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Possible other causative risk factors in patients with chronic renal disease who had a history of hemolytic uremic syndrome

To the Editor: Sharma *et al.*[1] reported the increased prevalence of chronic kidney disease in patients with hemolytic uremic syndrome (HUS) who had a positive history of diarrhea. The study sample included a retrospective cohort matched with healthy subjects without any chronic disease, including diabetes and hypertension. Of the 30 HUS patients, 12 were less than 12 years old, 5 were between 12 and 18 years old, and 6 were older than 18 years. According to the results of this study, there is a high risk of increase in albumin/creatinine ratio in HUS patients when compared with healthy subjects. However, with regard to the study setting, data about the history of HUS patients regarding chronic diseases such as type 1 diabetes mellitus, tubulointerstitial disease, and so on that could cause microalbuminuria and increased albumin/creatinine ratio was not detailed by the authors. Rachmani *et al.*[2] reported that increased albumin excretion rates, even in the upper normal range, could increase the progression of chronic kidney disease in diabetic patients. Onset of type 1 diabetes mellitus before the age of 20 is another established risk factor for increased cumulative prevalence of chronic kidney disease.[3] Acute interstitial nephritis is also associated with mild proteinuria in children.[4] Therefore, data about patients' history should be detailed in the article, including the diseases causing proteinuria as an exclusion criterion.

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The Authors Reply: We would thank Dr Turkmen for his comments[1] that serve to emphasize a relevant point about our observations. Our paper underlined the importance of rigorous selection criteria while analyzing the long-term renal sequelae (albuminuria, blood pressure, and estimated glomerular filtration rate) of diarrhea-positive hemolytic uremic syndrome (D + HUS).[1] The study hypothesis had two components: first, the selection of appropriate controls not exposed in an *Escherichia coli* outbreak being crucial to minimize confounding from occult renal injury that could be incurred during the outbreak exposure; second, sporadic D + HUS having a greater potential of chronic renal sequelae than outbreak D + HUS. As stated in the paper, the exclusion criteria ensured a healthy status for the controls by carefully excluding any chronic disease, including diabetes and hypertension, prior history of bloody diarrhea and/or HUS, acute renal disease, or a recent acute illness.[2] Dr Turkmen argued that chronic diseases such as type 1 diabetes in HUS patients might confound albuminuria. We wish to indicate that similar to the exclusion criteria in the controls none of the HUS patients had chronic diseases, including diabetes, hypertension, prior kidney disease, or a recent acute illness. No recent acute illness excluded a potential confounding effect of transient albuminuria.[3] As indicated in our paper, the HUS group had additional exclusions of outbreak D + HUS or suspected atypical HUS. An appropriate control arm that accounts for selection bias and for underappreciated confounders is crucial for an accurate estimation of chronic renal sequelae after D + HUS.

1. Turkmen K. Possible other causative risk factors in patients with chronic renal disease who had a history of hemolytic uremic syndrome. *Kidney Int* 2011; **80**: 124.
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