

# The Importance of a Disease Register for the Patients with Non-Celiac Gluten Sensitivity

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**Abstract** A new entity was included in the gluten diseases: the non-celiac gluten sensitivity. But the non-celiac gluten sensitivity is not yet clearly defined and its diagnosis is difficult. These lead us to implement a national register for the patients with non-celiac gluten sensitivity.

**Keywords:** non-celiac gluten sensitivity, celiac disease, disease register

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## 1. Introduction

In the last years, has been proposed a new nomenclature for the diseases induced by the ingestion of gluten (the protein present in wheat, rice, barley and oats). Besides celiac disease (CD) and wheat allergy (WA), the most studied forms of gluten-related disorders characterized by an evident immune mechanism (autoimmune in CD and IgE-mediated in WA), a new entity has been included, apparently not driven by an aberrant immune response: the non-celiac gluten sensitivity (NCGS).

Because the patients suffering from NCGS are a heterogeneous group and the diagnostic is being made only by excluding the CD and WA (in the absence of reliable biomarkers discovered yet), we considered to seek out the arguments that underline the importance of developing a specific disease register for this disorder. We reviewed the international literature through PubMed, using the search terms "celiac disease, "wheat allergy," " non-celiac gluten sensitivity".

## 2. Celiac disease, Wheat Allergy, Non-celiac Gluten Sensitivity

CD is a major health care problem, affecting people in any ages, which was reported worldwide prevalence of approximately 1% [1]. The diagnose of CD is being made on intestinal and extraintestinal symptoms, positive CD serology (anti tissue-transglutaminase, anti-endomysial antibodies, deaminated gliadin peptide antibodies and anti-gliadins antibodies), histology abnormalities (Marsh I-IIIc), presence of HLA DQ2/DQ8 haplotypes, negative

IgE-based assays, innate and adaptive immune response and positive response to gluten-free diet [2].

On the other hand, a significant percentage of the general population report problems caused by wheat and/or gluten ingestion, even though they do not have CD or WA, because they test negative both for CD-specific serology and histopathology and for immunoglobulin E (IgE)-mediated assays. Most patients report both intestinal and extra intestinal symptoms, and all report improvement of symptoms on a gluten-free diet. This clinical condition, originally described in 1980 has been named non-celiac gluten sensitivity (NCGS) [3]. Recent studies raised the possibility that, beside gluten [4] and wheat amylase trypsin inhibitors [5], low-fermentable, poorly-absorbed, short-chain carbohydrates [6] can contribute to symptoms (at least those related to IBS) experienced by NCGS patients.

It has been demonstrated that patients suffering from NCGS are a heterogeneous group, composed of several subgroups, each characterized by different pathogenesis, clinical history, and, probably, clinical course [4]. NCGS diagnosis can be reached only by excluding CD and WA. Recent evidence shows that a personal history of food allergy in infancy, coexistent atopy, positive for immunoglobulin G (IgG) antigliadin antibodies (50% of cases) and flow cytometric basophil activation test, with histology abnormalities Marsh 0-II, could be useful to identify NCGS patients [2,7].

Unfortunately, many patients with NCGS do not believe that gluten is responsible for their symptoms and they do not follow a gluten-free diet and, therefore, they don't solve their clinical condition. In the same time, due to poor physician's awareness of this disease, NCGS patients were commonly referred to psychiatrists because they were believed to have an underlying mental illness. [8,9,10,11]. In recent years, several studies explored the

relationship between the ingestion of gluten-containing food and the appearance of neurological and psychiatric disorders/symptoms like ataxia, peripheral neuropathy, schizophrenia, autism, depression, anxiety, and hallucinations [12]

There is a felt need of specialists to better define the different NCGS subgroup and to focus on researches that aim to identify reliable biomarkers for NCGS diagnosis [5]. In the same time, a proper screening for CD before a diagnosis of NCGS is made it is considered to be very important [13].

The scientific community gathered on the 3rd International Expert Meeting on Gluten Related Disorders (6–7 October 2014, Salerno, Italy) acknowledged that in the absence of sensitive and specific biomarkers, a close and standardized monitoring of the patient during elimination and re-introduction of gluten is the most specific diagnostic approach and hence could be used as the diagnostic hallmark of NCGS [12].

In this context it is important to take under consideration the introduction and use of a NCGS register.

A disease register represent a database, which contains information about the people, diagnosed with specific diseases in a defined population [14,15,16]. Based on the information documented in this register it is possible to achieve important objectives such as: monitor the disease's evolution, the active measures addressed to patients and to increase the level of medical knowledge which may support good medical practice in this field [14,17]. Beyond their importance in achieving these objectives, disease registers could be expensive and could demand a great deal of attention from the ethical point of view because of the concerns regarding data protection [14,18,19].

In order to have a functional and useful a NCGS register, the following objectives should be achieved:

1. Establish the kind of register that we want to implement: local register (serve one hospital and are files of all patients seen at a hospital with NCGS), or population based, central register (are as the local one, but include data from selected groups of contributing hospitals), or population based register (attempt to collect detailed information on all cases of NCGS in a population of known size and composition). A population based register will allow further the computing of some indicators, such incidence and prevalence, that are relevant for the population assisted (previous defined).

2. Define all the necessary items that should be included in the register: general data (e.g. location, name, gender, age, residence, logging date, date of current visit/admission, reason for the current presentation, etc.) and medical data (medical history, symptoms, clinical examination, laboratory examinations, other investigations and treatment). For the diagnostic should be take under consideration the diagnostic algorithm that has been already published [20]

3. Develop the platform that should fulfill the needs for interoperability and data security. In order to accomplish this, should be taken in account three possible solutions (depending on the final purpose, type of register and budget): a) open electronic health record (open EHR), an independent non-profit community facilitating the creation and sharing of health records by clinicians via open-source and standards-based implementations; b) EN/ISO-13606,

and c) Health Level Seven (HL7), currently the most widely implemented healthcare standard for clinical information exchange.

To achieve this objectives there are a several steps to follow in the development of a successful disease register[11]. These steps are:

- Set up an expert group which will guide the future development of the registry;
- Set up a steering group that should ensure that the register is run according to its stated aims and objectives, and that the rights of patients are respected;
- Obtain approval from a Research Ethics Committee;
- Establish arrangements for access to the data, thinking of the likely spectrum of users of the data;
- Consider arrangements for data security: physical security, encryption, passwords and procedural security (staff training and written records of procedures);
- Promote the register among those who contribute data
- Data considerations: clear definition of the cases, methods use to ascertain the cases, reliable identification of duplicate cases;
- Obtaining proper consent.

### 3. Conclusion

A register for NCGS patients should be consider to be implemented, first at local level, with the possibility of its extension at regional and national level. This specific disease register can provide tools for a more correct diagnosis and for more rigorous studies to establish the prevalence of NCGS in specific conditions and in the general population.

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