KAOHSIUNG MEDICAL UNIVERSITY HOSPITAL

Glycosuria and Renal Outcome in Non-Diabetic CKD Stage 3-5 Patients

Ming-Hsuan Tsai[1], Hugo You-Hsien Lin[2,3], I-Ching Kuo[2,3], Sheng-Wen Niu[2,3], Shang-Jyh Hwang[3], Hung-Chun Chen[3], Chi-Chih Hung[3]

[1] Post Baccalaureate, College of Medicine, Kaohsiung Medical University; [2]Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University; [3]Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital

INTRODUCTION

■Detection of glucose in urine (glycosuria) in non-diabetic patients is a sign of impaired renal tubular reabsorption.

■Glycosuria theroetically is more frequent in chronic kidney disease (CKD); however, the consequence of glycosuria is little known.

■In contrast, impaired renal tubular reabsorption could prevent renal tubules from the protein injury of glomerular filtrates.

■We aim at studying glycosuria and its association with renal outcome in non-diabetic CKD patients with proteinuria.

METHODS

■We recruited 988 non-diabetic CKD stage 3 to 5 patients with proteinuria between 2002 and 2009.

■Glycosuria was defined as more than one measurements of urine glucose by dipstick (+~++++) during the follow-up period and at least once in the first three tests.

■student's t test, cox proportional regression and multivariate logistic regression analysis were carried out and p value less than 0.05 was considered as significant.

Table 1. Characteristics of non-diabetic CKD stage 3-5 patients

	All (n=988)	non-glycosuria (n=687)	glycosuria (n=289)	P (t test)
Demographics and Medical History				
Age (yr)	60.9 ± 15.6	61.0 ± 16.2	60.5 ± 14.3	0.680
Gender (male) (n [%])	483 (49.6)	307 (44.7)	176 (61.3)	<0.001
BMI (Kg/m^2)	24.1 ± 4.1	24.3 ± 4.0	23.6 ± 4.2	0.006
Cormobidity (n [%])				
HTN	599 (61.5)	418 (60.8)	181 (63.1)	0.515
Hyperuricemia	181 (18.6)	153 (22.3)	28 (9.8)	<0.001
Cardiovascular disease	175 (18.0)	131 (19.1)	44 (15.3)	0.166
Medication (n [%])				
Other anti-HTN therapy	349 (35.8)	274 (39.9)	75 (26.1)	<0.001
RAS blocker	388 (39.8)	319 (46.4)	69 (24.0)	<0.001
Statin	169 (17.4)	138 (20.1)	31 (10.8)	<0.001
Smoker	80 (8.2)	63 (9.2)	17 (5.9)	0.092
Renal Function Status				
eGFR (ml/min/1.73 m^2)	19.1 1 ±3.3	22.8 ±13.8	10.6 ±6.6	<0.001
UPCR (mg/g)	1324(878.4-2235.7)	1214 (792.7-2039.7)	1582 (1047.7-2499.6)	<0.001
CKD stage (n [%])				
stage III	205 (21.0)	197 (28.7)	8 (2.8)	
stage IV	288 (29.6)	241 (35.1)	47 (16.4)	<0.001
stage V	481 (49.4)	249 (36.2)	232 (80.8)	
Cause of CKD (n [%])				
GN	573 (58.8)	389 (56.6)	184 (64.1)	
TIN	202 (20.7)	150 (21.8)	52 (18.1)	0.051
HTN	148(15.2)	115(16.7)	33(11.5)	
Others	51(5.2)	33(4.8)	18(6.3)	
Laboratory Data				
Hemoglobin (g/dl)	10.3 ± 2.3	10.8 ± 2.3	9.0 ± 1.7	<0.001
Albumin (g/dl)	3.9 ± 0.5	3.9 ± 0.5	3.9 ± 0.5	0.552
Blood glucose (mg/dl)	98.2 ± 16.4	97.6 ± 16.4	99.4 ± 16.5	0.129
Total cholestrol (mg/dl)	189(160-218)	191 (162-222)	184 (154-210)	0.002
Triglyceride (mg/dl)	118 (82-166)	124 (85-171)	103 (75-150)	<0.001
LDL (mg/dl)	109.4 ± 35.4	110.9 ± 36.5	105.3 ± 32.7	0.025
HDL (mg/dl)	43.3 ± 14.6	43.8 ± 14.7	42.1 ± 14.5	0.087
CRP (mg/l)	1.1 (0.5-4.4)	1.0 (0.4-4.4)	1.4 (0.5-4.9)	0.012
$HbA1_C$ (%)	5.4 ± 0.6	5.5 ± 0.5	5.3 ± 0.6	<0.001
Phosphorus (mg/dl)	4.7 ± 1.4	4.5 ±1.3	5.2 ± 1.4	<0.001
Calcium (mg/dl)	8.9 ± 0.8	9.0 ± 0.7	8.7 ± 0.9	0.000
Bicarbonate (mEq/l)	20.1 ± 4.5	21.1 ± 4.3	17.5 ± 3.9	0.000
Uric acid (mg/dl)	7.8 ± 2.0	8.2 ± 2.0	7.0 ± 1.7	<0.001
Mean BP (mmHg)	101.0 ± 14.1	101.4 ± 14.3	100.2 ± 13.6	0.223
Clinical Outcomes				
Follow-up days	1203± 559	1198 ± 582	1228 ± 636	0.482
RRT (n [%])	391 (39.6)	219 (22.2)	172 (17.4)	<0.001
Mortality (n [%])	150 (15.4)	104 (15.1)	46 (16.0)	0.725
CV events (n [%])	117 (12.0)	81 (11.8)	36 (12.5)	0.248

BMI: body mass index, MBP: mean blood pressure, HTN: hypertension, RAS: renin-angiotensin system, eGFR: estimated glomerular filtration rate, UPCR: urine protein to creatinine ratio, CKD: chronic kidney disease, GN: glomerular nephritis, TIN: tubulointerstitial nephritis, LDL: low-density lipoprotein, HDL: high-density lipoprotein, CRP: c-reactive protein, HbA1c: glycosylated hemoglobin, RRT: renal replacement therapy, CV: cardiovascular.

