Too Few Studies Provided a Link between Viral Infections and Celiac Disease

Iulian Diaconescu1*, Giulia Alexandru1, Rahela Carpa1, Iulia Lupan2, Corina Crisan3, Lucia Sur4, Genel Sur5, Anamaria Girbovan6

1Department of Microbiology, Babes Bolyai University, Cluj-Napoca, Romania
2Department of Molecular Biology, Babes Bolyai University, Cluj-Napoca, Romania
3Emergency Hospital for Children, Cluj-Napoca, Romania
4Department of Pediatrics I, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania
5Department of Pediatrics II, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania
6Department of Immunology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

*Corresponding author: mac_master_02@yahoo.com

Abstract Introduction. Celiac disease has a prevalence of 1% of the global population and it is increasing every year. Viral infections such as hepatitis C and hepatitis B are the most common liver diseases and studies show that there may be a link between them and celiac disease. Recent studies show attempts to find a link between viral infections and celiac disease. We focused our study on the association between viral infections and celiac disease. Material and Method. We studied 63 articles from the PubMed Database that revealed a possible connection between viral infections and celiac disease. Results. Since it is more frequent, hepatitis C is associated with the development of celiac disease, but celiac disease is not the autoimmune manifestation of hepatitis C. Patients with celiac disease have a significantly decreased response to hepatitis B vaccine. Other viruses that are associated with celiac disease are: rotavirus, adenovirus, eetrovirus and Epstein-Barr virus. Conclusions. The serological screening for celiac disease at hepatitis C patients, after starting treatment with interferon, is necessary. Also, it is justified the serological screening for celiac disease among adults infected with hepatitis B. Further studies are still needed to show the possible association of viral infections in the pathogenesis of celiac disease.

Keywords: celiac disease, viral infection, possible connection


1. Introduction

Anti-tissue transglutaminase antibodies (tTG) may occur during infections with hepatitis [1]. Environmental factors may also be involved in the pathogenesis of celiac disease (CD) [2]. The major pathogenic factors can be categorized into environmental effects and genetic variations. According to some studies, mostly are caused by hepatitis B virus or hepatitis C virus (3). Therefore, it is also important to identify the cellular reactions as response to the environmental factors that are capable of inducing an immune response associated with human leukocyte antigen (HLA) [4,5]. Our goal was to make a theoretical study of literature to find out the current state of knowledge about the possible association of CD with viral infections.

2. Materials and Methods

We used the keywords „celiac disease” and “viral infections” in the PubMed database. We found 63 articles, of which we studied just those articles that revealed a possible connection between viral infections and CD.

3. Results

3.1. Celiac Disease and Viral Hepatitis C

CD was associated with viral hepatitis C (HCV) and with chronic autoimmune liver disease. Given the fact that HCV was more frequent than autoimmune liver diseases, HCV seems to be the most common liver disease associated with the development of CD [6].

CD is not an autoimmune manifestation of HCV. That is why some researchers did not recommend screening for CD in patients with HCV [7]. Other researchers have argued that silent CD activation occurs during treatment with interferon in patients with HCV and CD should be suspected [8]. The prevalence of CD in patients with positive HCV was 0% (95% confidence interval: 0-0.59%): the IgA antiendomisium antibodies (EMA) were positive for 0.16% of patients, but histopathological examinations of intestinal biopsies were negative [9]. It was proposed that the serological screening of CD should be performed before and after starting treatment with interferon [10]. Later, a series of four CD patients with HCV associated have been described. It was showed that HCV infection
and CD may occur together. The conclusion was that chronic HCV and CD are not causally related [11].

Inflammatory non-intestinal diseases can trigger intolerance to gluten at sensitive people and HCV was considered as a suitable candidate. Interferon therapy could accelerate the symptoms in patients with silent CD. Symptoms that may occur are diarrhea, anemia, weight loss during therapy with interferon and positive tTG. As such, serology for CD should be considered in patients who develop diarrhea and / or weight loss during therapy with interferon [12].

3.2. Celiac Disease and Viral Hepatitis B

Some researchers have postulated that patients with CD may have a significant predisposition for lack of response to viral hepatitis B (HBV) vaccine. Patients with CD may have failed to induce humoral immune response necessary for long-term development of immunity; however, the responsible mechanism is still uncertain [13]. One of the theories claims that there is a relationship between the lack of response to HBV vaccine and certain genotypes of HLA. The response to HBV vaccine in children who have CD and gluten-free diet was not different from a healthy population [14]. An association between CD and HBV was not found in the pediatric population, however, the researchers acknowledged that further studies are needed in larger populations [15]. Some studies have focused on the possible pathogenic causes for no response at HBV vaccine in patients with CD [16]. Previous studies have suggested that vaccines for HBV may be less immunogenic in CD patients [17]. Recent studies showed that unprotected antibodies responses occurred more often in CD patients than in the unaffected population [18]. Other studies showed an increased prevalence of CD among patients with HBV. These patients were symptomatic and had significant changes in laboratory tests [19].

Despite major advances over the past decades, future studies are still needed to define the prevalence of CD in different etiologies of liver diseases and to prove any alleged association [20].

3.3. Celiac Disease and Rotavirus Viral Infection

Some prospective studies have shown that a high frequency of rotavirus infections can increase the risk of childhood CD in genetically predisposed people [21]. Gene-array analysis revealed that VP7 anti-rotavirus purified antibody modulates genes that are involved in modulating apoptosis, inflammation and alterations in the integrity of the epithelial barrier in the intestinal epithelial cells, resulting in all the typical characteristics of CD [22]. It was rumored the hypothesis about the involvement of rotavirus in triggering CD through molecular mimicry between human protein transglutaminase and dodecapeptide from VP7 protein of rotavirus, but current studies have shown that children with CD have immune reactivity to rotavirus [23].

3.4. Other Possible Viral Infections Associated with Celiac Disease

Serological IgA anti-adenovirus antibodies were detected in children with CD being in close relationship with CD regression [24]. Enterovirus infection was the first viral infection reported to be associated with CD. Some studies have shown that enterovirus infection during pregnancy was associated with CD development during childhood. Among the mothers whose children developed CD, 4% had IgA EMA, which may show a silent CD [25]. Respiratory syncytial virus infection was observed in children under two years diagnosed with CD before hospital admission [26]. Epstein-Barr virus has been detected in inflammatory cells and enterocytes of patients with refractory CD. Further studies are necessary to find if infection with Epstein-Barr virus contributes to the pathogenesis of refractory CD [27].

4. Conclusions

The serological screening of CD at HCV patients, after starting treatment with interferon, is necessary. Also, it is justified the serologic screening for CD among adults infected with HBV. Other viruses like rotavirus, adenovirus, enterovirus and Epstein-Barr virus could be associated with CD but few studies have reported the association of viral infections with CD.

Acknowledgements

Anamaria Girbovan received a grant from the University of Medicine and Pharmacy “Iuliu Hațieganu” Cluj–Napoca 2016, project no. 4995/21/08.03.2016.

References


Tjernberg AR, Ludvigsson JF. Children with celiac disease are more likely to have attended hospital for prior respiratory syncytial virus infection. Dig Dis Sci 2014; 59: 1502-1508.