



## Non-Celiac Gluten Sensitivity and Iron Deficiency Anemia Reversal through Nutrition: A Case Report

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### Abstract

Non-Celiac Gluten Sensitivity (NCGS) is becoming more clearly defined and accepted in the medical literature. Indirect evidence suggests that NCGS is more common than Celiac Disease [1], the latter affecting around 1% of the general population [2]. The National Health and Nutrition Examination Survey, found that 49 cases of NCGS were identified in 7,762 patients from 2009-2010 [3]. The University of Maryland, found the criteria for NCGS in 347 of 5,896 patients observed between 2004 and 2010, which represents 6% of the group evaluated [4]. This case reports on the successful treatment of NCGS and IDA in an individual patient, a 56-year-old Italian-American female using nutritional support. The patient continued conventional Irritable Bowel Syndrome (IBS) and Iron Deficiency Anemia (IDA) treatment while beginning functional nutrition therapy guided by laboratory testing from her physician. After three months of a whole-foods diet following a 'Low Glycemic Gluten Free Diet' (LGGFD) model, her symptomology associated with NCGS including constipation, bloating and stomach pain was reversed, she was off acid reflux medication, and follow-up laboratory studies revealed iron markers within normal range.

### Keywords

Non-celiac gluten sensitivity reversal, Iron deficiency anemia reversal, Nutrition intervention, Functional medicine, Gluten-free diet, Low-glycemic index diet

### Introduction

A 56-year-old, Italian-American post-menopausal female patient presented to an integrative medicine clinic in June 2016 with Irritable Bowel Syndrome (IBS) with constipation and Iron Deficiency Anemia (IDA), seeking nutrition advice to support improvement of symptoms of IBS including constipation, bloating, and stomach pain as well as for nutritional deficiencies, particularly anemia. Her history was significant for chronic fatigue, hypothyroidism, acid reflux, cold intolerance, hypoglycemic symptoms and dizziness. Her current medications included Levothyroxine, Esomeprazole Magnesium and iron polysaccharide (Ferrex 150). Prior to this, she suffered from anemia or borderline anemia for 25 years. The patient diagnosis and treatment are outlined in the timeline.

### Patient Case

This 56-year-old female came in with IBS with constipation, IDA. Her past medical history was significant for chronic fatigue, hypothyroidism, acid reflux, cold in-

tolerance, hypoglycemic symptoms, and dizziness. Her symptomology of constipation, bloating and stomach pain; deficiencies in vitamins B6 and B12, iron, magnesium and zinc; family history of Celiac Disease (CD); and negative biopsy testing for CD suggest NCGS. At the time of her first visit in June 2016, she was taking Levothyroxine and Ferrex 150 as directed and Esomeprazole Magnesium in consistently. She has a history of a wide variety of iron medication without success. She had a Standard American high-glycemic, dairy-free diet, and her medications were not adequately controlling her medical problems.

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**Received:** June 22, 2017; **Accepted:** August 26, 2017;  
**Published online:** August 28, 2017

**Citation:** Coetzee O, Mari A (2017) Non-Celiac Gluten Sensitivity and Iron Deficiency Anemia Reversal through Nutrition: A Case Report. J Hum Nutr 1(1):1-5

The patient was evaluated at an integrative nutrition clinic that used a functional medicine approach guided by laboratory testing and a Low Glycemic Gluten Free Diet (LGGFD) intervention ([Appendix](#)). The LGGFD offers two-fold benefits. The gluten-free component offers a reduction in potential irritants contributing to the case symptomology. The low-glycemic component has proven benefits for general health and was implemented also to address the patient's symptom of dizziness, which can be correlated to a high-glycemic diet or low iron. Foods with a high Glycemic Index (GI) are those which rapidly digest and absorb, creating fluctuations in blood sugar levels. Low-GI foods, by virtue of their slow digestion and absorption, produce gradual rises in blood sugar and insulin levels. She came in for follow-up visits at one month and then at 3.5 months.

Initial laboratory testing was indicative of IDA and B-vitamin, magnesium and zinc deficiencies ([Table 1](#)). These nutrient deficiencies are not uncommon in individuals with compromised intestinal mucosa. While the histological picture of CD was not present in this patient based on biopsy results, minor duodenal lesions and intraepithelial lymphocyte infiltration of the mucosa have been observed in NCGS patients [5]. While clearly defined histological criteria have not yet been established for NCGS [6], we cannot rule out a connection between compromised intestinal mucosa and nutrient deficiencies in this case nor can we ignore the improved histological picture of other gluten-specific diseases like CD after implementing the GDF.

