

Authors reply: The risk of renal comorbidities in celiac disease patients depends on the phenotype of celiac disease

Rakel Nurmi¹, Camilla Pasternack¹, Teea Salmi^{1,2}, Kaisa Hervonen^{1,2}, Inka Koskinen^{1,3}, Jutta Järvelin⁴, Heini Huhtala⁵, Pekka Collin^{1,6}, Jukka Mustonen^{7,8}, Katri Kaukinen^{1,8}, Satu Mäkelä⁸

From the ¹Celiac Disease Research Center, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; ²Department of Dermatology, Tampere University Hospital, Tampere, Finland; ³Department of Internal Medicine, Central Finland Health Care District, Jyväskylä, Finland; ⁴Department of Knowledge Brokers, Finnish Institute for Health and Welfare, Helsinki, Finland; ⁵Faculty of Social Sciences, Tampere University, Tampere, Finland; ⁶Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland; ⁷Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; and ⁸Department of Internal Medicine, Tampere University Hospital, Tampere, Finland

Running headline: Authors reply: Celiac disease and the risk of renal disorders

Dear Editor,

We thank Dr. Han and Dr. Gao for their interest and important comments [1] regarding our recently published article in the *Journal of Internal Medicine* [2]. Firstly, they requested more consideration with matching factors. Indeed, the aspect of adequate use of matching factors is important. In our study, patients were matched with reference individuals for age, sex, calendar period, and county. Han and Gao suggested some additional matching parameters to be used. Air pollution or racial factors should not explain the differences in the risk of renal comorbidities as reference individuals and patients resided in the same areas and as the Finnish population almost always represents Caucasian ethnicity [3]. We agree with Han and Gao that it would have been intriguing to adjust with body mass index (BMI), but unfortunately as a register-based study we had no access to data on height and weight. Furthermore, these parameters have likely changed during the long follow-up. It has been shown that celiac disease patients have significantly lower BMI than that in the general population [4]. Furthermore, they are also more often non-smokers compared to matched controls [5].

We agree with Han and Gao that the possible role of dapsone for kidney function should be investigated more in the future. Approximately 80% of the Finnish individuals with dermatitis herpetiformis use dapsone after diagnosis, and the treatment is usually needed for 2–3 years [6]. However, the exposure for dapsone was quite short-term when considering the whole median follow-up of 40 years in our study.

Han and Gao also commented on the definition of kidney disease. The collected diagnoses of glomerulonephritis, diabetic nephropathy, interstitial nephritis and end-stage renal disease can be considered to cover a comprehensive group of chronic kidney diseases in Finland and globally. As a register-based study, unfortunately we had no access to data on glomerular filtration rate or proteinuria during the follow-up. However, we agree that these markers should be used to evaluate the stage and the progression of kidney disease in clinical practice. To summarize, the intriguing association between renal disorders and celiac disease with its different phenotypes should be clarified more in further prospective studies.

Conflicts of interest: The authors declare no conflicts of interest.

References:

1. Han Q, Gao R. Regarding: The risk of renal comorbidities in celiac disease patients depends on the phenotype of celiac disease. *J Intern Med* 2022. [Epub ahead of print].
2. Nurmi R, Pasternack C, Salmi T, Hervonen K, Koskinen I, Järvelin J, et al. The risk of renal comorbidities in celiac disease patients depends on the phenotype of celiac disease. 2022. doi: 10.1111/joim.13532.
3. Official Statistics of Finland (OSF): Population structure [e-publication]. ISSN=1797-5395. Annual Review 2018. Helsinki: Statistics Finland [referred: 3.8.2022].
4. Ukkola A, Mäki M, Kurppa K, Collin P, Huhtala H, Kekkonen L, et al. Changes in body mass index on a gluten-free diet in coeliac disease: A nationwide study. *Eur J Intern Med*. 2012;**23**(4):384–8.
5. Snook JA, Dwyer L, Lee-Elliott C, Khan S, Wheeler DW, Nicholas DS. Adult coeliac disease and cigarette smoking. *Gut*. 1996;**39**(1):60–2.
6. Mansikka E, Hervonen K, Kaukinen K, Collin P, Huhtala H, Reunala T, et al. Prognosis of Dermatitis Herpetiformis Patients with and without Villous Atrophy at Diagnosis. *Nutrients*. 2018;**10**(5):641.

Correspondence:

Rakel Nurmi

Celiac Disease Research Center, Faculty of Medicine and Health Technology, Tampere University
FI–33520, Tampere, Finland.

Email: rakel.nurmi@fimnet.fi