr was measured using a modified Jaffe's reaction in an autoanalyzer at the OGHMA laboratory.

Assessment of kidney function

Kidney function was evaluated by eGFR, which was calculated using the new Japanese equation: eGFR (ml/min per 1.73 m^2) = 194 × serum creatinine$^{1.094}$ × age$^{0.287}$ × 0.739 (if female) [18]. For calculating eGFR, we applied the value of SCr in enzymatic methods, which was calculated by the following equation: SCr (enzyme) = (SCr (Jaffe) − 0.194)/1.079 [19].

Definition of anemia, clinical data, and analysis

Anemia was defined according to the Japanese Society for Dialysis Therapy (JSDT) guidelines and the kidney disease outcomes quality initiative (K/DOQI) guidelines, which take both age and sex into account: men, <40%; women aged <50 years, <32%; and women aged ≥50 years, <35% [20, 21]. Diabetes mellitus (DM) was diagnosed when fasting plasma glucose levels were >126 mg/dl. Subjects who were already on chronic dialysis were excluded from the screening registry. To analyze the effect of kidney function on the prevalence and risk of anemia, subjects were divided into following six groups: less than 15 ml/min per 1.73 m^2, from 15 to 29 ml/min per 1.73 m^2, from 30 to 44 ml/min per 1.73 m^2, from 45 to 59 ml/min per 1.73 m^2, from 60 to 90 ml/min per 1.73 m^2, and more than 90 ml/min per 1.73 m^2.

According to the recently published JSDT Guideline for Renal Anemia in Chronic Kidney Disease, anemia was defined as <35% in women [22]. We also analyzed using this definition in women.

Statistics

Statistical significance of differences in characteristics across participants was examined using the t test (continuous variables), and the Wald chi-square test (categorical variables) was carried out. We compared values of hematocrit and prevalence of anemia between the different levels of clinical variables such as BMI, age, and eGFR by Scheffé's multiple comparison methods after analysis of variance (ANOVA). Multiple logistic analysis was done to examine the correlates of anemia by variables such as eGFR category, sex, older age (>70 years), and BMI category. Data are expressed as mean (standard deviation, SD). A P value of less than 0.05 was considered statistically significant.

Results

OGHMA population

Of total of 143,948 OGHMA subjects, 94,602 (65.7%: 54,848 women and 39,754 men) had measurements of both SCr and hematocrit levels. The clinical characteristics of the screened subjects according to gender are summarized in

Table 1 Characteristics of screened subjects in 1993 in Okinawa, Japan

Variable	All (N = 94,602)	Men (N = 39,754)	Women (N = 54,848)	P value
Age (years)	54.7 ± 15.3	53.5 ± 15.7	55.6 ± 14.9	<0.0001
BMI (kg/m^2)	24.0 ± 3.4	24.1 ± 3.2	23.9 ± 3.5	<0.0001
SBP (mmHg)	127.4 ± 17.7	129.4 ± 16.8	126.0 ± 18.1	<0.0001
DBP (mmHg)	76.6 ± 10.5	78.6 ± 10.4	75.1 ± 10.3	<0.0001
Urine protein (%)	3504 (3.8)	1774 (4.5)	1730 (3.3)	<0.0001
Hematocrit (%)	41.4 ± 4.1	44.5 ± 3.3	39.2 ± 3.0	<0.0001
Estimated GFR (ml/min per 1.73 m^2)	79.3 ± 20.1	79.8 ± 18.6	78.9 ± 21.1	<0.0001
Anemia (%)	5450 (5.8)	3056 (7.7)	2399 (4.4)	<0.0001
Serum creatinine (mg/dl)	0.98 ± 0.21	1.10 ± 0.20	0.89 ± 0.17	<0.0001
Diabetes (FPG ≥ 126 mg/dl)	3103 (4.8)	1711 (6)	1392 (3.8)	<0.0001
Hypertension	28312 (30.0)	13309 (33.6)	15003 (27.4)	<0.0001
Age (years)				
20–29	5423 (5.7)	2773 (7.0)	2650 (4.8)	
30–39	11802 (12.5)	5746 (14.5)	6056 (11.0)	
40–49	17612 (18.6)	7723 (19.4)	9889 (18.0)	
50–59	19996 (21.1)	7684 (19.3)	12312 (22.4)	
60–69	22446 (23.7)	9035 (22.7)	13411 (24.5)	
≥70	17323 (18.3)	6793 (18.3)	10530 (19.2)	
Estimated GFR (ml/min per 1.73 m^2)				
≥90	25258 (26.7)	10709 (26.9)	14549 (26.5)	
60–89	54042 (57.1)	24100 (60.6)	29942 (54.1)	
45–59	13287 (14.0)	4360 (11.0)	8927 (16.3)	
30–44	1829 (1.9)	524 (1.3)	1305 (2.4)	
15–29	151 (0.2)	47 (0.1)	104 (0.2)	
<15	35 (0.04)	14 (0.04)	21 (0.04)	

SBP systolic blood pressure, *DBP* diastolic blood pressure, *FPG* fasting plasma glucose

Table 1. The prevalence of subjects aged 60 years or older was approximately 40%, which included about 20% of subjects 70 years or older (both genders). Male subjects were younger overall, but had a higher prevalence of diabetes, hypertension, and proteinuria than did female subjects. The prevalence of eGFR less than 60 ml/min per 1.73 m^2 was about 16%. The distribution of eGFR according to gender is shown in Fig. 1. As expected, the prevalence of anemia in women increased from 4.4% to 7.3% when the JSDT anemia criteria were applied; consequently the overall prevalence was 7.4% in overall subjects.

Relationship between kidney function and hematocrit

Table 2 shows the mean hematocrit levels and prevalence of anemia according to BMI category, age category, and eGFR category for men and women. The lower the BMI category or the higher the age category, the lower the mean hematocrit level and the greater the prevalence of anemia. At age 70 years, the prevalence of anemia was clearly high. The mean hematocrit levels decreased and the prevalence of anemia increased as kidney function decreased below an

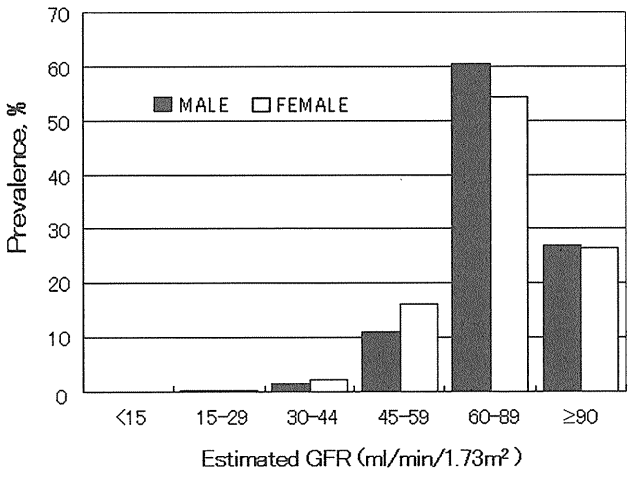

Fig. 1 Distribution of the estimated glomerular filtration rate in the cohort

eGFR of 60 ml/min per 1.73 m^2 among both men and women. In women, prevalence of anemia was 4.7% (age 20–29 years), 12.4% (age 30–39 years), 14% (age 40–49 years), 10.5% (eGFR ≥90 ml/min per 1.73 m^2), 5.7%