Initial laboratory testing also disclosed low Hemoglobin (Hb), Hematocrit (Hct), Mean Corpuscular

**Table 1:** Nutritional visit timeline (with diagnostic evaluation and interventions).

Three visits over three months	Nutritionist visit dates		
	6/13/15	7/12/16	9/27/16
<b>Medications</b>			
Levothyroxine	Yes	Yes	Yes
Esomeprazole Magnesium	Yes	No	No
Ferrex 150	Yes	No	No
<b>Dietary recommendations</b>			
LGGFD	Advised	Yes	Yes
Low FODMAP	Advised	No	No
Dairy free	No	Yes	Yes
<b>Dietary supplements</b>			
Generic probiotics	Yes	No	No
Hemagenics	No	Advised	Yes
Ultra Flora Balance	No	No	Advised
<b>Lifestyle recommendations</b>			
<b>Laboratory biomarkers</b>			
Hgb	10.2		12.9
Hct	32.5		38.8
MCV	80		90
MCH	25.1		29.9
MCHC	31.2		33.2
RDW	17.2		16.6
TIBC	422		321
UBIC	-		238
Iron	40		83
Iron Sat	9%		26%
Ferritin	-		29
<b>Vital signs</b>			
Blood pressure	132/68	125/70	115/65
Height	5' 4"	5' 4"	5' 4"
Weight (pounds)	133.5	127.6	125.2
BMI	22.9	21.9	21.5
Fat mass	42.2	38.4	37.0
Fat free mass	91.6	89.2	88.2
Body fat %	31.6	30.1	29.5
Total body water	67.0	65.2	64.9

Past medical history: IBS with constipation, IDA, bloating, stomach pain, chronic fatigue, hypothyroidism, acid reflux, cold intolerance, hypoglycemic symptoms, dizziness. Current history: NCGS, elevated RDW, uterine polyp.

Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC); Low-Normal Mean Corpuscular Volume (MCV); and High-Normal Red Cell Distribution Width (RDW) corresponding to anemia plus digestive inflammation or dysfunction with possible hypochlorhydria. With this case of a woman over 50 who is post-menopausal, her IDA is even more interesting and unlikely, and gluten exposure in sensitive individuals may cause inflammation.

In July 2016, she reported reversal of acid reflux symptoms and discontinued Esomeprazole Magnesium. She lost 6 lbs during the interim, which indicates inflammatory weight loss, as she is a small-framed person. The iron supplement Hemagenics® by Metagenics was recommended because it is formulated to provide support for red blood cell formation and better absorption with fewer side effects [7]. An ultrasound during the interim revealed a uterine polyp, for which follow-up with her OB/GYN was scheduled.

In September 2016 during the three-month follow-up visit, her laboratory testing showed iron markers within normal range, which may be attributed to improved integrity of the intestinal mucosa allowing for improved nutrient absorption and increased energy. She was advised to continue with iron supplementation for an additional three months to achieve optimal levels. Additionally, she was advised to begin taking a probiotic supplement to promote full restoration of balance in her intestinal biome after her long history of gastrointestinal distress. She reported reversal of symptoms of constipation and digestive discomfort when gluten remains eliminated from her diet.

### Patient Perspective

“I came to NHC (Natural Healthcare Center) with the frustration of a lifetime. No one had ever been able to figure out why my iron levels remained low even after infusions, medication and supplementation. I was first diagnosed with iron anemia more than 30 years ago. I have lived a life of chronic fatigue, I have had miscarriages, and I have had consistent IBS-related issues; and nothing worked. I am from an Italian background and have Celiac Disease in my family. However, I never tested positive for it, therefore the traditional medical community felt gluten was not the cause for my anemia. At NHC I came to realise there is a condition called NCGS and found out that it is becoming recognized in medicine as a real condition. My husband is a chef and cooks traditional Italian food. I never in all these years once considered not eating all the wonderful pasta and breads... because I wasn't a “Celiac”. I feel foolish now that I didn't try a gluten-free lifestyle before. I wasn't just gluten-free by eliminating wheat, but all grains. It was amazing to me how quickly

I improved when living this way. My IBS has resolved completely, as if it never existed. My iron has normalized for the first time ever, and I have energy. I am both happy and angry that something so simple had this profound an effect, and I should have known having Celiac in my family had to have some relevance even though I tested “negative”. The interpretation of my symptoms and blood work led the clinicians at NHC to pinpoint my lifelong struggle. I cannot be grateful enough”.

### Discussion

NCGS is characterized by intestinal and extraintestinal symptoms due to the ingestion of gluten-containing food in subjects without CD; these symptoms can identically mimic almost all those in CD [8]. Long-term IDA not responsive to iron prescriptions or supplementation should be taken into consideration in the presentation of NCGS and Irritable Bowel Disease (IBD)/IBS [9]. Practitioners encountering those with NCGS and IBD/IBS should search for new associations between not just Gluten-Free Diets (GFD) but all grains. Patients with Crohn's Disease and Ulcerative Colitis, seem to be more affected by gluten than the other inflammatory bowel diseases [9].

Carroccio, et al. [10], wanted to demonstrate that NCGS can be diagnosed through serologic, clinical and histological markers. Two hundred and seventy-six patients with NCGS were included in the study, compared to another 100 officially diagnosed CD patients and 50 with IBS. The NCGS patients showed higher percentages of anemia, food allergies, food allergies as infants, and coexistent atopy than the IBS controls. An interesting finding was that the histological picture of NCGS patients included eosinophil infiltration of the mucosa of the duodenum and colon, similar to CD. Their data confirmed an association between NCGS patients and those with CD.

