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Original Article

Fasting sugar, blood pressure, and uric acid are factors related to positive proteinuria and an impaired eGFR

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Abstract

Background: The aim of this study was to ascertain the relationships of blood pressure, fasting sugar level, triglyceride (TG) level, uric acid level, and body mass index (BMI) with proteinuria and the estimated glomerular filtration rate (eGFR) in a population from southern Taiwan.
Methods: The 20,900 subjects enrolled in this study had undergone a free adult health examination under the National Health Insurance scheme between September 2005 and June 2011. Factors such as blood pressure, blood sugar, TG, uric acid and BMI were examined in terms of their relationships with the eGFR (calculated according to the Taiwanese Modification of Diet in Renal Disease (Taiwanese-MDRD)) and proteinuria. The Chi-square test, Student's t-test or the Mann–Whitney U-test, and multivariate logistic regression analysis were employed.
Results: The prevalence of chronic kidney disease (CKD) was 66.7%. Multivariate logistic analysis showed that fasting sugar (OR = 1.12 and 1.65), blood pressure (OR = 1.09 and 1.12), and triglyceride levels (OR = 1.40 and 1.38) were factors related to positive proteinuria and an impaired eGFR.
Conclusion: CKD is prevalent in the southern Taiwanese population aged over 40 years, and we believe that controlling related risk factors could be an important method by which to prevent progression of CKD.

Keywords: Blood pressure; Chronic kidney disease; Fasting sugar; Uric acid

1. Introduction

Taiwan has gradually entered into an era of an aging society, as is also the case in some other developed countries,[1] and the prevalences of chronic diseases such as chronic kidney disease (CKD), etc., are also gradually increasing, notably in aging populations.[2] In addition, because diseases related to metabolic syndrome (MS)[3] and obesity or a higher body mass index (BMI) are becoming very important public health issues,

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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these conditions are gradually being subjected to increasing attention in the elderly population in Taiwan.

Some components of MS[3−5] have been reported to be related to CKD,[6,7] and the possibility of patients with MS developing kidney disease is related to insulin resistance. Obesity was observed to be linked to CKD in non-diabetic, non-hypertensive adults in a Korean study.[8] On the other hand, previous studies have reported that the uric acid level is related to CKD, and the role of uric acid in CKD is gradually being considered to be greater and highly important.[9−11] The uric acid level has also been shown to be related to the renin−angiotensin system and insulin resistance, two mechanisms that may be related to kidney damage.[10]

Taiwan is a developed country with very a high coverage rate of the National Health Insurance (NHI) system, which commenced in 1995. Adults aged above 40 years are eligible for a free adult health examination provided by the NHI. Due to some components of MS, obesity and uric acid level being known to be related to some chronic diseases, we aimed to reveal whether some components of MS, such as blood pressure, blood sugar, triglyceride (TG) and uric acid levels, as well as BMI, are associated with proteinuria and the estimated glomerular filtration rate (eGFR, calculated according to the Taiwanese Modification of Diet in Renal Disease (Taiwanese-MDRD)) in adults in southern Taiwan based on data obtained during adult health examinations provided by the Bureau of National Health Insurance (BNHI).

2. Methods

2.1. Subjects

Taiwanese adults who had undergone an examination under the health examination service of the BNHI from September, 2005 to June, 2011 were retrospectively enrolled from the database of the Department of Preventive Medicine of Kaohsiung Municipal Hsiao-Kang Hospital. All of the subjects lived in Kaohsiung City. Under the regulations of the BNHI from 1996 to June 2011, Taiwanese adults aged between 40 and 64 years were eligible to undergo this examination every 3 years, and those aged 65 and above could receive this examination every year. The procedure of the examination included taking a medical history, conducting a physical examination, taking a complete blood cell count, measuring fasting sugar, TG, blood urea nitrogen (BUN)/creatinine, and albumin/globulin levels, as well as a standard examination of urine.

