UPDATE ON GLUTEN SENSITIVITY
September 22, 2013

Gluten Sensitivity
Biomarkers and Epidemiology
The Ongoing Field Experience

Umberto Volta
Department of Medical and Surgical Sciences
University of Bologna, Italy
Coordinator of Italian Celiac Association Board

No relevant financial relationship to disclose

REVIEW

Cellular & Molecular Immunology (2013), 1–10

www.nature.com/cmi

Non-celiac gluten sensitivity: questions still to be answered despite increasing awareness

Umberto Volta, Giacomo Caio, Francesco Tovoli and Roberto De Giorgio

- No reliable epidemiological study on non-celiac gluten sensitivity (NCGS) has been published to date.

- In US NCGS prevalence has been reported to vary from 0.55% in primary care (NHANES) to 5.8% in tertiary care (Maryland Center).

- DBPC showed a high frequency of NCGS (28-30%) in IBS, which is present in 16-25% of the general population (possible high prevalence of NCGS?).

Non-celiac gluten sensitivity (NCGS) and celiac disease (CD) diagnosis in the period 2011-2013 at CD Center, University of Bologna, Italy

	Patients N°	Median Age	Sex F/M ratio
NCGS	180	44 (range 10-70)	4.3/1
CD	110	36 (range 14-64)	2.9/1

NCGS/CD = 1.6/1

Volta U et al, Cell Mol Immunol 2013

NCGS biomarkers

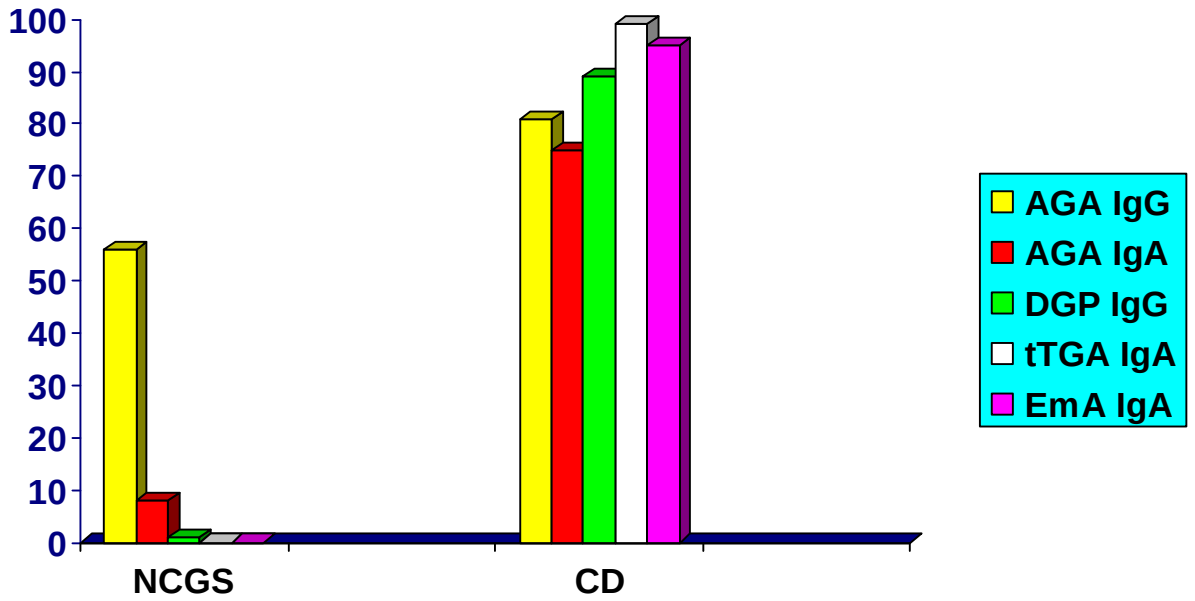
- Differently from celiac disease, no biomarker of NCGS has been identified so far.
- In vitro PBMC cytokine response to gluten has been assessed in NCGS patients without identifying a specific immune pattern.
- No genetic marker has been detected (no correlation with HLA-DQ2 and/or –DQ8).
- No antibody showed to be closely related to NCGS.
- With a wide variable prevalence, anti gliadin antibodies of first generation (AGA) were the only antibody found in a proportion of NCGS patients.

Volta U, De Giorgio R, Nat Rev Gastroenterol Hepatol 2012

Serological Tests in Gluten Sensitivity (Nonceliac Gluten Intolerance)

Umberto Volta, MD, Francesco Tovoli, MD, Ronny Cicola, MD, Claudia Parisi, MD, Angela Fabbri, MD, Maria Piscaglia, MD, Erica Fiorini, MD, and Giacomo Caio, MD

J Clin Gastroenterol. 2011 Dec 5. [Epub ahead of print]



- **Forty-four (56.4%) out of 78 NCGS patients were positive for AGA IgG, which were detected in 81% of celiac disease (CD) patients.**
- **Only 6 (7.7%) of NCGS patients showed AGA IgA positivity.**
- **Deamidated gliadin antibodies (DGP) IgG were consistently negative in NCGS patients except for one case at a very low titer positivity.**

AGA prevalence in other diseases and healthy controls

- **Connective tissue disorders 9%**
- **IBS without gluten sensitivity 13%***
- **Autoimmune liver diseases 21%**
- **Blood donors 2%**

AGA IgG is a marker neither specific nor highly sensitive for NCGS, but for the time being its positivity (especially at a high titer) in patients with suspected NCGS can contribute to this diagnosis.

