Urinary Gluten Immunogenic Peptides Correlation with Celiac Disease: A Systematic Review

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ABSTRACT

Background: *Current markers for monitoring of Celiac disease (CD) and outcome after gluten-free diet (GFD) are limited. Urinary gluten immunogenic peptide (UGIP) has been shown to correlate with gluten intake and mucosal damage in CD. Hence our study objective was to review the evidence of efficacy of UGIP as a biomarker for CD*

Method: *This systematic review was conducted using standards outlined in the PRISMA statement. Databases including PubMed, ProQuest, EBSCOHost, and Google Scholar were searched for relevant studies (randomized controlled trials (RCTs) and observational) up to March 2023. Newcastle Ottawa Scale and Cochrane Risk of Bias were used to assess the quality of included papers..*

Result: *T: Literature search identified 85 studies, and after assessment of eligibility, eight studies were eventually reviewed. UGIP concentration was found to correlate with degree of mucosal damage of CD (Marsh II-III). Although three observational studies found a correlation between gluten intake and UGIP concentration, two RCTs did not find UGIP reliable for determining GFD adherence. In addition, UGIP concentrations did not correlate with antibody titers and clinical symptoms.*

Conclusion: *UGIP may be useful for predicting degree of mucosal damage in CD. However, further studies are needed to evaluate its role in GFD adherence.*

Keywords*: Celiac disease, Gluten-free diet, Systematic Review, Urinary gluten immunogenic peptides*

ABSTRAK

Latar belakang: *Pemeriksaan untuk memantau penyakit celiac (CD) dan perbaikan setelah diet bebas gluten masih terbatas. Peptida imunogenik gluten urin (UGIP) telah ditunjukkan memiliki korelasi dengan asupan gluten serta kerusakan mukosa pada pasien CD. Oleh karena itu, studi ini bertujuan untuk meninjau bukti terkait penggunaan UGIP sebagai penanda CD.*

Metode: *Tinjauan sistematis ini dilakukan sesuai dengan pedoman pernyataan PRISMA. Pencarian literatur dilakukan menggunakan PubMed, ProQuest, EBSCOHost, dan Google Scholar untuk jurnal relevan yang diterbitkan hingga Maret 2023. Newcastle Ottawa Scale dan Cochrane Risk of Bias digunakan dalam penilaian*

kualitas studi.

Hasil: *Pencarian literatur mengidentifikasi 85 penelitian. Setelah dilakukan penilaian, delapan studi diikutsertakan dalam studi ini. Konsentrasi UGIP yang terdeteksi dalam urin berkorelasi dengan tingkat kerusakan mukosa pasien CD (Marsh II-III). Meskipun tiga studi observasi menyimpulkan bahwa ada korelasi antara asupan gluten dan deteksi UGIP, dua uji randomized controlled trials (RCT) menemukan bahwa UGIP tidak dapat diandalkan untuk menentukan kepatuhan terhadap GFD. Selain itu, konsentrasi UGIP tidak berkorelasi dengan titer antibodi dan gejala klinis..*

Kesimpulan*: UGIP dapat dipertimbangkan untuk membantu dalam memprediksi tingkat keparahan kerusakan mukosa pada pasien CD. Namun, studi lebih lanjut diperlukan untuk mengevaluasi perannya dalam memprediksi kepatuhan terhadap GFD..*

Keywords: *Celiac disease, Gluten-free diet, Systematic Review, Urinary gluten immunogenic peptides*

INTRODUCTION

Celiac disease (CD) is an immune-mediated disease characterized by inflammation of the small intestine.[1] This condition is a result of adaptive immune reaction to gluten products in susceptible individuals.[2] CD can develop at any age and varies between countries despite similar geographic conditions.[3] In many regions of the world, CD affects between 0.5 and 1 percent of the general population, with women being affected twice as frequently as men.[4] Genetic risk factors are particularly important for CD, predominantly the HLA gene, which is responsible for at least 40% of the genetically inherited risk for CD. In addition to genetic risk, environmental factors also contribute to an increased risk for CD.[1]