The data collected via this examination included age, gender, height, weight, and past medical history, such as history of diabetes mellitus, hypertension, etc. A history of diabetes mellitus (DM) was noted in those who had taken oral hypoglycemic agents (OHAs) or undergone insulin therapy to control blood sugar, and a history of hypertension was defined in subjects who were taking anti-hypertension drugs to control blood pressure. Subjects with severe systemic diseases such as end-stage renal disease with dialysis, congestive heart failure controlled with drugs (such as diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor blocker, beta adrenergic antagonist, etc.), severe hepatic or decompensated liver disease; those with historical records of chronic hepatitis B (CHB) or chronic hepatitis C (CHC), or who took hepatotoxicity or nephrotoxicity medication; and those with historical records of leukemia/lymphoma or any other hematologic disease were excluded from this study, because these conditions and the therapies for these diseases are associated with renal dysfunction, and could result in misleading analyses in this study. Additionally, if subjects had undergone two or more health examinations under the BNHI service during the period of enrollment, only the data from the first examination were included in the analysis. Subjects whose data were incomplete were also excluded from this study. Finally, 20,900 subjects in total were enrolled from 22,156 subjects in the database. This study was approved by the Institutional Review Board of Kaohsiung Municipal Hsiao-Kang Hospital.

2.2. Data collection

Fasting sugar, cholesterol, TG, and uric acid levels were measured after fasting for at least 12 h, and height and weight measurements were recorded for all subjects upon examination. All these data were included for analysis in this study. Urine standard analysis was performed within 4 h of registration, and blood samples were sent for testing within 4 h. BMI was calculated as weight/(height)^2 (kg/m^2). Blood pressure was measured in a sitting position, and no medicine was taken during the fasting period. The threshold values used in this study were as follows: systolic blood pressure (SBP) and diastolic blood pressure (DBP),[12] 120/80 mmHg; fasting sugar,[2] 100 mg/dL; TG,[4] 150 mg/dL; uric acid,[13] 7 mg/dL for males and 6 mg/dL for females; serum creatinine, 1.5 mg/dL for males and 1.2 mg/dL for females; urine protein, negative. According to the Steering Committee of the Regional Office for the Western Pacific Region of the World Health Organization (WPRO), the Asian standards for BMI (kg/m^2) were as follows[14]: underweight <18.5; normal 18.5−22.9; overweight 23−24.9; obese stage I 25−29.9; and obese stage II $\geq$ 30.

2.3. Estimated glomerular filtration rate (eGFR)

In this study, we used the eGFR calculated according to the Taiwanese Modification of Diet in Renal Disease (MDRD) equation: $1.309 \times \text{MDRD}^{0.912}$ (MDRD equation: $175 \times \text{SCr}^{-1.154} \times \text{Age}^{-0.203} \times 0.742$ (if female)), which is most suitable for Taiwanese subjects.[15]

We classified groups with differing eGFRs according to CKD stage, which was determined by the glomerular filtration rate and proteinuria based on the Kidney Disease Outcomes Quality Initiative (K/DOQI) definition: CKD stage 1 included participants with an eGFR $\geq$ 90 mL/min/1.73 m^2 with kidney damage (proteinuria); stage 2 was defined as an eGFR of 60−89 mL/min/1.73 m^2 with proteinuria; stage 3 as an eGFR of 30−59 mL/min/1.73 m^2 (including stage 3a as an eGFR of 45−59 mL/min/1.73 m^2 and 3b as an eGFR of 30−44 mL/min/1.73 m^2); stage 4 as an eGFR of 15−29 mL/min/1.73 m^2;

and stage 5 as an eGFR <15 mL/min/1.73 m^2.[16] The definition of positive proteinuria was one or more positive reactions by dipstick testing; if proteinuria was present as a trace reaction, the subject was classified as negative for proteinuria.

2.4. Statistical analysis

The Chi-square test with Yates's correction or Fisher's exact test was used to compare frequency between two groups, and Student's t-test or the Mann−Whitney U-test was used to compare group means. All tests were two-sided, and the significance levels were set at $\alpha = 0.05$. Multivariate logistic regression analysis was used to evaluate the odds ratios (ORs) and 95% confidence intervals for an eGFR < 60 mL/min/1.73 m^2 and positive proteinuria. Analyses were performed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA).

