

Long-term Trends and Influencing Factors of Glomerular Filtration Rate

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Abstract

Purpose: This study assessed chronic kidney disease (CKD) in Pingtung, Taiwan as indicated by the annual changes glomerular filtration rate (GFR) and risk factors of estimated glomerular filtration rate (eGFR).

Methods: This study utilized longitudinal data analysis to examine the 2011-2013 medical checkup results for adult at a Pingtung hospital. The participants' general information, physical examination results, and blood test results were analyzed. eGFR was calculated via the abbreviated modification of diet in renal disease (aMDRD) formula and used to determine eGFR stages based on the 2002 Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines.

Results: Data from a total of 9,702 participants were analyzed in this study. This study indicated that in Pingtung, from 2011 to 2013, male, aged ≥ 65 years and those who have metabolic syndrome and its components are abnormal have lower eGFR. Multiple linear regression analysis was applied to examine the risk factors influencing eGFR. The results showed lower eGFR in males, participants aged 65 and over, participants with metabolic syndrome, blood pressure, waist

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circumference, and triglyceride level abnormalities.

Conclusion: Predictors of eGFR decline included male gender, age of 65 years and over, metabolic syndrome, and abnormal blood pressure, waist circumference, and triglyceride levels.

Keywords: Chronic kidney disease, aMDRD formula, glomerular filtration rate, metabolic syndrome

1 Introduction

The improvements in medical care and living standards and changes in diet and lifestyle have resulted in growing incidence and prevalence rates for chronic kidney disease (CKD) and end stage renal disease (ESRD). Mortality rates in people with CKD have increased [1] and so have medical care burden and expenditures. Therefore, CKD prevention and cure has become an important issue in public health worldwide. Kidney diseases, such as nephritis, nephrotic syndrome, and nephropathy, were the tenth leading cause of death in Taiwan in 2012 and have been among the top ten leading causes of death in Taiwan for over a decade [2]. Due to the improvements in health care in Taiwan, many older adults and those with chronic diseases do not die from cardiovascular complications during the beginning stages of CKD. However, survivors suffer from impaired kidney function and require dialysis or transplantation. The number of dialysis patients increases by approximately 6% each year, indicating a decline in health in Taiwan and increasing annual insurance expenditures to NT\$30 billion [3].

The high incidence and prevalence of ESRD is an important issue in Taiwan. However, the prevalence of early stage CKD is even higher. The progression of early stage CKD into ESRD is associated with an increased mortality for those with cardiovascular diseases and imposes a heavy psychological and economic burden on individuals, families, and society. As such, countries worldwide have made efforts to prevent and cure this disease. Serum creatinine has been replaced by estimated glomerular filtration rate (eGFR) in the early diagnosis of CKD, which has greatly affected detection of early stage CKD in recent years, and the clinical diagnosis and treatment following the new Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines have been widely applied [4]. CKD is highly prevalent in southern Taiwan. However, the annual changes in CKD prevalence based on eGFR and eGFR risk factors have been rarely studied. Thus, this study examined the annual changes in eGFR-based CKD prevalence rates and identified risk factors for a lower eGFR.

2 Methods

Study design

This study utilized longitudinal data analysis to examine the medical health check results for adults at a hospital in Pingtung, Taiwan from 2011 to 2013. Participants' general information and physical examination and blood test results were analyzed.

Participants

The participants in this study were adults who had undergone a health check (or integrated screening). After excluding those who did not finish the physical examination or biochemical blood tests, the sample included a total of 9,702 participants.

Research instruments

Physical examination

(1) Waist circumference (WC): WC was measured to the nearest 0.1cm on bare skin midway between the lower rib margin and the iliac crest at the end of gentle expiration.

(2) Blood pressure (BP): Trained nurses measured the systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the left arm of seated participants twice according to a standardized protocol. A third BP measurement was made if the first two BP readings differed by more than 10 mm Hg. The average of the two closest readings was calculated to determine the reported BP for each participant.

(3) Biochemical determinations: Participants were required to fast for a minimum of 10 hours prior to the biochemical blood test which measured triglycerides, high-density lipoprotein cholesterol (HDL-C), and plasma glucose levels.

Definition of terms

Definition of eGFR: In the present study, the GFR was estimated using the Modification of Diet in Renal Disease (MDRD), and CKD was grouped into 5 stages based on the categorization of CKD by the National Kidney Foundation, Inc.: a participant whose eGFR ≥ 90 ml/min/1.73m² with proteinuria was in stage 1; those with eGFR ≥ 60 -89 ml/min/1.73m² with proteinuria were in stage 2; those with eGFR ≥ 30 -59 ml/min/1.73m² were in stage 3; those with eGFR ≥ 15 -29ml/min/1.73m² were in stage 4; those with eGFR < 15 ml/min/1.73m² were in stage 5.

