UNIVERSIDADE
BEIRA INTERIOR

Celiac disease and associated autoimmune conditions

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Dissertação para obtenção do Grau de Mestre em

Medicina

(mestrado integrado)

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abril de 2023

Declaração de Integridade

Eu, Ana Sofia Cruz Afonso Romano, que abaixo assino, estudante com o número de inscrição 40495 do Mestrado Integrado em Medicina da Faculdade de Ciências da Saúde, declaro ter desenvolvido o presente trabalho e elaborado o presente texto em total consonância com o **Código de Integridades da Universidade da Beira Interior**.

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Universidade da Beira Interior, Covilhã 21 / 04 /2023

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Agradecimentos

Primeiramente, gostaria de agradecer ao meu orientador, Dr. Pedro Marcos, pelo acompanhamento e orientação ao longo de toda a jornada que culminou neste trabalho.
Aos meus pais e irmãs, que me deram ferramentas para percorrer o meu caminho, mas nunca me largaram a mão e aplaudiram sempre todas as minhas conquistas.
Aos meus amigos, que permitiram que a Covilhã se tornasse numa casa e que todos os momentos fossem muito mais especiais.
Ao Nuno, que me acompanhou e torceu sempre pelo meu sucesso.

Abstract

Introduction: Celiac disease (CD) is a chronic, immune-mediated enteropathy that has been increasingly associated with other autoimmune conditions. The aim of this work was to review which autoimmune disorders have been associated with CD, highlighting the strength and clinical impact of that associations.

Methods: Review of the published literature in PubMed between 2002 and 2023. Systematic reviews, meta-analysis, case-control and cohort studies were preferred for analysis.

Results: CD has relevant associations with type 1 diabetes mellitus, autoimmune thyroid disorders (in particular, Hashimoto's thyroiditis), systemic lupus erythematosus, arthritis rheumatoid, autoimmune hepatitis, primary biliary cholangitis, Crohn's disease, ulcerative colitis, microscopic colitis, IgA nephropathy and psoriasis. Other autoimmune diseases such as autoimmune gastritis, Addison's disease, Sjogren's syndrome and non-infectious uveitis have been described as being potentially associated with CD, but the available data is weak to assume a relevant association.

Conclusion: This review confirms that CD has important associations with others autoimmune diseases. Physicians who manage patients with CD or with any other above-described autoimmune condition must be aware of that possible coexistence. This knowledge will allow early diagnosis and treatment of patients with concomitant diseases and the improvement of outcomes.

Keywords

Celiac disease;gluten enteropathy;associated conditions;autoimmune diseases;risk

Resumo

Introdução: A doença celíaca é uma doença crónica imunomediada que tem sido cada vez mais associada a outras patologias autoimunes. O objetivo do presente trabalho foi rever quais são as doenças autoimunes comumente associadas à doença celíaca, destacando a evidência científica e o impacto clínico dessas associações.

Métodos: Revisão da literatura publicada na PubMed entre 2002 e 2023. Para análise foi dada preferência a revisões sistemáticas, meta-análises, caso-controle e estudos de coorte.

Resultados: A doença celíaca tem apresentado associações relevantes com as seguintes patologias: diabetes mellitus tipo 1, doenças autoimunes da tiroide (nomeadamente, tiroidite de Hashimoto), lúpus eritematoso sistêmico, artrite reumatoide, hepatite autoimune, colangite biliar primária, doença de Crohn, colite ulcerosa, colite microscópica, nefropatia por IgA e psoríase. Outras doenças autoimunes tais como a gastrite autoimune, a doença de Addison, a síndrome de Sjogren e a uveíte não-infeciosa, têm sido descritas com alguma frequência em doentes com doença celíaca, contudo os dados disponíveis são insuficientes para assumir uma associação relevante.

Conclusão: Esta revisão confirma que a doença celíaca apresenta associações importantes com outras doenças autoimunes. Médicos que avaliem e sigam doentes com doença celíaca ou com qualquer umas das doenças autoimunes acima referidas devem ser conhecedores dessa possível coexistência. Esse conhecimento poderá permitir o diagnóstico e tratamento precoce de utentes com doenças concomitantes e, consequentemente, uma melhoria dos resultados clínicos.

Palavras-chave

Doença celíaca;enteropatia ao glúten;doenças associadas;doenças autoimunes;risco.