3. Results

In total, 20,900 subjects were enrolled in this study, including 8841 (42.3%) males and 12,059 (57.7%) females. Due to the regulations of the adult health examination service under the National Health Insurance, the average age of those enrolled in this study was above 45 years, with a mean age of 56.91 ± 10.73 years (males, 58.01 ± 11.13; females, 56.03 ± 10.34, $p < 0.001$). The basic characteristics of all subjects are presented in Table 1. The prevalences of hypertension and diabetes mellitus were 25.7% and 8.9%, respectively, and the rates of abnormal measurements of blood pressure, BMI, fasting sugar, TG, uric acid (male/female) and serum creatinine levels, and urine protein were 68.9%, 66.0%, 37.5%, 28.5%, 29.1% (36.4%/23.7%), 3.5% and 13.0%, respectively. Significant gender differences were identified for all factors. The average eGFR of all subjects was 57.47 ± 9.75 mL/min/1.73 m^2, and there were differences between groups with different eGFRs according to gender ($p = 0.001$). The average eGFR was slightly higher in the male subjects than in the female subjects, but no significant difference was noted ($p = 0.69$). The prevalence of CKD in this study cohort was 66.7%, and we observed that CKD was more prevalent in the female subjects than in the male subjects (65.6% vs. 67.5%, $p < 0.001$). In addition, CKD stage 3a was

Table 1
Basic characteristics of the 20,900 subjects enrolled in the study.

	All subjects	Male	Female	*p*
Case number, *n* (%)	20,900 (100.0)	8841 (42.3)	12,059 (57.7)	
Mean age[g], years	56.91 ± 10.73	58.01 ± 11.13	56.03 ± 10.34	**<0.001**
History of DM, *n* (%)	1866 (8.9)	970 (11.0)	896 (7.4)	**<0.001**
History of hypertension, *n* (%)	5365 (25.7)	2560 (29.0)	2805 (23.3)	**<0.001**
Mean blood pressure (BP)				
Systolic BP[g]	129.54 ± 18.84	130.50 ± 17.59	128.83 ± 18.84	**<0.001**
Diastolic BP[g]	78.77 ± 11.55	80.12 ± 11.55	77.86 ± 11.46	**<0.001**
Blood pressure ≥ 120/80 mmHg, *n* (%)	14,404 (68.9)	6384 (72.2)	8020 (66.5)	**<0.001**
Mean BMI[g]	24.68 ± 3.64	25.13 ± 3.42	24.35 ± 3.77	**<0.001**
BMI ≥ 23 kg/m^2, *n* (%)	13,800 (66.0)	6515 (73.7)	7285 (60.4)	**<0.001**
Fasting glucose ≥ 100 mg/dL, *n* (%)	7467 (35.7)	3737 (42.0)	3750 (31.1)	**<0.001**
Triglyceride ≥150 mg/dl, *n* (%)	5959 (28.5)	3095 (35.0)	2864 (23.7)	**<0.001**
Abnormal uric acid[a]	6073 (29.1)[a]	3220 (36.4)[b]	2853 (23.7)[c]	**<0.001**
Abnormal serum creatinine[d]	737 (3.5)[d]	605 (6.8)[e]	132 (1.1)[f]	**<0.001**
Positive urine protein	2707 (13.0)	1408 (15.9)	1299 (10.8)	**<0.001**
eGFR (mL/min/1.73 m^2)[g]	57.47 ± 9.75	57.50 ± 9.78	57.45 ± 9.72	0.69
≥ 90, *n* (%)	76 (0.4)	30 (0.3)	46 (0.4)	**0.001**
60−89, *n* (%)	7614 (36.4)	3354 (37.9)	4260 (35.3)	
30−59, *n* (%)	12,977 (62.1)	5351 (60.5)	7626 (63.2)	
15−29, *n* (%)	190 (0.9)	89 (1.0)	101 (0.8)	
<15, *n* (%)	43 (0.2)	17 (0.2)	26 (0.2)	
CKD, *n* (%)	13,938 (66.7)	5803 (65.6)	8135 (67.5)	**0.03**
Stage 1	8 (0.1)	7 (0.1)	1 (0.0)	**<0.001**
Stage 2	725 (5.2)	407 (7.0)	318 (3.9)	
Stage 3a	11,655 (83.6)	4629 (79.8)	7026 (86.4)	
Stage 3b	1317 (9.4)	639 (11.0)	678 (8.3)	
Stage 4	190 (1.4)	104 (1.8)	86 (1.1)	
Stage 5	43 (0.3)	17 (0.3)	26 (0.3)	

