Asymptomatic Hyperuricemia and the Risk of New-Onset Chronic Kidney Disease in Japanese Males over 40 Years of Age: A long-term retrospective cohort study

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INTRUDUCTION

Hypertension and diabetes as predictive factors for chronic kidney disease (CKD). However, it is not clear if asymptomatic hyperuricemia without gouty attacks is a risk factor for CKD. The aim of this study was to determine the associations between new-onset CKD and asymptomatic hyperuricemia, low serum high-density lipoprotein cholesterol (HDL-C), hypertension, diabetes and obesity in male factory workers over 40 years of age in Kanagawa, Japan.

METHODS

Study Population

The participants were all male factory workers over 40 years of age who had undergone annual medical examinations from 1990 to 2007. This retrospective cohort study covered a maximum period of 18 years. To investigate the effects of asymptomatic hyperuricemia, 41 participants with a history of gouty attacks were excluded from the analysis.

Disease Criteria

The presence of hyperuricemia, low serum HDL-C, hypertension, diabetes, and obesity were based on data from the participants' first-year medical examinations.

Hyperuricemia	**: uric acid > 7.0 mg/dL**
Low serum HDL-C	**: HDL-C < 40 mg/dL**
Hypertension	**: SBP ≥ 140 mmHg or DBP ≥ 90 mmHg**
Diabetes	**: fasting blood sugar ≥ 126 mg/dL**
Obesity	**: body mass index ≥ 25 kg/m^2.**

Outcomes

The endpoint was new-onset CKD. New-onset CKD was defined as the time point when estimated glomerular filtration rate (eGFR) fell below 60 mL/min/1.73 m2. The eGFR was calculated based on the participant's age and serum creatinine (Cr) level, using the equation determined by the Japanese Society of Nephrology.

$$eGFR = 194 \times Cr^{-1.094} \times Age^{-0.287}$$

Statistical Analysis

The associations between new-onset CKD and the presence of hyperuricemia, low serum HDL-C, hypertension, diabetes, and obesity were analyzed. Cox regression analysis was performed to derive a hazard ratio and 95% confidence interval (CI) for each covariate using age, hyperuricemia, low serum HDL-C, hypertension, diabetes and obesity, the follow-up period (months) as the survival variable. The hazard ratio was determined to be significant when the P value was < 0.05. In addition, Kaplan-Meier curves and log-rank tests were used to estimate the cumulative incidence of the covariates showing a significant hazard ratio.

RESULTS

The study involved 1,285 participants with a mean (± standard deviation [SD]) follow-up period of 95.2 (± 66.7) months. Of these participants, 100 (7.8%) developed CKD during the follow-up period, and their mean (±SD) follow-up period was 89.3 (±62.0) months. The mean (±SD) follow-up period for participants who did not develop CKD was 95.7 (±67.1) months.

Table 1 shows the baseline characteristics of the participants.

Table 1. Baseline characteristics of participants

	Participants (n = 1,285)	%
Age (yrs)		
40	433	33.7
41 – 45	273	21.2
46 – 50	276	21.5
51 – 55	220	17.1
≧56	83	6.5
Uric acid (mg/dL)		
＞7.0	166	12.9
≦7.0	1,119	87.1
HDL-C (mg/dL)		
＜40	153	11.9
≧40	1,132	88.1
Blood pressure (mmHg)		
SBP≧140 or DBP≧90	255	19.8
SBP＜140 and DBP＜90	1,030	80.2
Fasting blood sugar (mg/dL)		
≧126	51	4.0
＜126	1,234	96.0
Body mass index (kg/m^2)		
≧25.0	255	19.8
＜25.0	1,030	80.2

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Table 2 shows the prediction for new-onset CKD during followed-up period. Of the participants with hyperuricemia at baseline, 32 (19.3%) developed CKD during the follow-up period. The results of Cox regression analysis revealed that the hazard ratio for new-onset CKD in the participants with hyperuricemia was 3.99 (95% CI: 2.59–6.15), showing a significant association between hyperuricemia and new-onset CKD.