Metabolic syndrome: Metabolic syndrome status was defined according to the criteria set by the Health Promotion Administration, Ministry of Health and Welfare in 2007. Any three of the following five criteria were grounds for identifying metabolic syndrome: (1) abdominal obesity: waist circumference (WC) ≥ 90 cm in men and ≥ 80 cm in women; (2) raised triglycerides (TG): ≥ 150 mg/dL; (3) reduced HDL-C: HDL-C < 40 mg/dL in men and < 50 mg/dL in women; (4) hypertension: blood pressure of at least 130/85mmHg or taking antihypertensive

medication; and (5) raised fasting plasma glucose (FPG) ≥ 100 mg/dL and/or taking anti-glycemic medication.

Ethics

This study analyzed secondary numerical data from participants' health checks and integrated screening results. Before using the data, consent was obtained from the hospital. During data collection, all the data were anonymized in order to adhere to ethical principles. This study was approved by the institutional review board before data collection.

Statistical analyses

The present study analyzed data using SPSS 17.0 (SPSS for Windows release 17.0), with a significance level of $\alpha = .05$. Inferential statistics applied the Chi-square, independent t test and multiple linear regression model for analytics.

3 Main Results

The data from 9,702 participants were analyzed in this study. The analysis results for the changes in GFRs over three years in Table 1 show a significant annual increase in the number of participants with $eGFR < 60$ ml/min/1.73m². An $eGFR < 60$ ml/min/1.73m² was more prevalent in males and aged 65 and over compared to females and under 65 years (Table 2). Participants with abnormal metabolic syndrome and its components were found to have significantly lower eGRF than those without such abnormalities. Similar conclusions can be drawn from Table 3. The yearly results in Table 4 show significantly lower eGRFs were observed in males, aged 65 and over, and participants with abnormal metabolic syndrome and its components. Table 5 shows risk factors influencing eGFR. The results indicated that lower eGFR was related to male gender, age ≥ 65 years, metabolic syndrome, and abnormal BP, WC, and triglyceride levels.

4 Discussion

CKD is not easily detected in its early stages. CKD severity and stage can be determined mainly based on GFR and renal injuries. A lower GFR is associated with a higher mortality rate, prevalence of cardiovascular diseases, and hospitalization rate [5,6]. This study revealed an increase in the number of people with eGRF-based CKD (stage1-5) in southern Taiwan from 2011 to 2013; the prevalence rates for CKD were 18.5%, 17.5%, and 22.7%, respectively. Previously reported prevalence rates of CKD in Taiwan include 9.8%, 11.9%, and 16.1%, as found in a 1999-2003 insurance data analysis [7], a study among people aged 20 or over in 1994-2006 [1], and a study on people aged 40 or over [8],

respectively. These prevalence rates correspond to the findings in this study. CKD prevalence has been found to vary from country to country, with prevalence rates reaching 7.85% in India, 10.1% in Singapore, 11.9% in Thailand, 12.7% in Norway, and 11% in the US [9-11].

According to the Framingham Heart Study and four other longitudinal cohort studies, CKD can increase the mortality rate, particularly, that caused by cardiovascular diseases (including coronary artery, cerebrovascular, and peripheral vascular diseases and heart failure) [12]. Initiating risk factors for CKD in an average adult include unalterable factors (such as aging, genetic diseases, ethnic factors, and gender) and alterable factors (such as diabetes, metabolic syndrome, high BP, obesity, cardiovascular diseases, anemia, primary nephrotic syndrome, genitourinary disorders, and albuminuria) [3]. This study found that male gender, old age (≥ 65 years), and abnormal metabolic syndrome and its components are related to a lower eGFR, thus, increasing the risk of CKD.

CKD is currently considered a serious issue in public health [13]. Awareness of CKD risk factors is important for its prevention and cure. Risk factors can be alterable or unalterable. Age, gender [14], ethnicity, and genetic diseases are unalterable factors, while controllable factors include impaired kidney function, diabetes [15], high cholesterol, obesity [16], metabolic syndrome, smoking, high-protein diet, and anemia. Aging is a risk factor for CKD, with middle-aged and older adults being more prone to CKD. CKD risk grows with age and its prevalence is much higher among people aged 60 and over [8]. This study also noted lower eGFRs in participants aged 65 and over which was consistent each year and lower eGFRs in stages 1-5 for older participants compared to those under the age of 65.