DM: diabetes mellitus; BP: blood pressure; eGFR: estimated glomerular filtration rate, as measured using the Taiwanese-MDRD (Taiwanese modification of diet in renal disease); BMI: body mass index; CKD: chronic kidney disease.
Bold represents $p < 0.05$.
[a] Male ≥7 mg/dL, female ≥6 mg/dL.
[b] Male ≥7 mg/dL.
[c] Female ≥6 mg/dL.
[d] Male >1.5 mg/dL, female >1.2 mg/dL.
[e] Male >1.5 mg/dL.
[f] Female >1.2 mg/dL.
[g] Mean ± standard deviation.

most prevalent in this study (83.6%) in all subjects, and was more prevalent in the female subjects than in the male subjects (79.8% vs. 86.4%) (Table 1).

The percentage of patients with CKD gradually decreased year on year from 2005 to 2011 (Fig. 1), from 76.3% in 2005 to 62.9% in 2011. In addition, the trend test for the percentage of subjects with CKD analyzed by year showed a significant difference ($p < 0.01$).

We also conducted comparisons of some items between the group with an eGFR ≥60 mL/min/1.73 m^2 and the group with an eGFR <60 mL/min/1.73 m^2. With the exception of the mean fasting sugar and mean TG levels, the other items differed significantly between the two groups ($p < 0.05$) (Table 2). According to multivariate logistic analysis, fasting sugar ≥100 mg/dL (OR = 1.12, 95% CI = 1.40−1.27), an abnormal blood pressure level (OR = 1.09, 95% CI = 1.02−1.16), and an abnormal uric acid level (OR = 1.40, 95% CI = 1.31−1.50) were significant factors associated with positive urine protein ($p < 0.05$) (Table 2).

The results of analyses of the urine protein level are shown in Table 3. With the exception of gender, all other items were found to be significantly related to a positive urine protein measurement. According to multivariate logistic analysis, fasting sugar ≥100 mg/dL (OR = 1.65, 95% CI = 1.51−1.79), an abnormal blood pressure level (OR = 1.12, 95% CI = 1.02−1.23), TG ≥ 150 mg/dL (OR = 1.47, 95% CI = 1.35−1.61), BMI ≥ 23 kg/m^2 (OR = 1.23, 95% CI = 1.12−1.36) and an abnormal uric acid level (OR = 1.38, 95% CI = 1.26−1.05) were significant factors associated with positive urine protein ($p < 0.05$). In addition, an abnormal serum creatinine level and an eGFR <60 mL/min/1.73 m^2 were associated with positive proteinuria.

Finally, we analyzed the risk factors in patients with CKD at stages 3a, 3b, 4 and 5 (Table 4). Uric acid was a risk factor in patients with CKD stage 3a, 3b, 4 and 5; blood pressure was a risk factor in CKD stage 3a and 3b; and fasting sugar was a risk factor in CKD stage 3b and 5. In addition, the OR gradually increased with the severity of CKD.

4. Discussion

Our study demonstrated that the prevalence rates of a history of hypertension and DM were higher than those reported previously (17.9% and 5.6%) by Huang et al.[17] Furthermore, the results of this study also indicated higher rates of abnormal blood pressure and fasting sugar, TG, uric acid and serum creatinine levels than reported in two previous studies.[17,18] According to data reported by the Ministry of the Interior, Taiwan, R.O.C., the percentage of people over 40 years of age is gradually increasing (from 36.3% in 2000 to 49.0% in 2014).[19] This may be a cause of the findings discussed above, in that the gradually aging society in Taiwan has resulted in gradually increasing rates of abnormal measurements, as shown in this study.

An extreme rate of eGFR decline has been identified in black populations relative to Asians, Caucasians and Hispanics.[20] In addition, white men with CKD have been reported to have a higher mortality.[20,21] Therefore, race is one of the major factors affecting eGFR decline and progression of CKD. In the present study of subjects living in Taiwan, we did not identify those who were Taiwanese aboriginals, which prevented us from exploring whether differences existed between Taiwanese subjects and other races. This issue will be examined in the future.