The gluten-free diet (GFD) is the only effective therapy for CD, which requires strict adherence from patients.[5] The objective of this restrictive diet is to alleviate symptoms and to attain restoration of the intestinal mucosa. However, since gluten is a complex protein found in a wide variety of foods, some patients may inadvertently come into contact with gluten despite their efforts to avoid it.[6] CD patients who repeatedly consume gluten, even insignificant amounts, may develop damage to the intestinal mucosa.[7] The current techniques for monitoring compliance of GFD are restricted in their effectiveness, as food questionnaires, celiac serology, and clinical symptoms are unable to offer a precise assessment of adherence. The validity of dietary questionnaires is controversial because patients may not accurately report their gluten consumption. While celiac serological testing is useful for diagnosis and monitoring adherence to a GFD, it has limitations. Antibody levels take a long time to normalize, and occasional accidental gluten exposure cannot be detected, making it unsuitable for strict GFD monitoring. Additionally, serological testing is weakly correlated with mucosal healing. The presence of clinical symptom improvement does not necessarily indicate adherence to a gluten-free diet, as those who strictly adhere to the diet may nonetheless suffer symptoms. Likewise, the improvement of symptoms during clinical follow-up may not be a reliable indicator of adherence to a GFD.[8]

In the CD pathogenesis, gluten immunogenic peptide (GIP) plays a key role in activating the immune system and triggering the T lymphocytes. GIP is able to pass through the intestinal mucous membranes and trigger an immune response.[9] Specific antibodies can be used to detect GIP in urine and stool samples from CD patients. High concentrations of urine GIP (UGIP) have been found to correlate with gluten uptake and inadequate intestinal mucosal recovery upon biopsy.[10] In terms of comparing urine with stool samples, urine samples have several advantages. Urine samples simplify the collection, transport, and storage of samples, are noninvasive, and more cost-effective.[11] Hence our study objective was to review the evidence of efficacy of UGIP as a biomarker for CD.

METHODS

The systematic review was carried out following the guidelines of the PRISMA protocol.[12] We conducted a comprehensive literature search on databases including PUBMED, EBSCOhost, and Proquest databases using specific keywords like “gluten immunogenic peptides,” “celiac disease,” “gluten-free diet,” “adherence,” and “mucosal healing.” The search was limited to articles in the English language published between 2012 until March 2023.

Following a thorough search, the verification of article duplication was conducted utilizing Sysrev, a journal management system based on open-source technology. All relevant studies were included.Exclusion criteria were review articles, conference abstracts, and articles not in English. All studied outcomes were assessed for quality (risk of bias) using the Newcastle Ottawa Scale (NOS)[13] and the Cochrane RoB tool.[14] Reviewers independently reviewed and examined all the literatures. Disagreements were resolved through discussion. Data extractions were performed by all authors.

RESULT

Based on the keywords used, 85 articles were initially found. The subsequent screening and review process is summarized in Figure 1. After filtering duplicates, 68 articles were left for evaluation. A screening for titles and abstracts was performed, and 59 articles were excluded. Five additional articles were excluded from this search, i.e., three articles in the form of scientific posters and two articles in the form of review article. In this study, a total of eight articles were reviewed (Table 1), with five studies showing a low risk of bias and three studies showing a high risk of bias (Table 2 and 3).

Monachesi et al. assessed the diagnostic accuracy of UGIP determination in detecting gluten contamination of the gluten-free diet (GFD) by the implementation of six gluten challenges. The investigation revealed that the ability of UGIP determination to monitor the GFD was inadequate. The presence of UGIP was still observable in those following a stringent gluten-free diet (34%) and/or after undergoing the zero-gluten challenge (41%) (P=0.579). On the other hand, UGIP was mostly found to be negative in subjects after consuming a significant amount of gluten (up to 1 gram) ($P > 0.05$). Subjects doing the gluten contamination elimination diet (GCED) showed a better result, in which UGIP was found to be positive (33%) only after consuming gluten, even in a small amount (5 or 10 mg).[15] Burger et al. evaluated the applicability of self-test UGIP for diagnostic purposes and correlated the test results with reported symptoms by giving the subjects capsules containing placebo and gluten. All subjects were positive for celiac disease confirmed by biopsy, and all subjects had negative UGIP and CD antibodies at baseline. UGIP was detected in 47% and 86% of subjects after consuming 50 mg and 500 mg, respectively. The percentage of UGIP detected in the gluten capsule group was always higher than in the

