



**UNIVERSITI TEKNOLOGI MARA (UiTM)**

**ASSOCIATION BETWEEN GLUTEN SENSITIVITY AND EPILEPSY BASED ON  
HLA-DQ GENOTYPING TOGETHER WITH CELIAC DISEASE-RELATED  
ANTIBODY**

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## **TITLE PAGE**

### **Title**

Association between Gluten Sensitivity and Epilepsy based on HLA-DQ genotyping together with Celiac Disease Related Antibody

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## ABSTRACT

**Introduction :** Gluten sensitivity (GS) is a common autoimmune disease that has been reported to affect 1 in every 100 people worldwide. (1, 2) GS is associated with several neurological conditions including epilepsy. (3) About 95% of people diagnosed with gluten intolerance were genetically predisposed through the human leukocyte antigen (HLA), HLA-DQ 2 and HLA-DQ 8. (4, 5) **The** purpose of this study is to investigate the association between epilepsy and gluten sensitivity based on HLA-DQ genotyping, alpha-gliadin antibody (AGA), and tissue transglutaminase antibody (anti-tTG).

**Method:** A case-control study was conducted with a target sample size of 100 patients. 50 epilepsy patients and 50 non-epileptic adults matched for age, gender, and race were recruited. All patients were subjected to an interview, clinical examination and venous blood sampling. AGA and anti-tTG antibodies were detected using a commercially available ELISA kit. The blood sample were also sent for genotyping of HLA-DQ alleles represented by 6 single nucleotide polymorphisms (SNPs) [(i) DQ2.2 (rs2395182; rs7775228 rs4713586); (ii) DQ2.5 rs2187668; (iii) DQ7 (rs4639334) and (iv) DQ 8 (rs7454108)].

**Results:** The overall seroprevalence of gluten sensitivity in the study group was 40%. Out of this 21 (42%) patients were from epilepsy group. HLA-DQ 2.2 genotype was found to be strongly associated with epilepsy where 9 epileptic patients were positive for HLA-DQ 2.2 [p-value 0.003]. However, the seroprevalence of HLA-DQ 8 was 18 (36%) in the epileptic group and 19 (38%) in the control group [p-value=0.836]. The AGA was positive in 4 (8%) epilepsy patients while anti-tTG antibody was negative in both study groups. Overall, there was no association seen between gluten sensitivity seropositivity and epilepsy in our study [OR 0.85 (CI 0.380-

1.885), (p-value 0.838)]. Nevertheless, we found that 8 out of 21 epileptic patients with gluten sensitivity used more than 1 anti-seizure medication. (p-value 0.014).

**Conclusion:** Our study showed no association between GS and epilepsy. However, the seroprevalence of HLA-DQ 2.2 genotype was significantly higher in epileptic patients and those epileptic patients with GS required multiple anti-seizure medications.

Keywords: *Epilepsy, gluten sensitivity (GS), human leukocyte antigen (HLA), anti-gliadin antibody (AGA), anti-tissue Transglutaminase antibody (tTG)*

## INTRODUCTION

Gluten is a protein found in wheat, barley, and rye. Adverse reaction to gluten is known as a gluten sensitivity (GS) which comprises of celiac disease (CD), wheat allergies (WA), and non-celiac gluten sensitivity (NCGS). Recently there has been a growing interest in GS as subjects worldwide have reported that ingestion of gluten causes intestinal and extraintestinal symptoms.

The epidemiology of GS is not well established, mainly due to lack of diagnostic test to confirm the diagnosis. Traditionally, diagnosis of GS is mainly based on clinical criteria, intestinal biopsy and exclusion of other disorders. The data available is limited and largely variable. In the USA, two different surveys in 2010 showed GS prevalence of 0.6% and 6% in the general population. (6, 7) Another multi-centre study in Italy showed GS prevalence of 3.19%. (8) However, these studies have major limitations because the diagnosis of GS was highly presumptive in all the patients, being based exclusively on clinical criteria and self-reported symptoms by patients. In Malaysia, there is only one study done by Theresa et al on prevalence of CD antibodies in Malaysia that suggests CD is likely to be under-diagnosed. (1)

Although GS is commonly known to cause gastrointestinal symptoms, studies have shown that it is also associated with neurological conditions. (9-12) Neurological manifestations of GS are becoming widely recognized and has been reported worldwide. GS is associated with several neurological conditions such as dementia, ataxia, peripheral neuropathy, and epilepsy. (3) However, the relation between GS and epilepsy is still uncertain. Research investigating the association between epilepsy and GS is limited and previous studies have contradicting results where some suggested association while other have not. (13) A systemic review by Julian et al, found an association between epilepsy and CD or gluten intolerance where epilepsy is more prevalent in patients with CD or gluten intolerance and vice versa. (4) There are also literatures