RESULTS

■The mean age was 60.9 years, eGFR was 19.1 mL/min per 1.73 m^2 and urine protein-to-creatinine ratio was 1324 mg/g.

■Percentage of glycosuria was 2.4%, 12.8% and 46.9% in non-diabetic CKD stage 3, 4 and 5, respectively. It was also higher in those with heavy proteinuria.

■ In multivariate logistic regression, glycosuria was associated with eGFR, proteinuria, hemoglobin, albumin, and phosphorus.

■In survival analysis, glycosuria was associated with a decreased risk for end-stage renal disease (ESRD) (hazard ratio= 0.79; CI=0.63-0.98; *p=0.035*) and for rapid renal function progression (odds ratio= 0.64; CI=0.43-0.95; *p=0.003*); but glycosuria was not associated mortality or cardiovascular events.

Table 2-1. Cox regression for ESRD, mortality and CV events

	Non-glycosuria	Glycosuria	*p*-value
ESRD [a]			
Unadjusted HR (95% CI)	1 (reference)	2.55 (2.08-3.11)*	<0.001
HR (95% CI) for Model 1	1 (reference)	0.73 (0.58-0.90)*	0.004
HR (95% CI) for Model 2	1 (reference)	0.74 (0.59-0.92)*	0.007
HR (95% CI) for Model 3	1 (reference)	0.79 (0.63-0.98)*	0.035
Mortality [a]			
Unadjusted HR (95% CI)	1 (reference)	1.05 (0.74-1.48)	0.801
HR (95% CI) for Model 1	1 (reference)	0.88 (0.60-1.28)	0.495
HR (95% CI) for Model 2	1 (reference)	0.92 (0.62-1.35)	0.653
HR (95% CI) for Model 3	1 (reference)	0.82 (0.56-1.21)	0.312
CV events [a]			
Unadjusted HR (95% CI)	1 (reference)	1.50 (0.99-2.27)	0.057
HR (95% CI) for Model 1	1 (reference)	1.16 (0.73-1.84)	0.522
HR (95% CI) for Model 2	1 (reference)	1.20 (0.75-1.91)	0.440
HR (95% CI) for Model 3	1 (reference)	1.09 (0.68-1.73)	0.731

HR, Hazard ratio; CI, Confidence interval; eGFR, estimated glomerular filtration rate; UPCR, Urine protein-to-creatinine ratio; CVD, Cardiovascular disease; MBP, Mean blood pressure; BMI, Body mass index.
[a] Model 1 adjusts for age, gender, eGFR, log-transformed UPCR; model 2 adjusts for covariates in model 1 plus CVD, MBP; model 3 adjusts for covariates in model 2 plus hemoglobin, albumin, log-transformed CRP, BMI, log-transformed cholesterol and phosphorus.

Table 2-2. Logistic regression for rapid renal progression

	Non-glycosuria	Glycosuria	*p*-value
Unadjusted OR (95% CI)	1 (reference)	0.63 (0.45-0.89)*	<0.001
OR (95% CI) for Model 1 [a]	1 (reference)	0.63 (0.43-0.92)*	0.008
OR (95% CI) for Model 2 [b]	1 (reference)	0.65 (0.44-0.95)*	0.009
OR (95% CI) for Model 3 [c]	1 (reference)	0.64 (0.43-0.95)*	0.003

OR, Odds ratio; CI, Confidence interval; eGFR, estimated glomerular filtration rate; UPCR, Urine protein-to-creatinine ratio; MBP, Mean blood pressure; BMI, Body mass index.Models were the same as table 2-1.

Supplement Table 1. Logistic regression for glycosuria

Variables	β	95% CI of β	*p*-value
Age	0.992	0.981 - 1.004	0.205
Gender (male)	1.239	0.875 - 1.754	0.226
BMI	0.986	0.945 - 1.028	0.509
MBP (mmHg)	0.991	0.979 - 1.003	0.146
Cardiovascular disease	0.706	0.452 - 1.102	0.126
eGFR (ml/min/1.73 m^2)	0.887	0.862 - 0.913	<0.001
Log(UPCR)	4.304	2.295 - 8.069	<0.001
Hemoglobin (g/dl)	0.824	0.620 - 1.096	0.183
Albumin (g/dl)	1.563	1.067 - 2.289	0.022
Blood glucose(g/dl)	1.007	0.998 - 1.017	0.136
Hemoglobin (g/dl)	0.873	0.777 - 0.980	0.022
Log(cholesterol)	0.674	0.134 - 3.404	0.633
Ln(CRP)	1.172	0.961 - 1.429	0.117
Phosphorus (g/dl)	0.774	0.670 - 0.894	0.001

CONCLUSIONS

■Glycosuria was associated better renal outcome in non-diabetic CKD stage 3-5 patients. This may indicate that impaired renal tubular reabsorption of filtered protein is associated with less renal function progression.

KEY WORDS glycosuria, renal tubule, chronic kidney disease, ESRD

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H) Clinical Nephrology, CKD. H1) Lab methods, progression & risk factors for CKD 1-5, nutrition in CKD, renal diseases (except GNs and cystic diseases).
Chi-Chih Hung

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