Index

Abbreviations List

Anti-tTG	Anti-transglutaminase antibody
CI	Confidence interval
GFD	Gluten-free diet
HLA	Human leukocyte antigen
HR	Hazard ratio
IgA	Immunoglobulin A
IgG	Immunoglobulin G
OR	Odds ratio
RR	Risk ratio

1. Introduction

Celiac disease (CD) is a chronic, immune-mediated enteropathy that occurs in genetically predisposed individuals and has gluten as a trigger.[1, 2] In the past, CD was considered a rare disease. However, CD has emerged as an important condition with a global prevalence of 1.4%, which varies according to age (higher in children than adults: 0.9% vs 0.5%, p<0.001), gender (higher in women than men: 0.6% vs 0.4%, p<0.001) and region (higher in Western countries than in Asia and Africa).[3]

The clinical spectrum of CD is wide, which explains the challenging diagnosis and underdetection. Its classic clinical manifestations are more common in children than in adults who tend to present fewer and atypical symptoms. The usual signs and symptoms of CD include chronic diarrhea, weight loss and abdominal pain.[1, 4] Nonetheless, others such as constipation, flatulence, abdominal distention and fatigue may occur. Nearly 50% of all patients may suffer from extraintestinal manifestations, such as dermatitis herpetiformis, atrophic glossitis, anemia, hyposplenism, metabolic bone disorders, abnormal liver tests, and neuropsychiatric disturbances.[4]

The diagnosis of CD relies on three tiers: (1) serological tests - usually through the measurement of anti-transglutaminase immunoglobulin A (anti-tTG IgA) and immunoglobulin A (IgA) serum levels, but measuring anti-endomysial IgA and immunoglobulin G (IgG) antibodies (particularly the anti-deamidated gliadin peptide antibody IgG), can be useful when anti-tTG IgA titer is lower than 10 U/mL with normal IgA levels, and when there is a total IgA deficiency; (2) duodenal histology - patients with positive serological test should undergo an upper endoscopy with duodenal biopsies, as should all other patients from whom the level of clinical suspicion is high even though serological tests return negative; histopathological findings characteristic of CD (increased intraepithelial lymphocytes, villus atrophy and crypt hyperplasia) must be classified according to the modified Marsh classification; (3) genetic testing - useful in ruling out CD, since the absence of human leukocyte antigen (HLA)-DQ2 and -DQ8 haplotypes virtually excludes CD diagnosis.[1, 4-6] In general, a positive serology associated with a compatible histology confirms the CD diagnosis. Serological tests and duodenal biopsies must be done on a gluten-containing diet to avoid false negative results.[4]

The cornerstone of CD treatment continues to be a gluten-free diet (GFD), which means that foods containing wheat, rye, and barley (or their derivatives) must be avoided.[5]

Since CD is a systemic immune-mediated inflammatory disease of the small bowel increasingly associated with other conditions namely autoimmune diseases,[6] this

review aims to revisit and summarize which autoimmune disorders have been associated with CD, highlighting the strength and clinical impact of that associations.

2. Methods

A narrative review was performed based on studies published in PubMed between 2002 and 2023 using keywords such as “celiac disease”, “gluten enteropathy”, “associated conditions”, “autoimmune diseases” and “risk”. Articles written in English or Portuguese were reviewed. Studies of interest for full-text analysis were selected according to the information contained in titles and abstracts. Systematic reviews, meta-analysis, case-control and cohort studies were preferred.

3. Results

CD has been particularly associated with type 1 diabetes mellitus, with HLA-DQ2.5 and HLA-DQ8 being the higher-risk genes enhancing the coexistence of these two conditions.[7, 8] A large population-based study, including 26605 patients with type 1 diabetes mellitus, found a prevalence of CD of 6.0% (95% Confidence Interval [CI] 5.0-6.9).[9] Nine longitudinal cohort studies covering 11157 children and adolescents have demonstrated a weighted pooled prevalence of CD in patients with type 1 diabetes mellitus of 5.1% (95% CI 3.1-7.4).[10] According to a more recent meta-analysis that analyzed 87 studies, the weighted prevalence of CD in type 1 diabetes mellitus patients is around 4.5% (95% CI 4.0-5.5).[7]

Hashimoto's thyroiditis and Graves' disease are autoimmune thyroid disorders that have been frequently associated with CD.[11] The prevalence of CD in patients with autoimmune thyroid disease is 1.6% (95% CI 1.3-1.9), a higher value than in general population.[11, 12] It is also well described that Hashimoto's thyroiditis is more commonly associated with other autoimmune diseases than Grave's disease.[13, 14]

A pooled analysis of CD and risk of future systemic lupus erythematosus found a 3-fold increased risk of systemic lupus erythematosus in CD patients compared to the general population (Hazard Ratio [HR] 3.5, 95% CI 2.5-4.9).[15] The same study described that the probability of developing systemic lupus erythematosus during the first year after CD diagnosis is higher than 5 years after CD diagnosis (HR 8.9, 95% CI 3.4-23.0 vs HR 2.5, 95% CI 1.6-4.1).[15] The univariate analysis of a case-control study including 5018 patients with systemic lupus erythematosus and 25090 age- and sex-matched controls described a significantly higher prevalence of CD in patients with systemic lupus erythematosus than in controls (0.8% vs 0.2%, $p<0.001$).[16] The multivariate analysis of that case-control study found that lupus was significantly associated with CD (Odds Ratio [OR] 3.9, 95% CI 2.6-6.0).[16]