Wen et al.[22] reported that the prevalence of CKD among 462,293 Taiwanese subjects aged over 20 years who participated in a standard medical screening program was 12%, while in a study of a population from central Taiwan, Lee et al.[23] reported a prevalence of 17.1%. According to this study, the prevalence of CKD was 66.7%, with a significantly

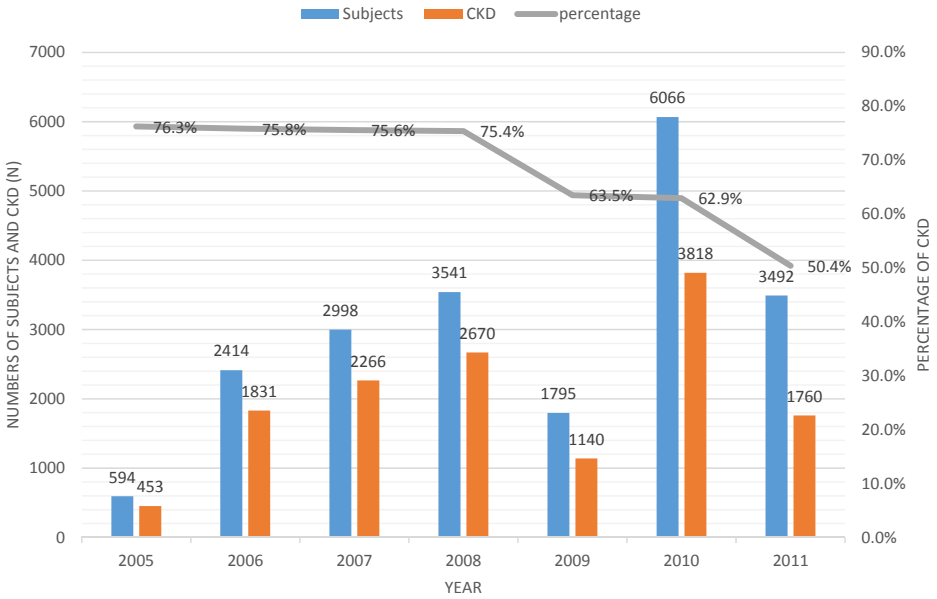

Fig. 1. Percentage of subjects with chronic kidney disease (CKD) from 2005 to 2011. Percentage of subjects with CKD gradually decreased year on year; trend test for percentage of subjects with CKD by year: $p < 0.01$.

Table 2
Univariate and multivariate analysis of the eGFR level using a cut-off point of 60 mL/min/1.73 m^2.

	Univariate analysis			*Multivariate analysis*		
	eGFR ≥60 mL/min/1.73 m^2	eGFR <60 mL/min/1.73 m^2	*p*	Odds ratio	95% Confidence interval	*p*
Case number, *n* (%)	7690 (36.8)	13,210 (63.2)				
Mean age[a], years	55.42 ± 10.35	57.77 ± 10.85	**<0.001**			
Male, *n* (%)	3384 (44.0)	5457 (41.3)	**<0.001**			
Mean fasting sugar[a]	102.35 ± 31.61	102.93 ± 31.90	0.20			
Fasting sugar ≥ 100 mg/dL, *n* (%)	2648 (34.4)	4819 (36.5)	**0.003**	1.12	1.04−1.27	**0.007**
History of DM, *n* (%)	671 (8.0)	1249 (9.5)	**<0.001**			
Mean blood pressure (BP)						
Systolic BP[a]	128.68 ± 17.83	130.05 ± 18.58	**<0.001**	1.09	1.02−1.16	**0.008**
Diastolic BP[a]	78.49 ± 11.37	79.93 ± 11.64	**0.009**			
Systolic/diastolic blood pressure ≥ 120 or 80 mmHg, *n* (%)	5170 (67.2)	9234 (69.9)	**<0.001**			
History of hypertension, *n* (%)	1730 (22.5)	3635 (27.5)	**<0.001**			
Mean triglyceride[a]	133.18 ± 122.17	134.46 ± 102.70	0.41			
Triglyceride ≥ 150 mg/dL, *n* (%)	2099 (27.3)	3860 (29.2)	**0.003**	1.01	0.95−1.08	0.755
Mean BMI[a]	24.55 ± 3.65	24.76 ± 3.64	**<0.001**			
BMI ≥ 23 kg/m^2, *n* (%)	4952 (64.4)	8848 (67.0)	**<0.001**	1.03	0.97−1.10	0.342
Uric acid[a]	5.60 ± 1.56	5.85 ± 1.60	**<0.001**	1.40	1.31−1.50	**<0.001**
Male ≥ 7 mg/dL, *n* (%)	1125 (33.2)	2095 (38.4)	**<0.001**			
Female ≥ 6 mg/dL, *n* (%)	759 (17.6)	2094 (27.0)	**<0.001**			

