

Invited Editorials

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Editorial: noncoeliac gluten sensitivity – a disease of the mind or gut?

Authors' reply

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We thank Aziz *et al.* for their thoughtful commentary on our recent article.^{1, 2} They raise important issues, of which we would agree, with a few qualifying statements.

No studies have been performed to show that gluten is the cause of depression or its improvement. However, psychiatric symptoms are known to be common in many chronic health conditions. In coeliac disease, anxiety and depression are typical in untreated patients, and improvement in mental state is often shown following gluten withdrawal.^{3, 4}

The idea that our findings mimic those in coeliac disease does not take this nonspecific effect of illness into account. We can find no studies in the literature that implicate gluten as the causative agent of depression in

coeliac disease. This improvement in psychological functioning may be the result of symptomatic resolve and enhanced perception of health and psychological well-being.⁵

In contrast, the induction of current feelings of depression following the consumption of gluten in this study points to a causative (not associative) role of gluten on mental state. The mechanistic action by which gluten might induce these changes in noncoeliac gluten sensitivity (NCGS) remains unknown. While it was hypothesised that gluten may induce depression as a consequence of changes in brain serotonin, gluten exorphins or changes in gut microbiota, we believe that it was unlikely to be via the induction of low-grade gut inflammation or changes in intestinal permeability. No changes to any biomarkers of these events were identified in this or previous well controlled studies,^{6, 7} although duodenal biopsies were not performed after challenges with gluten or placebo.

We wholeheartedly agree with Aziz *et al.* regarding the limitations of this study. Only a relatively small number of patients were studied and psychological end-points were limited to one scale. The association between gluten-specific acute changes in current feelings of depression requires a larger and more detailed examination. Only with clinical trials that include increased duration of gluten exposure, expansion of psychological, and other, end-points and adequate power will it be determined whether gluten does have

a specific effect on the psychological state of patients fulfilling the criteria of NCGS, as our pilot has suggested.

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Editorial: anti-viral therapy for prevention of perinatal HBV transmission – extending therapy beyond birth and the risk of post-partum flare

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Nguyen and colleagues studied the risk of post-partum hepatitis B virus (HBV) flares according to the duration of anti-viral therapy to prevent perinatal transmission of HBV.¹ The study comprised a nonrandomised historical opt-in observational cohort of 91 hepatitis B carriers (101 pregnancies) with HBV DNA >7 log IU/mL treated with lamivudine or tenofovir in the last trimester of pregnancy.

Patients were subdivided according to treatment duration, i.e. 2 weeks, 12 weeks or no therapy. Onset of post-partum flare, defined as an ALT >5× ULN, was similar between the three groups, occurred early post-partum (<10 weeks), and usually resolved spontaneously. HBeAg seroconversion rates did not differ between the groups.

Other studies investigating the effect of treatment duration on post-partum hepatitis defined a flare as ALT >1.5–2× ULN,² thus the relatively high ALT flare definition in this study may have underestimated the actual incidence of post-partum flares. Treatment was not standardised and determined at the treating physician's

discretion. Thus, as with any nonrandomised comparison, hidden biases cannot be ruled out and make the conclusions somewhat tenuous.

The lack of a standardised protocol for treatment initiation and continuation precludes interpretation of whether post-partum flares are due to differences in treatment responses vs. maternal immunological changes. We acknowledge that it may be difficult, if not impossible, to perform a randomised controlled trial and to withhold anti-viral treatment in mothers with high viral load, given the potential risk of immunoprophylaxis failure.^{3–5} Thus, whether anti-viral therapy in pregnancy has a significant effect on post-pregnancy flare risk remains unclear.

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