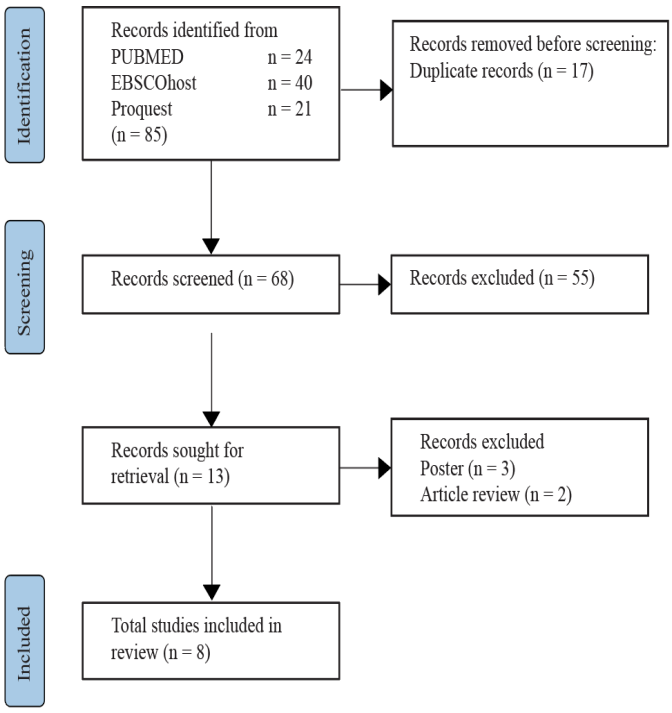

Figure 1. Article Selection

placebo group, but no significance was observed in the outcome.[16]

Three studies compared UGIP concentrations between gluten-free diet (GFD) group and gluten-containing diet (GCD) group. In two studies, Moreno et al.[10] and Ruiz-Carnicer et al.[17] showed that all healthy individuals and CD patients who did not adhere to GFD had detectable UGIP in their urine samples. Some CD patients who adhered to long-term GFD also had positive results, but UGIP concentrations were lower than in the GCD group.[10,17] In the study by Moreno et al. UGIP was detected in 48% of adult CD patients and 45% of pediatric CD patients following GFD, but 70-71% of them were below the limit of quantification (QL) (< 6.25 ng/mL), compared with the GCD group, in which 100% of patients were above QL. Moreno et al. also found that 50 mg of gluten correlated with a higher excretion of GIP in urine samples, compared with 25 mg of gluten from a study of four healthy participants.10 A similar observation was found in the study by Ruiz-Carnicer et al. in which all participants in GCD (healthy and CD patients) group gave positive results in urinary GFD excretion, and most were above QL (100% in the healthy and 82% in CD patients). While GIP could be detected in the urine of 58% of CD patients with a GFD, but only 10% were above QL.[17] In the third study, Coto L et al. demonstrated a direct association between the quantity of gluten consumed and the rate of positive UGIP. In the Coto L et al study, [20] healthy participants were recruited to follow a dietary regimen for 12 days in which they ingested 50 mg and 2 g of gluten. Only 15% were positive for UGIP in participants who consumed 50 mg of gluten, but in those who consumed 2 g of gluten, 90% were positive. Higher concentrations of UGIP were found primarily between 6-9 hours after gluten consumption.[18]

Three studies examined the correlation between UGIP and antibody titers. Two studies found no significant correlation between GIP and CD antibody measurements.10,17 Ruiz et al found that 16% of

