

# Screening for celiac disease among the personnel in active service of an Italian Armed Force

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## Abstract

**Introduction and objective.** Celiac disease (CD) affects the 1% of the general population worldwide. Because of its clinical variability, roughly the 70% of CD patients are not correctly diagnosed and not adequately treated. Active military personnel represent an interesting cohort for a CD screening. Upon the enrollment in the Armed Forces, a complete health check is carried out to exclude any diseases. Aim of the present work is to assess the CD prevalence among the personnel of Carabinieri Corps, an Italian armed force, through a serological screening.

**Results and discussion.** Out of 291 militaries (281 M, 10 F age range: 18.2-61.5) enrolled, 2 resulted affected by CD (prevalence: 0.7%); 1 to have high serological anti-TG and EMA level without duodenal mucosal lesions and 1 to have high serological anti-TG, but not EMA.

**Conclusion.** These results show that the CD prevalence among a cohort of Italian militaries is similar to that of the general population.

## Key words

- celiac disease
- screening
- military personnel
- gluten-free diet

## INTRODUCTION

Celiac disease (CD) is a permanent inflammatory enteropathy, triggered in genetically predisposed individuals, by dietary gluten. Gluten is the alcohol protein fraction of some cereals, such as wheat, barley and rye. CD is the most frequent food intolerance worldwide, with a globally estimated prevalence of 1% [1].

CD is usually defined as a clinical chameleon. In fact, this condition might show up with a wide range of signs and symptoms, involving different organs and systems: anemia, hypertransaminasemia, oral aftosis, recurrent miscarriages, osteoporosis, and chronic fatigue are just some of these. In addition, the CD-associated symptoms can range for very mild to severe [1]. These forms of CD are diagnosed casually during a screening program in the healthy population or among the first-grade relatives of CD patients, that are known to have a 10-fold risk to develop these conditions, respect to the general population [2]. Because of its clinical variability, CD is very under-diagnosed. The data from the

Italian Ministry of Health report that in our Country roughly 200,000 patients are diagnosed with CD, out of 600,000 estimated to be affected. Therefore, the 70% of CD patients are not diagnosed and consequently are consuming gluten in their diet [3]. The long-lasting exposure to dietary gluten maintains the symptoms and signs related to CD and, most of all, increases the risk to develop the life-treating complications of CD, such as intestinal adeno-carcinoma and T-cell lymphoma [4].

At the moment, the only effective treatment for CD is a strict a life-long withdrawal of gluten from the diet. A gluten-free diet (GFD) determines the remission of the CD-related symptoms and histological lesions in the duodenal mucosa and prevents the onset of the neoplastic complications [1].

Military personnel represent an interesting cohort for a screening of CD prevalence. At the moment of the enrollment in the Italian Armed Forces, a complete health check is carried out to exclude any diseases, including CD.

Several epidemiological studies on CD have been performed among the military personnel, in active service or retired. A first paper, in 1999, described retrospectively, the clinical features of 458 individuals, dismissed with the diagnosis of CD from the US military hospitals in the period 1986-1995 [5]. In 2011, Langgreden *et al.* reported the risk of developing a cancer in a cohort of 4,5 millions of US Veterans. Although this study did not investigate the CD prevalence in the cohort, it concluded that CD is a risk factor for intestinal and esophagus cancer [6]. More recently, a case-control analysis including 13,7 millions of US militaries in active service reported an increasing prevalence of CD over the years, ranging from 1.3/100,000 in 1999 to 6.5/100,000 in 2008 [7]. While it is out of doubt that the prevalence of CD is raising worldwide, this paper is likely to over-estimate the dimension of CD prevalence. It did not take in account several confounding factors, such as the ascertainment bias and the different access to health services that the US militaries have in the different Region of service [8].

It is clear that, despite the body of evidence available on the CD epidemiology among military personnel, data on the real prevalence of CD lack.

So, the aim of the present work is to assess the CD prevalence among the personnel of Carabinieri Corps, an Italian armed force, through a serological mass-screening program.