CKD severity and stages were categorized in this study based on eGFR. Multiple linear regression analysis was employed to analyze eGFR predicting factors. The results indicated that eGFR was 17.159 ml/min/1.73m² lower in participants aged 65 and over than in younger participants, 12.999 ml/min/1.73m² lower in males than in females, and lower in participants with abnormal metabolic syndrome, BP, WC, or triglyceride levels. One study observed 2,858 adult patients for 8.5 years and found that age, high BP, diabetes, and low-density lipoprotein cholesterol are important factors that can cause a kidney disease [17]. Four of the main diseases related to ESRD include diabetes (43.2%), chronic glomerulonephritis (25.1%), high BP (8.3%), and chronic interstitial nephritis (2.8%), among which diabetes is the leading cause of ESRD [18]. Some studies reported that GFR decreases by 10-12 ml/min per year in diabetic patients with ESRD whose BP is not controlled; moreover, continuous high BP and albuminuria accelerate the deterioration of kidney function [19]. Dyslipidemia is another possible reason for inflammation and GFR decline [20]. CKD patients were found to have a higher risk of cardiovascular diseases than other patients. High blood cholesterol is one of main causes of atherosclerosis. One clinical study showed that dyslipidemia can cause atherosclerotic renal disease, glomerulosclerosis, and GFR decline, leading to an impaired kidney function [21]; this is consistent with

the findings in this study. With regard to the lower eGFR observed in participants with abnormal WC, a past study noted an abnormally high proportion of eGFRs <60 among patients with a body mass index (BMI) ≥ 27 Kg/m², and that higher BMI was found to be related to higher CKD incidence and risk of ESRD [22,23]. The results of this study were also similar.

Studies examining normal kidney function identified hyperuricemia as a risk factor for CKD [24]. Due to the recent exclusion of the uric acid test from the physical examination, this study could not analyze the effect of uric acid on CKD. However, uric acid was found to directly or indirectly damage the kidneys. An excess of uric acid is related to the risk factors of CKD, including high BP, diabetes, and cardiovascular diseases, through which it can cause deterioration of kidney function and metabolic syndrome [25]. Therefore, uric acid should be considered in future research.

The results of this study can serve as reference for local health care trends. Understanding the regional eGFR changes and influencing factors can benefit long-term health promotion and health care resource utilization.

Limitations

The data used in this study were collected only from one hospital; thus, the results may not be generalizable to the general population due to selection bias. However, given the large sample size, the results can still serve as a reference for other studies. Using health check data for analysis, this study did not include all the potential factors influencing CKD and, thus, has limited the inferences.

5 Labels of figures and tables

Table 1. GFR-based CKD stages in 2011-2013 (n=9702)

Variable	2011 (n=1203)		2012 (n=3391)		2013 (n=5108)		p value
	n	%	n	%	n	%	
CKD Stage							<.001
non CKD	980	81.5	2797	82.5	3950	77.3	
stage1(≥ 90)*	45	3.7	98	2.9	202	4	
stage2(60-89)	36	3	124	3.7	288	5.6	
stage3(30-59)	127	10.6	313	9.2	577	11.3	
stage4(15-29)	10	0.8	43	1.3	69	1.4	
stage5(<15)	5	0.4	16	0.5	22	0.4	

*eGFR: $\text{ml/min}/1.73\text{m}^2$

Table 2. Correlation between demographic characteristics and metabolic syndrome components and GFR (n=9702)

Variable	Non CKD (n=7727)		stage 1 (n=345) (≥90) [#]		stage 2 (n=448) (60-89) [#]		stage 3 (n=1017) (30-59) [#]		stage 4 (n=122) (15-29) [#]		stage 5 (n=43) (<15) [#]		p value
	n	%	n	%	n	%	n	%	n	%	n	%	
Gender													<.001
Male	3799	74.1	184	3.6	312	6.1	725	14.1	80	1.6	25	0.5	
Female	3928	85.8	161	3.5	136	3.0	292	6.4	42	0.9	18	0.4	
Age													<.001
< 65 years	4626	88.1	232	4.4	181	3.4	169	3.2	24	0.5	16	0.3	
≥ 65 years	3101	69.6	113	2.5	267	6.0	848	19.0	98	2.2	27	0.6	
WC													<.001
Normal	4591	83.5	185	3.4	205	3.7	450	8.2	50	0.9	19	0.3	
Abnormal	3136	74.6	160	3.8	243	5.8	567	13.5	72	1.7	24	0.6	

No (< 3 abnormal metabolic components)	5539	84.2	204	3.1	230	3.5	528	8.0	64	1.0	17	0.3
Yes (≥ 3 abnormal metabolic components)	2188	70.1	141	4.5	218	7.0	489	15.7	58	1.9	26	0.8

Note: Two-tailed chi-squared test; significance level $\alpha=0.05$.

^a blood pressure of at least 130/85mmHg or taking antihypertensive medication.

^b raised fasting plasma glucose (FPG) ≥ 100 mg/dL and/or taking anti-glycemic medication.