Tabel 1. Summaries of the studies

No	Studies	Study Design	Participants (n)	GFD Adherence & Gluten Detection	Antibody titers	Clinical Symptoms Correlation	Mucosal Damagee	Risk of Bias
1	Moreno ML et al. (2017[10]	Prospective observational study	134	UGIP (+) in GFD group after 4-6h and 1-2 days of gluten intake	-	-	All patients with mucosal damage (Marsh II/ III) had quantifiable UGIP	Low risk (NOS score 9)
2	Stefanolo JP et al. (2020)[20]	Prospective observational study	53	69.8% patients on GFD have detectable UGIP	(+) correlation with serum IgA-DGP titers	UGIP more frequently detected in asymptomatic CD patients	-	Low risk (NOS score 9)
3	Ruiz-Carnicer A et al. (2020)[17]	Prospective observational study	112	-	-	-	94% CD patients with mucosal damage had detectable UGIP	Low risk (NOS score 9)
4	Costa AF et al. (2019)[19]	Prospective observational study	44	UGIP testing was consistent with dietary reports in 65.9% of patients.	-	UGIP more frequently detected in asymptomatic CD patients	-	High risk (NOS score 6)

No	Studies	Study Design	Participants (n)	GFD Adherence & Gluten Detection	Antibody titers	Clinical Symptoms Correlation	Mucosal Damagee	Risk of Bias
5	Burger JPW et al. (2022)[16]	Prospective double blinded placebo-controlled crossover study	15	-	-	-	All patients with mucosal damage (Marsh III) had quantifiable UGIP	Low Risk of Bias (ROB Cochrane)
6	Moreno et al (2021)[21]	Clinical Trial	4	-	-	-	All patients with mucosal damage (Marsh II/ III) had quantifiable UGIP	High risk (NOS score 6)
7	Coto L et al. (2021)18	Prospective study	20	95% patients had detectable UGIP after consuming 2 g of gluten	-	-	Low risk (NOS score 9	
8	Monachesi et. al. (2021)15	Randomized, double-blind, controlled study	25	GIP still detected after 3 days of GFD	No correlation with serum IgA anti-transglutaminase	-	-	Low Risk of Bias (ROB Cochrane)

patients with positive UGIP who followed the GFD were also positive for CD antibodies (anti-tTG or AGA), and the remaining 84% of positive UGIP were negative for CD antibodies (k = 0.080, p = 0.210).[17] Costa et al. performed serological testing and found that 21 out of 42 patients had antibody concentrations above the upper limit of normal. Nine out of 42 and 18 out of 42 had positive concentrations for IgA tTG and IgA DGP, respectively. Out of the 25 asymptomatic serologically tested patients, 3 were found to have UGIP, whereas among the 19 serologically tested symptomatic patients, UGIP was not detected in any case.[10] Stefanolo et al. reported that during the 4-week study period, positive excretion of GIP was positively correlated with serum IgA DGP antibody titers (r = 0.49; P < 0.0002) in symptomatic (r=0,6; P=0.009) and asymptomatic (r = 0.45; P<0.007) patients.[19] Thus, urinary excretion GIP did not correlate with antibody titers.

There are two studies evaluating the correlation of UGIP with mucosal damage from intestinal biopsies. Moreno et al. stated that the majority of adult CD patients (86%) with detectable urine GIP had histologic abnormalities (Marsh II-III) (Spearman correlation r=0.75) and 52% of GIP-negative patients had no mucosal damage (Marsh 0-I). The study by Ruiz-Carnicer et al. also observed that individuals with detectable UGIP had a considerably higher mucosal injury (Marsh II-III), whereas patients with negative UGIP had no mucosal damage (Marsh 0-I). The degree of intestinal mucosal injury was significantly correlated with urine GIP in both investigations (r = 0.75 in Moreno et al. and p < 0.001 in Ruiz-Carnicer et al. .10,17

Three studies examined the correlation between the presence of symptoms and UGIP concentrations.17,19,20 Ruiz-Carnicer et al discovered that 27% of patients who tested positive for UGIP had CD symptoms, but only 19% of individuals who tested negative for UGIP had CD symptoms. However, the majority of UGIP-positive and UGIP-negative patients did not have symptoms of CD11. Costa et al. and Stefanolo et al. found that qualitative measure of UGIP from asymptomatic CD patients were higher than in symptomatic patients.[17,19] Costa et al. showed no positive GIP in symptomatic CD patients, and only

three were found positive in asymptomatic patients. Meanwhile, Stefanolo et al. detected positive GIP in urine samples at 43.1% in asymptomatic patients compared with 27.8% in symptomatic patients (p = 0.04). Using a 5-point Likert scale, Burger et al. examined five symptoms: nausea, bloating, diarrhea, abdominal discomfort, and decreased energy. The study found that the most reported symptom with a higher score was abdominal pain.[20]