Volta U et al. Dig Dis Sci 2008
***Caio G et al, poster presentation at the 15th ICDS, Chicago 2013**

Prospective Survey on Non Celiac Gluten Sensitivity by Coeliac Disease Italian Association (AIC)

- The project, started at the end of 2012 and still in progress, aimed to provide a picture of NCGS in Italian Centers for Gluten-Related Disorders by collecting the following data through a questionnaire:

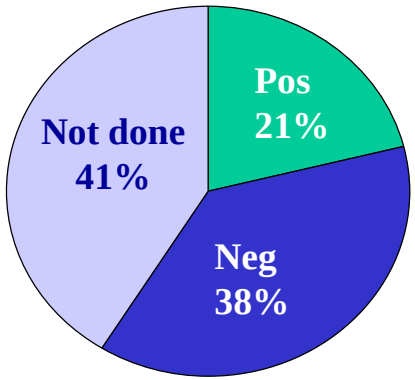
  1) symptoms and signs of onset; 2) frequency and timing of symptoms; 3) duration of symptoms before diagnosis, 4) who was the first to think about NCGS; 5) associated disorders; 6) 1st and 2nd generation antibodies to gliadin; 7) HLA typing; 8) Duodenal biopsy.
- In the first 6 months of this survey, 400 NCGS (F/M 5,5:1, median age 55 years, range 14-80 years) were enrolled.
- The most frequent intestinal symptoms were abdominal pain (84%), bloating (81%), diarrhea (52%), whereas among extraintestinal symptoms the most common were fatigue (75%), headache (55%), anxiety (40%) and foggy mind (38%). About 20% of the enrolled pts were 1st degree relatives of celiacs.

AIC Associazione Italiana Celiachia 30 anni 1979-2009

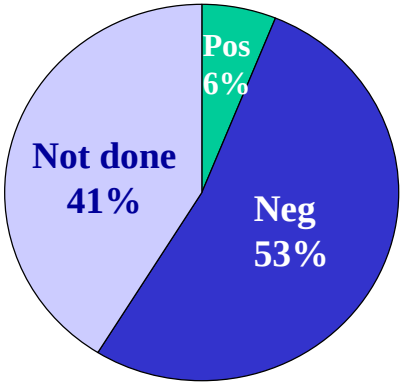
Scientific Board for Non Celiac Gluten Sensitivity (NCGS)
Coordinators: U. Volta, G.R. Corazza, E. Tosi (President AIC), O. Lovello (President F.C.)
Members M.T. Bardella, A. Calabrò, G.R. Corazza, C. Corposanto, O. Lovello, C. Pilo, A. Pucci, E. Tosi, R. Troncone, U. Volta

1st and 2st GENERATION GLIADIN ANTIBODIES IN NCGS

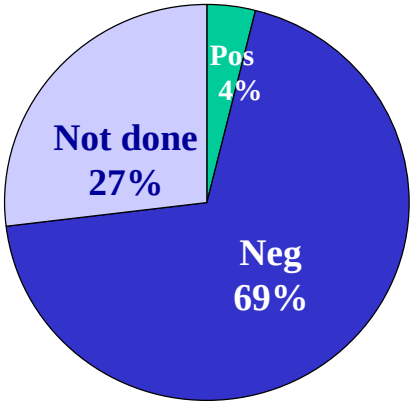
AGA IgG



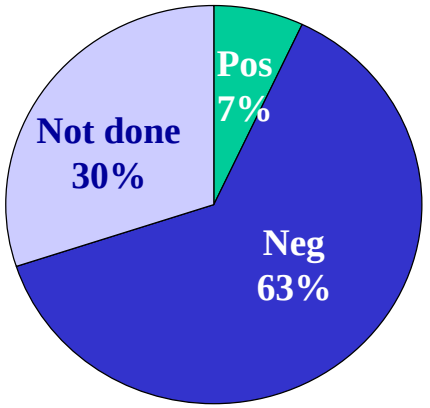
AGA IgA



DGP IgG



DGP IgA



AIC SURVEY

Take home message

- Increasing awareness of NCGS with many open issues still to be puzzled out, including epidemiology and biomarkers.

- Current facilities for the diagnosis of NCGS are comparable to those for celiac disease in the early 1970s when celiac markers such as tissue tranglutaminase and endomysial antibodies had not been discovered yet.

- The identification of NCGS biomarkers is the first step for defining the real prevalence of this new syndrome in the general population, as already happened for celiac disease.