**MATERIALS AND METHODS**

The study has been approved by the Ethical Committee of the Istituto Superiore di Sanità (protocol n. 568/16) and the diagnosis of CD is made according to the National Guidelines of the Italian Ministry of Health – revision 2015 [9]. All the Carabinieri admitted in the period February 2017-August 2018 to the Carabinieri Health Service (Infermeria Presidiaria della Legione Carabinieri Lazio) in Rome, Italy, were asked to enroll in the study. After signing the informed consent, a 5 ml blood sample was withdrawn from a peripheral vein and collected in a vacutainer blood-tube containing a serum separating gel, centrifuged at 1900 rpm for 15 minutes without brake to separate plasma from cells. The plasma was tested for the anti-transglutaminase (tG) IgA levels by a commercially available ELISA kit (Eurospital, Trieste, Italy; normal level <9 UI/ml) at the laboratory of the Unit of Human Nutrition and Health of Istituto Superiore di Sanità. Those patients resulted to have an anti-tG plasma

titre above the positivity cut-off, are investigated for plasma EMA and eventually, undergo to duodenal biopsy. These two examinations were performed at the Department of Gastroenterology, Columbus Hospital – Catholic University, Rome.

**RESULTS**

In the study, 291 militaries (281 M, 10 F; age range: 18.2-61.5) were enrolled. Out of them, 3 patients resulted to have the anti-TG plasma titre above the cut-off (Table 1).

Patient 1 was a 39.8-years old, male military, that at the moment of the enrollment in the study did not report any symptom or disease. When interviewed more in depth after the result of the anti-TG determination, he reported to suffer from frequent oral aphthosis and mild dyspepsia. After the CD diagnosis, he was put on a GFD with a complete remission of the above-mentioned symptomatology.

Patient 2 resulted positive to both anti-TG and EMA, but he did not show the diagnostic alteration of celiac duodenal mucosa. He was diagnosed with potential CD and according with the guidelines, he is still consuming gluten in the diet and undergoes periodically to clinical and serological examination.

Patient 3 showed an anti-TG titre slightly positive. He did not perform the duodenal biopsy since the EMA negativity and the anamnestic record that he was affected by an autoimmune chronic kidney disease. So, the serum presence of the anti-TG is likely to be related to the concomitant auto-immune nephropathy.

Finally, we included in the series a military already diagnosed with CD, treated with a GFD. His serum anti-TG levels resulted below the cut-off, showing a clinical remission of the condition.

The overall prevalence of overt CD in our cohort resulted to be 0.7% (2/291).

**DISCUSSION**

The main result of this study is that the prevalence of CD among the military personnel in service is quite similar to that of the general population [10]. This result is surprising, at the light of the fact that all the militaries undergo a complete health check-up upon the enrollment, that excludes, among the other conditions, the present of overt CD and CD autoimmunity. So, the 2 celiac militaries developed the CD after the enrolment in the Arma of Carabinieri, that occurred when they were 19 and 21 years old, respectively.

**Table 1**  
Clinical features of patients with overt celiac disease (CD) or CD-autoimmunity

Patient (n)	Sex	Age (years/months)	anti-tG (UI/ml)	EMA	Mucosal histology (Marsh classification)
1	M	39,8	53	+++	IIIa
2	M	45,4	50	+	I
3	M	41,9	20	-	Not performed
4*	M	45,1	<9	-	Not performed

\*Patient diagnosed with CD out of this study, already on a gluten free diet at the moment of enrolment in the study.

Our study also confirms that CD may present with very mild signs and symptoms, that very often lead to misdiagnosis CD. The Patient 1 in our series did not report any symptoms or signs when interviewed before the anti-TG determination. Then, when checked with the patient more accurately his medical history after the positive result of the anti-TG, he reported some mild but frequent gastro-intestinal symptoms. When these symptoms remitted after 6 months on a GFD, the patient recognized how much these affected his well-being.