Moreno et al. conducted a study to evaluate UGIP as means of confirming Refractory Celiac Disease (RCD) that might be classified as "exposed to gluten". The study analyzed four patients who were diagnosed with refractory celiac disease type 1 and had anomalies in the histology of their duodenum as observed in reevaluation biopsies. Three individuals who had aberrant histological findings in their duodenal biopsies were found to have positive UGIP using lateral flow immunoassays. As a result, they were reclassified as being exposed to gluten rather than having RCD. The patients completed a comprehensive food questionnaire on their usage of gluten products.[10]

Table 2. Risk of Bias Assessment using NOS for the studies

	Moreno ML et al. (2015)	Stefanolo JP et al. (2020)	Ruiz-Carnicer A et al. (2020)	Costa AF et al. (2019)	Moreno et al (2021)	Coto L et al. (2021)
Representative of the exposed group	+	+	+	+	-	+
Selection of the unexposed group	+	+	+	-	-	+
Confirm the exposure	+	+	+	+	+	++
Outcome of interest not present at the start of study	+	+	+	-	+	+
Control for important factors or additional factors	++	++	++	+	+	+
Outcome assessment	+	+	+	+	+	+
Follow up long enough for outcome to occur	+	+	+	+	+	+
Adequacy of follow up of cohorts	+	+	+	+	+	+
Total quality scores	9 (low risk)	9 (low risk)	9 (low risk)	6 (high risk)	6 (high risk)	9 (low risk)

Table 3. Risk of bias assessment using Cochrane recommendations for the studies

	Monachesi et al.	Burger JPW et al.
Random sequence generation	Low risk	Low risk
Allocation concealment	Unclear risk	Low risk
Blinding of participants and personnel	Low risk	Low risk
Blinding of outcome assessment	Low risk	Low risk
Incomplete outcome data addresses	Low risk	Low risk
Selective reporting	Low risk	Low risk
Other biases	Low risk	Low risk
Overall risk	Low risk	Low risk

DISCUSSION

Patients with CD who adhered to GFD observe a notable amelioration in their symptoms. Therefore, diagnostic modalities that assess adherence to GFD, as well as unintentional gluten intake in CD patients are of immense importance. While three observational studies established a correlation between gluten intake and UGIP detection, two RCTs indicated that UGIP is not a dependable indicator of adherence to a GFD. Furthermore, UGIP can also be used to predict the extent of mucosal damage in CD patients. Hence, the UGIP does not correlate with symptom severity and antibody titers.

The studies included in this review found mixed results regarding the role of UGIP as a monitoring tool for GFD adherence. Gluten can be absorbed by the intestinal mucosa and filtered by the kidneys, then excreted in the urine.[22,23] UGIP have shown to increase with higher gluten consumption.[18] Compared with stool samples, urine samples have several advantages in terms of simplifying the collection, transport, and storage of samples, being noninvasive, and being more cost-effective.[24] In addition, urine samples can be collected sooner than stool samples after discontinuation of a gluten-free diet because GIP is removed more rapidly in urine samples (24-48 hours) than in stool samples (2-7 days). However, stool tests for GIP may be more sensitive than urine samples due to the larger time window for detection of GIP.[25]

GFD adherence was not correlated by increased concentrations of serum gliadin (AGA), transglutaminase 2 (TGA), or deamidated gliadin peptide (DGPA), with IgA+G DGPA showing the best results for monitoring GFD adherence among all serological types. Antibody titers did not detect accidental gluten exposure because it takes longer for antibody titers to normalize.[24] The use of serology is limited to detecting a lack of adherence but not the strictness of GFD. Ruiz-Carnicer et al found that only 16% of patients with Marsh classification II-III had positive serologic results.[17] The GIP-positive result, which was associated with worse histologic damage, was 39%, higher than the serologic result. Another study by Gerasimidis et al. also reported that gluten exposure was undetectable using anti-tTG antibodies.[26]

The absence of UGIP was associated with healing of the small intestinal mucosa in celiac patients, although the complete histologic resolution of CD-associated intestinal lesions may require up to two years.[19, 27] In all patients with Marsh II/III, UGIP were significantly detected.[28,9]

This review has a number of constraints. The sample size was relatively small in all reported studies. Subjective information provided by study participants regarding previous gluten or GFD consumption might also influence the results of individual studies. Additionally, a duodenal biopsy was not performed as a gold standard test for CD in several studies.

