JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
LETTER TO THE EDITOR

Comment on a recent article titled 'Hepatocyte nuclear factor 1B deletion, but not intragenic mutation, might be more susceptible to hypomagnesemia'

To the Editor,

In a recent issue of the *Journal of Diabetes Investigation*, Wang *et al.*[1] report that individuals with an *HNF1B* gene deletion are more likely to have hypomagnesemia than people with an intragenic mutation. This was based on an analysis of published data from 539 cumulative cases and the odds ratio was 3.1 (95% confidence interval 1.8–5.4). In 2016, we published data on a small series of patients with HNF1B-associated disease (n = 38) and found that the median serum magnesium level was lower in those with a 17q12 microdeletion (0.58 mmol/L, interquartile range [IQR] 0.53–0.69) compared with those with a mutation (0.7 mmol/L, IQR 0.67–0.75; P = 0.01). However, we also found that 'renal function was worse in the mutation group with a median estimated glomerular filtration rate (GFR) of 42.6 mL/min/1.73 m^2 (IQR 31–60) compared with 81.4 (IQR 56–91) in the deletion group, P = 0.002'[2]. This finding was corroborated in a much larger series of individuals with HNF1B-associated disease (n = 201) described by Dubois-Laforgue and colleagues[3]. They found that patients with an *HNF1B* mutation had a worse renal prognosis than those with a 17q12 deletion, as they had a higher frequency of chronic kidney disease stages 3–4/end-stage renal disease and a lower median eGFR at follow-up (42.5 vs 75 mL/min/1.73 m^2, respectively; P = 0.008). Wang *et al.* do not comment on renal function in the 539 analyzed cases in their paper; we suggest that the higher prevalence of hypomagnesemia in those with an *HNF1B* deletion is likely to be explained by a higher eGFR in this group compared with those with an intragenic mutation.

They also present a case of an individual with a spontaneous heterozygous *HNF1B* whole-gene deletion with dorsal pancreatic agenesis, multiple renal cysts and hypomagnesemia. They state in the abstract that 'magnesium supplementation effectively alleviated the symptoms of diarrhea' although this was started at the same time as digestive enzymes and other medications. His symptoms of severe diarrhea and significant weight loss are typical of pancreatic insufficiency, which we would usually confirm by fecal elastase measurement. It seems more likely that the improvement in his symptoms was due to starting treatment with digestive enzymes, which usually need to continue long-term. Oral magnesium supplementation itself can be associated with diarrhea as a side-effect and is usually ineffective in HNF1B-associated disease due to the renal magnesium wasting that is seen[4].

ACKNOWLEDGMENTS

AH is supported by the National Institute for Health Research (NIHR) Exeter Clinical Research Facility and the NIHR Exeter Biomedical Research Centre, Exeter, UK.

DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: N/A.

Informed consent: N/A.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

Rhian Clissold[1], Coralie Bingham[1], Andrew Hattersley[2]

[1]*Exeter Kidney Unit, Royal Devon University Healthcare NHS Foundation Trust, Exeter, UK,* [2]*Institute of Biomedical and Clinical Sciences, University of Exeter College of Medicine and Health, Exeter, UK*

REFERENCES

1. Wang Y, Xiao X, Lin Q, *et al.* Hepatocyte nuclear factor 1B deletion, but not intragenic mutation, might be more susceptible to hypomagnesemia. *J Diabetes Investig* 2023. https://doi.org/10.1111/jdi.14084.
2. Clissold R, Shaw-Smith C, Turnpenny P, *et al.* 17q12 microdeletions but not intragenic *HNF1B* mutations are associated with a neurodevelopmental phenotype. *Kidney Int* 2016; 90: 203–211.
3. Dubois-Laforgue D, Cornu E, Saint-Martin C, *et al.* Diabetes, associated clinical spectrum, long-term prognosis and genotype/phenotype correlations in 201 adult patients with hepatocyte nuclear factor 1B (HNF1B) molecular defects. *Diabetes Care* 2017; 40: 1436–1443.
4. Adalat S, Woolf A, Johnstone K, *et al.* HNF1B mutations associate with hypomagnesemia and renal magnesium wasting. *J Am Soc Nephrol* 2009; 20: 1123–1131.

Correspondence
Rhian Clissold
Tel.: +44-01392-402535
E-mail address: rhian.clissold@nhs.net

Received 21 November 2023; accepted 12 December 2023

Doi: 10.1111/jdi.14137