BMI: body mass index; eGFR: estimated glomerular filtration rate, as measured using the Taiwanese-MDRD (Taiwanese Modification of Diet in Renal Disease); DM: diabetes mellitus; BP: blood pressure.
Comparison of factors: age: BMI: <23 kg/m2 = 0, ≥23 kg/m^2 = 1; fasting sugar: <100 mg/dL = 0, ≥100 mg/dL = 1; triglyceride: <150 mg/dL = 0, ≥150 mg/dL = 1; uric acid: male <7 mg/dL/female <6 mg/dL = 0, male ≥7 mg/dl/female ≥6 mg/dL = 1; blood pressure: blood pressure <120/80 mmHg = 0, else = 1. Bold represents $p < 0.05$.
[a] Mean ± standard deviation.

higher prevalence in female than in male subjects, and a lower average eGFR value and a younger age were present as compared with the results of a previous study performed in central Taiwan (57.54 ± 9.75 vs. 78.6 ± 21.3 mL/min/1.73 m^2; 56.91 ± 10.73 vs. 64.0 ± 11.4 years).[23] These results showed that the prevalence of CKD is higher in southern Taiwan, which implied that this condition might be an important public health issue in that region. The prevalence of CKD in this study was higher than that reported in previous Taiwanese studies,[17,18] possibly due to the higher prevalence of hypertension and DM, and the fact that the subjects included in the study were 40 years of age and above, being only those who were eligible to participate in free health examinations provided by the NHI. Furthermore, other factors such as subjects' education level, socioeconomic level, etc., have been suggested to be related to CKD[22]; these factors were not recorded during health examinations, and were therefore not able to be analyzed in this study. Further research should be conducted in the future to address this issue.

Lee et al.[23] also reported that the MDRD value was significantly higher in males. The results of this study, which used the Taiwanese-MDRD formula to calculate the eGFR, showed that a greater proportion of female subjects had an eGFR <60 mL/min/1.73 m^2, and the female subjects had a lower average eGFR value than the male subjects. As in this study all subjects were above the age of 40, these results were considered reasonable. In addition, a number of risk factors, including blood pressure, fasting sugar and uric acid levels, were significantly different between the group with an eGFR <60 mL/min/1.73 m^2 and that with an eGFR of ≥60 mL/min/1.73 m^2, and almost all factors exhibited higher proportions of abnormal percentages in the group with an eGFR <60 mL/min/1.73 m^2. Therefore, we concluded that a cut-off value for the eGFR of 60 mL/min/1.73 m^2 could be a suitable indicator of CKD, despite the formula for CKD being different.

Hyperglycemia can induce direct mesangial expansion, perhaps via increased matrix production or glycosylation of matrix proteins, after which thickening of the glomerular basement membrane (GBM) occurs, which can result in glomerular sclerosis caused by intraglomerular hypertension.[24] These pathological mechanisms can lead to decreases in the GFR and proteinuria. Previous studies found that the blood sugar level is related to CKD[25] and proteinuria,[26,27] and oxidative stress has been identified as a possible cause.[28] In addition, many conditions are related to proteinuria, such as hypertension, DM, and an abnormal uric acid level.[29] In this study, multivariate analysis showed that the fasting sugar level was related to positive proteinuria and an impaired eGFR, which was in concordance with the findings of previous studies.