The cumulative incidence of CKD was analyzed by the Kaplan-Meier method using the three variables (hyperuricemia, low serum HDL-C, and hypertension) showing significant associations with new-onset CKD in the Cox proportional hazards model (Figure 1). Concerning hyperuricemia, low serum HDL-C and hypertension, the log-rank tests showed P values of <0.01 (Figure 1-A), 0.01 (Figure 1-B) and <0.01 (Figure 1-C), respectively.

Table 2. Associations between predictors and new-onset CKD during a maximum period of 18 years foll

Predictors	Duration±SD (months)	Cases	Incidence (%)	Hazard ratio	95% CI
Uric acid (mg/dL)					
＞7.0	76.3±63.3	32	19.3	3.99	2.59, 6.15
≦7.0	98.0±66.8	68	6.1	1.00	
HDL-C (mg/dL)					
＜40	89.3±61.5	18	11.8	1.69	1.00, 2.86
≧40	96.0±67.4	82	7.2	1.00	
Blood pressure (mmHg)					
SBP≧140 or DBP≧90	83.5±62.8	33	12.9	2.00	1.29, 3.11
SBP＜140 and DBP＜90	98.1±67.4	67	6.5	1.00	
Fasting blood sugar (mg/dL)					
≧126	95.1±66.0	3	5.9	0.56	0.17, 1.77
＜126	95.2±66.8	97	7.9	1.00	
Body mass index (kg/m^2)					
≧25.0	93.2±66.4	34	12.5	1.35	0.87, 2.10
＜25.0	95.7±66.8	66	6.5	1.00	

Figure 1. Kaplan-Meier curves and Log-rank tests of CKD incidence

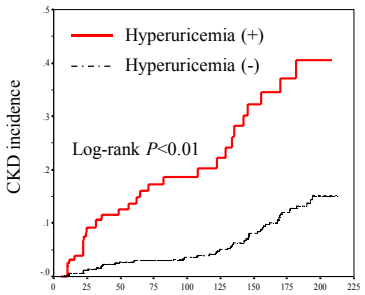

Figure 1-A CKD incidence with or without hyperuricemia

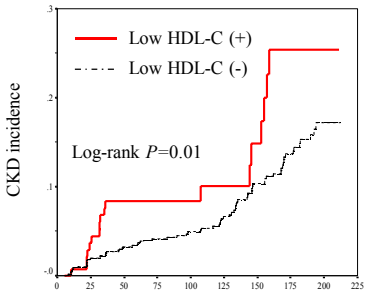

Figure 1-B CKD incidence with or without low HDL-C

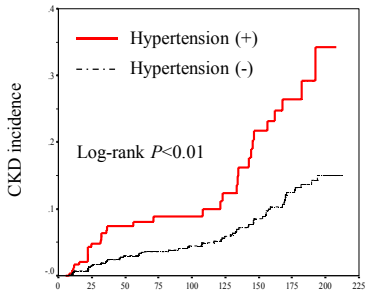

Figure 1-C CKD incidence with or without hypertension

DISCUSSION

We investigated the associations between new-onset CKD and asymptomatic hyperuricemia without gouty attacks, low serum HDL-C, hypertension, and diabetes in Japanese male factory workers over 40 years of age. The results showed a significantly higher incidence of new-onset CKD in participants with asymptomatic hyperuricemia. A significantly higher incidence of new-onset CKD was also found in participants with low serum HDL-C and hypertension. The incidence of new-onset CKD tended to be higher, but not significantly, in obese participants, whereas no significant increase in the incidence of new-onset CKD was found in those with diabetes.

In conclusion, the results of this study suggest that asymptomatic hyperuricemia without gouty attacks is a predictive factor for new-onset CKD. Therefore, the appropriate treatment might reduce the number of patients of CKD.