中文題目：已痊癒的和進行中的 C 型肝炎病毒感染以及第一基因型是腎功能正常者出現蛋白尿的危險因子: 以人群為基礎之橫斷型研究

英文題目：Resolved and current hepatitis C virus infection and genotype 1 are risk factors of albuminuria among individuals with preserved kidney function: a population-based cross-sectional study

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***Background**:*

Albuminuria is a manifestation of kidney damage and a risk factor of chronic kidney disease (CKD) progression. Additionally, it is a predictor of adverse health outcomes including end-stage renal disease (ESRD), cardiovascular events, and mortality. Previous studies have demonstrated the association between hepatitis C virus (HCV) seropositivity and risk of albuminuria. However, whether past (resolved) and current (chronic) HCV infection are similar in risk of albuminuria is relatively undetermined. In addition, the impact of HCV RNA genotype on risk of kidney damage remains unknown. Accordingly, we conducted a population-based study to investigate the association of resolved and current HCV infection and HCV genotype on risk of albuminuria.

***Method:***

In this cross-sectional study, the study population were adult participants of 2005-2018 National Health and Nutrition Examination Survey (NHANES) aged 19 to 79 years (n=38,150). After excluding individuals who were pregnant (n=721), received dialysis in the past 12 months (n=128), missed tests for HCV infection (n=3,607), serum creatinine (n=249), and urinary albumin & creatinine (n=9,318), or those with estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 $m^2$ (n=1,675), a total of 22,452 participants were eligible for this study. Participants who were tested negative for HCV antibody screening were defined as no history of HCV infection. Those who were tested positive for HCV screening were further tested by HCV RNA test. Individuals with positive HCV RNA test was defined as current HCV infection, while those with negative result were further tested by confirmation test. A positive or intermediate result was defined as past (resolved) HCV infection, while a negative result was defined as no history of HCV infection. The eGFR was calculated by isotope dilution mass spectrometry (IDMS) traceable Modification of Diet in Renal Disease (MDRD) Study equation [GFR = 175 × (standardized serum creatinine)$^{-1.154}$ × (age)$^{-0.203}$ × 0.742(if the subject is a woman) × 1.212 (if the subject is black)].

The outcome of interest was albuminuria, which was defined as urinary albumin creatinine ratio (ACR) of ≥ 30 mg/g. Among the 22,452 participants, only 4,408 (19.6%) individuals had two urinary ACR tests. Therefore, we separated our analysis for those who had at least one and those who had two ACR of ≥ 30 mg/g, respectively.

Other covariates included histories of diabetes mellitus or hypertension, which were defined as self-reporting diagnosis with the disease or taking medications. Cardiovascular disease (CVD) was

defined by self-reported history of congestive heart failure, coronary heart disease, angina, or heart attack; gout and old stroke were also defined by self-reported history of the diseases.

For the analytical analysis, continuous variables were presented as mean ± standard deviation and were tested by Student's *t* tests when appropriately. Categorical variables were presented as numbers (percent) and were compared by $\chi^2$ tests. Tests were two-tailed with a significance level of 0.05. Simple and multivariable logistic regression analysis were performed to explore the association between status of HCV infection and albuminuria. In the multivariable logistic regression model, we adjusted for age, sex, eGFR, body mass index (BMI), as well as self-reported diabetes and hypertension, all of which were known risk factors associated with albuminuria. Data were presented as odds ratio (OR) and 95% confidence interval (CI). Statistical analysis was performed using IBM SPSS V22.

***Results:***

The study participants were 45.6±16.2 years old in average and 49.2% were males, with 36.7% Whites, 21.5% Blacks, and 27.2% Hispanics. Compared with individuals without history of HCV infection (n=22,029), those with past (n=161) and current HCV infection (n=262) tended to be older, male, more likely to have a history of diabetes, hypertension, cardiovascular disease (CVD), gout, and previous stroke, and have higher systolic and diastolic blood pressure. The overall prevalence of albuminuria was 9.7%, higher among individuals with past (18.0%) and current HCV infection (17.9%) compared with those without HCV infection (9.5%), $p<0.001$. By multivariable logistic regression analysis, our results showed that both past (resolved) (OR 1.75, 95% CI 1.15-2.67, $p<0.01$) and current (chronic) HCV infection (OR 1.77, 95% CI 1.26-2.48, $p<0.001$) were risk factors of albuminuria compared with no history of HCV infection. When restricting our analysis for those who had two urinary ACR tests (n=4,408), our results showed that current HCV infection (OR 2.79, 95% CI 1.04-7.46, $p<0.05$) is an independent risk factor of albuminuria compared with no history of HCV infection, while the association between resolved HCV infection and albuminuria attenuated. Furthermore, we showed that HCV RNA genotype 1 was significantly associated with higher risk of albuminuria (OR 2.09, 95% CI 1.45-2.99, $p<0.001$). When restricting our analysis for those who had two urinary ACR tests, the association between genotype 1 HCV infection and albuminuria was still significant (OR 3.45, 95% CI 1.10-10.80, $p<0.05$). Our results did not show the association between HCV RNA genotype 2 and albuminuria.

***Conclusions:***

This cross-sectional study demonstrated that both past and current HCV infection were associated with the prevalence of albuminuria. The association was more significant with HCV virus RNA genotype 1 infection. Future studies are warranted to determine whether treatment of HCV infection might ameliorate albuminuria and reduce subsequent risk of kidney failure.