Hypertension can lead to hyaline arteriolosclerosis. Arterial hypertension leads to hyaline accumulation in the walls of small arteries and arterioles, which thickens the walls and narrows the lumina. The damage to glomeruli caused by hyaline arteriolosclerosis results in impaired glomerular filtration and an increase in protein filtration.[30,31] Previous studies found that hypertension is related to CKD,[32] and similarly, we found that blood pressure was related to positive proteinuria and an impaired eGFR in this study. This result supports the hypothesis that controlling blood pressure can decrease damage to renal function.

Table 3
Univariate and multivariate analysis of urine protein.

	Univariate analysis			*Multivariate analysis*		
	Negative	Positive	*p*	Odds ratio	95% Confidence interval	*p*
Case number, *n* (%)	18,193 (87.0)	2707 (13.0)				
Mean age[a], years	56.90 ± 10.76	56.96 ± 10.54	0.80			
Male, *n* (%)	7433 (40.9)	1408 (52.0)	**<0.001**			
Mean fasting sugar[a]	100.59 ± 27.21	117.06 ± 50.91	**<0.001**			
Fasting sugar ≥ 100 mg/dL, *n* (%)	6150 (33.8)	1317 (48.7)	**<0.001**	1.65	1.51−1.79	**<0.001**
History of DM, *n* (%)	1399 (7.7)	467 (17.3)	**<0.001**			
Mean blood pressure (BP)						
Systolic BP[a]	129.02 ± 17.96	133.00 ± 20.33	**<0.003**			
Diastolic BP[a]	78.41 ± 11.34	81.18 ± 12.60	**<0.001**			
Systolic/diastolic blood pressure ≥ 120 or 80 mmHg, *n* (%)	12,407 (68.2)	1997 (73.8)	**<0.001**	1.12	1.02−1.23	**0.017**
History of hypertension, *n* (%)	4348 (23.9)	1017 (37.6)	**<0.001**			
Mean triglyceride[a]	129.15 ± 96.13	166.51 ± 174.82	**<0.001**[b]			
Triglyceride ≥ 150 mg/dL, *n* (%)	4895 (26.9)	1064 (39.3)	**<0.001**	1.47	1.35−1.61	**<0.001**
Mean BMI[a]	24.52 ± 3.55	25.71 ± 4.05	**<0.001**			
BMI ≥ 23 kg/m^2, *n* (%)	11,791 (64.8)	2009 (74.3)	**<0.001**	1.23	1.12−1.36	**<0.001**
Uric acid[a]	5.69 ± 1.56	6.19 ± 1.76	**<0.001**			
Male ≥ 7 mg/dL, *n* (%)	2642 (35.5)	578 (41.1)	**<0.001**	1.38	1.26−1.51	**<0.001**
Female ≥ 6 mg/dL, *n* (%)	2385 (22.2)	468 (36.0)	**<0.001**			
Serum creatinine	1.05 ± 0.25	1.24 ± 0.63	**<0.001**			
Male > 1.5 mg/dl	383 (5.2)	132 (9.4)	**<0.001**			
Female > 1.2 mg/dl	413 (3.8)	109 (8.4)	**<0.001**			
eGFR	69.72 ± 13.24	63.21 ± 16.41	**<0.001**			
< 60 mL/min/1.73 m^2	3782 (20.8)	972 (35.9)	**<0.001**			

DM: diabetes mellitus; BP: blood pressure; eGFR: estimated glomerular filtration rate, as measured using the Taiwanese-MDRD (Taiwanese Modification of Diet in Renal Disease); BMI: body mass index.
Comparison of factors: age: BMI: <23 kg/m2 = 0, ≥23 kg/m2 = 1; fasting sugar: <100 mg/dL = 0, ≥100 mg/dL = 1; triglyceride:<150 mg/dL = 0, ≥150 mg/dL = 1; uric acid: male <7 mg/dL/female <6 mg/dL = 0, male ≥7 mg/dl/female ≥6 mg/dL = 1; blood pressure: blood pressure <120/80 mmHg = 0, else = 1. Bold represents $p < 0.05$.
[a] Mean ± standard deviation.
[b] Mann−Whitney test.

