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Letter to the Editor

Is liver steatosis diagnostic of non-alcoholic fatty liver disease in patients with hereditary fructose intolerance?

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Hereditary fructose intolerance
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Dear Editor,

Recently, Aldámiz-Echevarría et al. reported on sixteen patients, aged 3–48 years, affected by, genetically confirmed, hereditary fructose intolerance (HFI), all in dietary treatment of fructose, sorbitol and sacarose exclusion [1]. All subjects except one had normal BMI values and their HOMA index was within the normal range. In nine of these patients, imaging techniques demonstrated fatty liver corresponding to grade 1 hepatic steatosis, and three of them had hepatomegaly. Based only on the finding of hepatic steatosis the authors suggested that these patients were affected by non-alcoholic fatty liver disease (NAFLD), surprisingly unrelated to obesity, overweight or insulin resistance. They finally conclude that since NAFLD seems highly prevalent in HFI patients, new specific therapeutic approach for these patients should be identified [1].

We disagree with theses conclusions and specifically with the fact that the simple imaging demonstration of liver steatosis, particularly in adolescents and young adults with HFI with normal BMI and without evidence of insulin resistance, allow a diagnosis of NAFLD. Our opinion is based on the knowledge of the natural history of pediatric HFI and in particular on the study by Odièvre et al. who showed that although infants with severely symptomatic HFI normalize clinical and biochemical findings after being fed a fructose-free diet, they still present hepatomegaly for years afterwards as well as persistence, or even increase, of fatty vacuolization of hepatocytes on serial liver biopsies with disappearance of fibrosis [2]. Moreover, in the same study, fatty vacuolization of hepatocytes was always present in homozygous infants despite receiving a fructose-free diet from birth after HFI was recognized in older siblings [2].

These findings strongly suggest that liver steatosis is almost constantly present in young patients with HFI both after being placed on a fructose-free diet and when fructose-free since birth. Steatosis, therefore, represents a marker of their metabolic disturbance and persists for years and potentially for life. This might explain the high prevalence of steatosis found by Aldámiz-Echevarría et al. in their patients who had a quite wide range of age. Moreover the low sensitivity of ultrasound to detect mild liver steatosis may suggest an even higher prevalence.

The presence of liver steatosis in children and young adolescents carries a high risk of metabolic disorder and requires a detailed diagnostic work-up. The diagnosis of NAFLD should be based on the detection of fatty liver combined with recognized risk factors (mainly central obesity/overweight) and on the exclusion of other liver diseases such as, for instance, HFI [3].

Obviously any adult patient with HFI may develop NAFLD in the course of its life, but in this case obesity or overweight, and/or evidence of insulin resistance, at least, should be identified.

Conflicts of interest

There is no conflict of interest to declare.

CRediT authorship contribution statement

Giuseppe Maggiore: Conceptualization, Writing - original draft. **Silvia Nastasio:** Validation, Writing - review & editing. **Marco Sciveres:** Validation, Writing - review & editing.

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