CONCLUSION

UGIP concentration may predict the severity of mucosal damage caused by CD. Although observational studies found a correlation between gluten intake and UGIP but RCTs did not find UGIP reliable for determining adherence to GFD and that UGIP concentrations did not correlate with antibody titers and clinical symptoms. More studies with larger sample sizes are needed to determine the relationship between UGIP and CD severity.

REFERENCES

1. Ludvigsson JF, Murray JA. Epidemiology of Celiac Disease. Gastroenterology Clinics of North America. 2019;48(1):1–18.
2. Parzanese I, Qehajaj D, Patrinicola F, Aralica M, Chiriva-Internati M, Stifter S, et al. Celiac disease: From pathophysiology to treatment. World J Gastrointest Pathophysiol. 2017;8(2):27-38. doi:10.4291/wjgp.v8.i2.27
3. Lebwohl B, Rubio-Tapia A. Epidemiology, Presentation, and Diagnosis of Celiac Disease. Gastroenterology. 2021;160(1):63–75.
4. Gujral N, Freeman HJ, Thomson AB. Celiac disease: prevalence, diagnosis, pathogenesis and treatment. World J Gastroenterol 2012; 18:6036.
5. Melini V, Melini F. Gluten-Free Diet: Gaps and Needs for a Healthier Diet. Nutrients. 2019;11(1):E170.
6. Comino I, Fernández-Bañares F, Esteve M, Ortigosa L, Castillejo G, Fambuena B, et al. Fecal gluten peptides reveal limitations of serological tests and food questionnaires for monitoring gluten-free diet in celiac disease patients. Am J Gastroenterol. 2016;111:1456–65.
7. Catassi C, Fabiani E, Iacono G, D'Agate C, Francavilla R, Biagi F, et al. A prospective, double-blind, placebo controlled trial to establish a safe gluten threshold for patients with celiac disease. Am J Clin Nutr. 2007;85:160–6.
8. Wieser H, Ruiz-Carnicer Á, Segura V, Comino I, Sousa C. Challenges of Monitoring the Gluten-Free Diet Adherence in the Management and Follow-Up of Patients with Celiac Disease. Nutrients. 2021;13(7):2274.
9. Cebolla Á, Moreno M de L, Coto L, Sousa C. Gluten Immunogenic Peptides as Standard for the Evaluation of Potential Harmful Prolamin Content in Food and Human Specimen. Nutrients. 2018;10(12):E1927.
10. 10. Moreno M de L, Cebolla Á, Muñoz-Suano A, Carrillo-Carrion C, Comino I, Pizarro Á, et al. Detection of gluten immunogenic peptides in the urine of patients with coeliac

disease reveals transgressions in the gluten-free diet and incomplete mucosal healing. Gut. 2017;66(2):250–7.