[#] eGFR: ml/min/1.73m².

Table 3. Correlation between demographic characteristics and metabolic syndrome components and eGFR (n=9702)

Variable	eGFR		<i>t</i>	<i>P</i> value
	N	Mean±SD		
Gender			-29.34	<.001
Male	5125	81.79±23.37		
Female	4577	97.04±27.36		
Age			39.99	<.001
< 65 years	5248	98.16±24.37		
≥ 65 years	4454	78.18±24.66		
WC			10.58	<.001
Normal	5500	91.47±25.93		
Abnormal	4202	85.74±26.78		
BP (mmHg)			16.51	<.001
Normal	5396	92.91±25.77		
Abnormal (≥130/85mg/dL)	4306	84.08±26.48		
Triglycerides			7.65	<.001
Normal	7110	90.22±26.42		

Abnormal ($\geq 150\text{mg/dL}$)	2592	85.59 \pm 26.25		
HDL			3.25	.001
Normal	6658	89.60 \pm 25.48		
Abnormal	3044	87.65 \pm 28.43		
FPG			11.57	<.001
Normal	5608	91.61 \pm 25.89		
Abnormal ($\geq 100\text{mg/dL}$)	4094	85.36 \pm 26.78		
Metabolic syndrome			13.73	<.001
No (<3 abnormal metabolic components)	6582	91.56 \pm 25.67		
Yes (≥ 3 abnormal metabolic components)	3120	83.57 \pm 27.25		

Table 4. Correlation between demographic characteristics and metabolic syndrome components and eGFR in 2011-2013

Variable	2011 (n=1203)			2012 (n=3391)			2013 (n=5108)		
	n	t-value	p value	n	t-value	p value	n	t-value	p value
		Mean±SD			Mean±SD			Mean±SD	
Gender		-10.91	<.001		-19.09	<.001		-19.62	<.001
Male	624	82.11±23.86		1672	81.06±22.59		2829	82.16±23.72	
Female	579	98.76±28.67		1719	97.16±26.42		2279	96.52±27.71	
Age		19.94	<.001		23.20	<.001		29.40	<.001
< 65 years	672	99.27±25.41		1875	97.84±24.23		2701	98.11±24.21	
≥ 65 years	531	78.56±25.80		1516	78.57±23.83		2407	77.85±24.93	

WC		3.48	0.001		5.87	<.001		8.10	<.001
Normal	666	92.60±27.58		2002	91.41±25.03		2832	91.24±26.15	
Abnormal	537	87.06±27.26		1389	86.07±26.76		2276	85.23±26.78	
BP (mmHg)		5.66	<.001		11.17	<.001		10.90	<.001
Normal	680	94.02±26.55		1948	93.45±23.79		2768	92.24±26.23	
Abnormal (≥130/85mg/dL)	523	85.07±28.06		1443	83.51±26.34		2340	84.21±26.28	
Triglycerides		1.83	0.068		4.06	<.001		6.22	<.001
Normal	907	90.96±27.74		2569	90.24±25.93		3634	90.03±26.43	
Abnormal (≥150mg/dL)	296	87.59±26.92		822	86.05±25.50		1474	84.95±26.51	

HDL		0.91	0.363		0.78	0.438		3.72	<.001
Normal	645	90.80±26.57		2002	89.46±25.21		2832	89.48±25.45	
Abnormal	558	89.35±28.67		1389	88.69±27.36		2276	86.24±29.03	
FPG		4.32	<.001		6.16	<.001		8.78	<.001
Normal	765	92.71±27.14		1889	91.65±25.72		2954	91.35±25.67	
Abnormal (≥100mg/dL)	438	85.62±27.75		1502	86.17±25.77		2154	84.73±27.27	
Metabolic syndrome		4.60	<.001		8.30	<.001		10.30	<.001
No (<3 abnormal metabolic components)	800	92.75±26.72		2352	91.65±25.29		3430	91.21±26.68	

Yes (≥ 3 abnormal metabolic components)	403	84.91 \pm 28.50		1039	83.73 \pm 26.38		1678	83.15 \pm 27.48	
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Table 5. Regression Analysis of Risk Factors of GRF

	Unstandardized Coefficient β^*	Standardized Coefficient β Distribution	p-value
(Constant)	107.480		<0.001
Age	-17.159	-0.323	<0.001
Gender	-12.999	-0.245	<0.001
Metabolic syndrome	-2.100	-0.037	0.005
BP	-2.743	-0.052	<0.001
WC	-2.820	-0.053	<0.001
Triglycerides	-2.372	-0.040	<0.001

*Reference group for analysis variables: <65 years old, female, without metabolic syndrome, normal BP, normal WC, normal triglyceride levels

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