Uric acid has also been found to be related to the renin−angiotensin system and insulin resistance,[10] and the oxidant/anti-oxidant capacities of uric acid and other metabolites have been reported to be relevant to impaired renal function.[33] Previous studies have also reported that the uric acid level is correlated with a decreasing GFR[34] and positive proteinuria,[35−37] and is even an indicator of CKD.[35−37] In this study, uric acid level was a factor related to an impaired eGFR. In addition, the uric acid level was also found to be significantly related to positive proteinuria in this study. Our results were therefore in accordance with those of previous studies, and implied that the uric acid level is a vital indicator of CKD in Taiwanese subjects.

Table 4
Multivariate analysis of risk factors related to CKD stages 3a, 3b, 4 and 5.

Factor	Odds ratio	95% Confidence interval	*p*
Risk factors of CKD stage 3a			
Blood pressure	1.068	1.003−1.137	0.039
Uric acid	1.297	1.212−1.389	<0.001
Risk factors of CKD stage 3b			
Blood pressure	1.268	1.10−1.455	0.001
Fasting sugar	1.846	1.547−2.202	<0.001
Uric acid	2.330	2.054−2.643	<0.001
Risk factors of CKD stage 4			
Uric acid	2.520	1.858−3.419	<0.001
Risk factors of CKD stage 5			
Fasting sugar	3.016	1.426−6.383	0.004
Uric acid	3.951	2.095−7.453	<0.001

Comparison of factors: age: fasting sugar: <100 mg/dL = 0, ≥100 mg/dL = 1; uric acid: male <7 mg/dL/female <6 mg/dL = 0, male ≥7 mg/dl/female ≥6 mg/dL = 1; blood pressure: blood pressure <120/80 mmHg = 0, else = 1.

An increased BMI and decreased renal function are likely to be associated with risk factors such as low-grade inflammation, oxidative stress, hyperlipidemia, increased sympathetic activity, hyperfiltration caused by insulin resistance, the renin−angiotensin system, and elevated cytokine levels. All these risk factors can result in atherosclerosis.[38] Previous studies have reported that the eGFR is likely to be affected by BMI[39−41]; however, in this study, BMI was not related to impairment of the eGFR, and was related only to positive proteinuria. In addition, the TG level was also unrelated to impairment of the eGFR, and was related only to positive proteinuria in this study. Previous studies have shown that dyslipidemia with inflammation might decrease renal function,[42] and it has been reported that a high TG level predicts a risk of development of proteinuria in both male and female subjects.[43] One study reported that the TG level is associated with a moderate decline in the eGFR,[44] which implied that the TG level might also be an indicator of risk of CKD. Therefore, we believe that BMI and TG are not risk factors related to

impairment of eGFR, but the ORs were greater than 1, and therefore controlling BMI and the TG level to within the reference ranges might be a method by which to prevent progression of CKD, especially in subjects older than 40.

We also analyzed the risk factors related to different CKD stages (3a, 3b, 4, 5). Uric acid level was a risk factor related to all stages of CKD, and blood fasting were also risk factors related to various stages of CKD (3a, 3b, 5). These three risk factors were all found to be related to CKD stage 3b, and we believe that controlling these factors is very important during this stage of CKD in order to prevent progression of impairment of the eGFR.

A limitation of this study was that the results only reflected populations of subjects aged 40 or above who were eligible to undergo a free BHI health examination. As a result, the researchers were unable to ascertain the status of populations under 40 years of age, due to which selection bias might be the reason for the high prevalence of CKD in this study. Moreover, the data obtained during health examinations under the BNHI did not include HDL, and consequently the researchers were unable to analyze the association of CKD with MS.

In conclusion, according to the findings of this study, CKD is prevalent in southern Taiwan, a fact that indicates that prevention of CKD and decreasing the rate of progression of CKD are important public health issues. Blood pressure, fasting sugar and uric acid levels were found to be risk factors of impairment of the eGFR and positive proteinuria, and as the population is gradually aging, the proportion of subjects with abnormal measurements of these factors is also increasing, resulting in impairment of function of human organs among older Taiwanese residents, including CKD. Therefore, from the results of our study, we believe that controlling blood pressure, fasting sugar and uric acid levels could be an important method by which to decrease the progression of CKD in Taiwan, in turn reducing medical expenditure and the burden of management of CKD.

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