11. Silvester JA, Comino I, Rigaux LN, Segura V, Green KH, Cebolla A, et al. Exposure sources, amounts and time course of gluten ingestion and excretion in patients with coeliac disease on a gluten-free diet. Alimentary Pharmacology & Therapeutics/ 2020; 52(9):1469–1479. doi:10.1111/apt.16075
12. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.
13. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. 2014.
14. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials BMJ 2011; 343 :d5928 doi:10.1136/bmj.d5928
15. Monachesi C, Verma AK, Catassi GN, Franceschini E, Gatti S, Gesuita R, et al. Determination of Urinary Gluten Immunogenic Peptides to Assess Adherence to the Gluten-Free Diet: A Randomized, Double-Blind, Controlled Study. Clin Transl Gastroenterol. 2021 Oct 6;12(10):e00411. doi: 10.14309/ctg.0000000000000411. PMID: 34613954; PMCID: PMC8500619.
16. Burger JPW, van Lochem EG, Roovers EA, Drenth JPH, Wahab PJ. Dose-Escalating (50-500 mg) Gluten Administration Leads to Detectable Gluten-Immunogenic-Peptides in Urine of Patients with Coeliac Disease Which Is Unrelated to Symptoms, a Placebo Controlled Trial. Nutrients. 2022 Apr 23;14(9):1771. doi: 10.3390/nu14091771. PMID: 35565738; PMCID: PMC9105321.
17. Ruiz-Carnicer Á, Garzón-Benavides M, Fombuena B, Segura V, García-Fernández F, Sobrino-Rodríguez S, et al. Negative predictive value of the repeated absence of gluten immunogenic peptides in the urine of treated celiac patients in predicting mucosal healing: new proposals for follow-up in celiac disease. The American Journal of Clinical Nutrition. 2020;112(5):1240–51.
18. Coto L, Sousa C, Cebolla A. Dynamics and Considerations in the Determination of the Excretion of Gluten Immunogenic Peptides in Urine: Individual Variability at Low Gluten Intake. Nutrients. 2021 Jul 29;13(8):2624. doi: 10.3390/nu13082624. PMID: 34444783; PMCID: PMC8398346.
19. Costa AF, Sugai E, Temprano M de la P, Niveloni SI, Vázquez H, Moreno ML, et al. Gluten immunogenic peptide excretion detects dietary transgressions in treated celiac disease patients. WJG. 2019;25(11):1409–20.
20. Stefanolo JP, Tálamo M, Dodds S, Temprano M de la P, Costa AF, Moreno ML, et al. Real-World Gluten Exposure in Patients With Celiac Disease on Gluten-Free Diets, Determined From Gliadin Immunogenic Peptides in Urine and Fecal Samples. Clinical Gastroenterology and Hepatology. 2021 ;19(3):484-491.e1.
21. Moreno ML, Sánchez-Muñoz D, Sanders D, Rodríguez-Herrera A, Sousa C. Verifying Diagnosis of Refractory Celiac Disease With Urine Gluten Immunogenic Peptides as Biomarker. Front Med (Lausanne). 2021 Jan 18;7:601854. doi: 10.3389/fmed.2020.601854. PMID: 33537327; PMCID: PMC7848017.
22. Slot ID, van der Fels-Klerx HJ, Bremer MG, Hamer RJ. Immunochemical Detection Methods for gluten in food products: Where do we go from here? Critical Reviews in Food Science and Nutrition. 2015;56:2455–66. doi:10.1080/10408398.2013.847817.
23. Syage JA, Kelly CP, Dickason MA., Ramirez AC, Leon F., Dominguez R, Sealey-Voyksner JA. Determination of gluten consumption in celiac disease patients on a gluten-free diet. The American Journal of Clinical Nutrition. 2018;107(2), 201–207. doi:10.1093/ajcn/nqx049.
24. Jing J, Gao Y. Urine biomarkers in the early stages of diseases: current status and perspective. Discov Med. 2018;25(136):57-65. PMID: 29579412.
25. Porcelli B, Ferretti F, Biviano I, Santini A, Cinci F, Vascotto M, et al. Testing for fecal gluten immunogenic peptides: a useful tool to evaluate compliance with gluten-free diet by celiacs. Ann Gastroenterol. 2020;33:631–637
26. Gerasimidis K, Zafeiropoulou K, Mackinder M, Ijaz UZ, Duncan H, Buchanan E, et al. Comparison of Clinical Methods With the Faecal Gluten Immunogenic Peptide to Assess Gluten Intake in Coeliac Disease. J Pediatr Gastroenterol Nutr. 2018;67:356–360
27. Wieser H, Ruiz-Carnicer Á, Segura V, Comino I, Sousa C. Challenges of Monitoring the Gluten-Free Diet Adherence in the Management and Follow-Up of Patients with Celiac Disease. Nutrients. 2021;13(7):2274.
28. Coto L, Sousa C, Cebolla A. Individual variability in patterns and dynamics of fecal gluten immunogenic peptides excretion after low gluten intake. Eur J Nutr. 2022;61:2033–2049