It is further encouraging to see how the literature is beginning to mention NCGS as a criterion on its own. In the review of Makharia, et al. [11], they state, “The complex of symptoms associated with these diseases, such as diarrhea, constipation or abdominal pain may overlap for the gluten related diseases, and furthermore they can be similar to those caused by various other intestinal diseases, such as Irritable Bowel Syndrome (IBS)”. They further go on to say that NCGS is likely to have a heterogeneous association with intestinal inflammation, intestinal tight junction dysregulation and intestinal microbiota imbalances. They conclude by suggesting another potential inducer of innate immune response, “amylase-trypsin inhibitor”, a protein present in wheat endosperm which, along with alpha-gliadin, could be a major issue in NCGS. Volta, et al. [1] postulates that there is a strong dietary link between tight junction disruption in NCGS and IBS.

El-Salhy, et al. [3] bring up a point of contention in the literature investigation. They feel the evidence is not clear that alpha-gliadin is the major culprit in NCGS rather than the carbohydrates, fructans and galactans found in wheat might be the issue. Further investigation is warranted to explore the carbohydrate connection in wheat and the “amylase-trypsin inhibitor” mentioned earlier. These two might be cofactors to alpha-gliadin in mucosal disruption.

CD-related enteropathy leads to multiple nutritional deficiencies involving macro- and micronutrients [4]. One may postulate that NCGS might have the same effect as seen in the case study above. The GFD presents the only nutritional therapy for CD. Various studies have indicated that maintaining a GFD will result in the improvement or reversal of most of the nutritional deficiencies [12]. A GFD should not be motivated by finding “Gluten-Free Substitutes”. It should, rather, be motivated by a “whole-food paleo-style nutrient-dense glycemic-controlled completely grain-free” approach. All grains contain prolamines that can be just as destructive as alpha-gliadin [1].

According to Caruso, et al. [13], reduced levels of iron, folate, vitamin B12, vitamin D, zinc and magnesium are common in untreated CD patients probably due to loss of brush border proteins and enzymes needed for the absorption of these nutrients. This picture of reduced levels of nutrients stands true for our case study above, which suggests that further research is needed to investigate the potential for a higher degree of intestinal epithelium destruction in some NCGS cases. Caruso, et al. further states that the removal of gluten from the diet leads to histological recovery and normalization of iron, vitamin and mineral levels. IDA appears to be the most common extraintestinal sign of CD and usually resolves with adherence to a GFD. One may postulate that the same can be applied to NCGS.

Caruso, et al. [13] looked at the frequency and clinical relevance of nutrient deficiency in CD and whether and when nutrient supplementation was needed. The common denominators seemed to be iron, magnesium, zinc, B-vitamins and others. Taking into consideration that most of these nutrients are absorbed in the duodenum, more research needs to be done on this area of digestion and absorption in NCGS patients.

Botero-Lopez, et al. [14] studied the digestive and absorptive involvement in atypical presentation of CD. Their study focused on the status of iron, copper and zinc in patients with Typical CD (TCD) and Atypical CD (ACD). One hundred and nine subjects were in the study; 39 were Healthy Controls (HC), 19 ACD and 54 TCD. The outcome for this study indicated that TCD

and ACD had very similar issues when it came to iron, copper and zinc absorption, whereas the HC group was different. In short, the micronutrient deficiencies were very similar in both ACD and TCD.

Infantino, et al. [15] in a very recent publication might bring us closer to an actual medical diagnosis with NCGS. To date, there is no biomarker to diagnose NCGS, however studies have reported 50% of patients with suspected NCGS tested positive for Anti-Gliadin Antibodies (AGA), in specific, the IgG class. His conclusion: “Therefore, in the presence of clinical symptoms that suggest NCGS, IgG AGA positivity, together with negative anti-tTG, EMA, and Anti-Deamidated-Gliadin-Peptide (DGP) antibodies, NCGS diagnosis might be suspected”.

## Conclusion

The complications of IBS if left untreated or mismanaged can lead to diarrhea, constipation, hemorrhoids, malnourishment, heart problems, and overall poor quality of life [16]. As one of the possible root causes of IBS, NCGS should be considered in the presence of the symptomatology and nutrient deficiencies discussed in this case report. The general medical community does not seem to accept the clinical significance of NCGS causing nutrient depletions and malabsorption regardless of the information expressed through this paper. This case has outlined a functional medicine approach to dietary intervention that provides a reversal for NCGS and IDA. It lays emphasis on the fact that NCGS and CD portray very similar nutrient deficiencies in clinical practice and might be overlooked by many clinicians. This highlights the need to revisit the current definition of NCGS, which minimizes disruption of the intestinal epithelium.

This patient reversed her symptoms of NCGS and achieved laboratory iron markers within normal range over a period of three months. A low glycemic gluten free nutritional intervention was associated with improvement and reversal of her symptoms of NCGS and IDA.

## Acknowledgements

This case report followed the CARE guidelines for case reports. Oscar Coetzee is a professor and Doctor of Clinical Nutrition at the Maryland University of Integrative Health in Laurel, Maryland. Angela Mari is a Master’s student of Clinical Nutrition at the Maryland University of Integrative Health in Laurel, Maryland.

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