It is still controversial whether the most suitable diagnostic strategy for CD is the mass screening or the case finding [11]. The case finding as it is performed at the moment, misses most of the cases of overt CD [12], on the other hand mass screening is expensive, lack of a validated non-invasive blood test and we do not still have ultimate evidences to set an age which CD certainly develops within. Our study shows that the best strategy to make the hidden part of the celiac iceberg emerged is a way between the mass screening and the case finding and it might be a screening in the high-risk group. High-risk groups are to be identified on the basis of a careful evaluation of clinical symptoms and signs, associated autoimmune diseases, consanguinity for CD and CD-autoimmunity.

We diagnosed a military with potential CD. This form of CD is characterized by the serological positivity for EMA and/or anti-TG in absence of significant mucosal lesions (Marsh 0 and 1, according to the Marsh-Oberhuber classification). At the current stage of the knowledge, this form of CD is more frequent in children and quite rare in adults. The current guidelines suggest keeping these individuals on a free diet and follow them periodically, since most of the cases solves spontaneously, with the disappearance of the serum CD-specific antibodies [13].

Individuals with CD properly treated with a strict and long-life GFD has a normal quality of life and physical performances [14]. As proof of the fact, a treated CD individual can serve unconditionally as military in Arma the Carabinieri as well as in the other Italian Armed Forces. The Directive IGESAN/PS-15 of the General Inspectorate of the Military Health Service – Italian Armed Forces dated in 2015, verbatim states that: “*for those diagnosed with CD after the enrolment into the Armed Force, this diagnosis does not imply any leave provision*”. This normative offers a high protection for celiac militaries, that can receive a diagnosis of CD and the life-saving treatment, without being forced to leave their job and their position in the Armed Force. So, further and larger screening program for CD could be performed among the Armed Force personnel to increase the number of CD diagnosis.

The CD prevalence found in this study is similar to that found in previous screening program in adults, in Europe and worldwide. Mustalahti *et al.* have report-

ed a CD prevalence among adults ranging from 0.3% in German, 0.7% in Italy to 2.4% in Finland [15]. An anti-TG IgA-based screening performed in Wyoming, United States, has described a prevalence of overt CD of 0.80% among healthy individuals [16]. In Brazil, the serum anti-TG IgA have been found in 1.5% of blood donors and the 66.7% of them have presented also the mucosal histological lesions, pathognomonic of CD [17]. Finally, in Australia, the screening for CD in blood donors has brought to the CD diagnosis the 0.96% of the screened population [18].

This study has two limitations. The first is the M/F ratio of the cohort, that is very unbalanced towards the male sex. The M/F ratio in this study reflects that of the militaries of the Arma dei Carabinieri, where only the 5% are females. On the contrary, CD is a condition much more frequent in women than men with a ratio 2.5/1. Nevertheless, we have found in our population a CD prevalence similar to that of general population, where the women are predominant [3]. This finding might suggest that the higher CD prevalence among women respect to the men should be due to some referral bias, such as the more severe symptoms at onset of the disease in the women.

The other limitation consists in the relatively small number of militaries included in our series. The main problem in a mass screening for CD in an adult population is to make acceptable to people that do not feel complaining any health problem, the possibility that they have a condition, whose treatment will limit their dietary choices and consequently, their social life.

In conclusion, our study reports that the prevalence of CD among militaries in service is equivalent to that in the general population. This finding supports the hypothesis that it is worth identifying the misdiagnosed CD cases among the Armed Forces, with a program based firstly on a careful clinical identification of mild symptoms, signs, associated diseases and consanguinity and then on serological testing for at risk individuals.

#### **Authors' contribution**

MP conceived the experimental design, enrolled the patients and drafted of the paper. OV performed the ELISA kit and drafted the paper. SC and SR maintained the study database and drafted the paper. IDV performed the clinical analysis in patients found positive at the screening. EB conceived the experimental design, enrolled the patients and drafted the paper. MS supervised the study, gave critical advices and drafted the study. All the Authors contributed to the final version of the paper and approved it.

#### **Conflict of interest statement**

None to be declared.

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