The relation between CD and rheumatoid arthritis has been also described.[17, 18] Despite having different pathophysiologies, these conditions share several clinical aspects, being rheumatological symptoms common in CD patients and gastrointestinal manifestations frequent in rheumatoid arthritis patients.[19] A bidirectional two-sample mendelian randomization study concluded that individuals with CD may have a higher risk of developing rheumatoid arthritis (OR 1.5, 95% CI 1.2-1.8).[20]

A recent meta-analysis demonstrated that the prevalence of CD in autoimmune hepatitis patients is around 3.5% (95% CI 1.6-5.3), significantly higher than in the general population.[21] A cross-sectional study analyzing 2799 healthy participants and 100 patients with autoimmune liver disease revealed that the prevalence of CD in patients

with autoimmune hepatitis is around 3.0%.[22] In the same study, the authors concluded that the prevalence of CD in autoimmune hepatitis patients could be at least of 4.0%.[22] In Italy, 47 patients with autoimmune hepatitis were studied, and, it was concluded that the crude prevalence rate of CD was around 6.4% (95% CI 1.3-18.6), a higher value than the observed in general population that was 0.5% (95% CI 0.3-0.8).[23]

According to an extended review of the literature, the mean prevalence of CD in primary biliary cholangitis is around 3.1%, but the reverse (the mean prevalence of primary biliary cholangitis in CD) is just 0.4%.[24] A cross-sectional study that included 100 participants with some autoimmune liver disease obtained a mean prevalence of CD in patients with primary biliary cholangitis around 12.5%.[22] A recent meta-analysis analyzing 10 studies obtained a weighted prevalence of CD in primary biliary cholangitis patients around 7.8% (95% CI 5.0–12.0).[25] A large unicentric study comparing the prevalence of CD between a cohort with primary biliary cholangitis and a cohort with other liver diseases found that CD is much more commonly diagnosed in patients with primary biliary cholangitis than in patients with other liver diseases (11.8% vs 2.9%, $p<0.01$).[26]

Concerning CD and inflammatory bowel disease, a systematic review that analyzed 27 studies concluded that CD patients have 11-fold more risk of inflammatory bowel disease than the general population (OR 11.1, 95% CI 8.6-14.4). This review also analyzed the reverse and concluded that patients with inflammatory bowel disease seem to have a moderately higher risk of CD (OR 2.2, 95% CI 1.9-2.6).[27] The investigators also described that patients with CD harbor increased risk for both classic forms of inflammatory bowel disease: Crohn's disease (OR 10.4, 95% CI 4.5-23.8) and ulcerative colitis (OR 6.9, 95% CI 4.8-10.2).[27] A recent meta-analysis including 65 studies found an increased risk of CD in patients with inflammatory bowel disease (RR 3.9, 95% CI 2.2-7.0) and an increased risk of inflammatory bowel disease in patients with CD (RR 9.9, 95% CI 4.0-24.2).[28] This meta-analysis also reports that Crohn's disease is more associated with CD than ulcerative colitis (RR 3.2, 95% CI 1.8-5.6 vs RR 2.8, 95% CI 1.8-4.4).[28] Furthermore, another meta-analysis demonstrated a statiscally significant association between CD and microscopic colitis (OR 8.3, 95% CI 5.9-11.6).[29] CD was prevalent in both types of microscopic colitis: 5.2% (95% CI 2.2-12.1) in collagenous colitis and 6.3% (95% CI 3.4-11.5) in lymphocytic colitis.[29]

According to a population-based prospective cohort study, individuals with CD could also have 3-fold more risk of developing IgA nephropathy (HR 3.0, 95% CI 1.2-7.6).[30] This association is reinforced by a meta-analysis describing an increased risk of IgA nephropathy in CD patients (RR 2.6, 95% CI 1.3-5.4).[31]

In literature, there is a meta-analysis that describes a significant association between psoriasis and CD: OR 2.2 (95% CI 1.7-2.7) for CD in patients with psoriasis and OR 1.8 (95% CI 1.4-2.4) for psoriasis in patients with CD.[32] This meta-analysis also revealed a significantly increased risk of new-onset psoriasis in CD (HR 1.8, 95% CI 1.6-1.9).[32] Another meta-analysis including 12912 individuals with psoriasis and 24739 controls revealed that patients with psoriasis harbor a 3-fold increased risk of CD compared to participants without psoriasis (OR 3.1, 95% CI 1.9-5.0).[33] A case-control study, including 12502 patients with psoriasis and 24285 age- and sex-matched controls, described a prevalence of CD higher in patients with psoriasis than in controls (0.29% vs 0.11%, $p<0.001$). [34] This study concluded that psoriasis was associated with CD (OR 2.7, 95% CI 1.7-4.5).[34]

Other autoimmune diseases such as autoimmune atrophic gastritis,[35, 36] Addison's disease, [13, 37] Sjogren's disease,[18] and non-infectious uveitis,[38, 39] have been described in some studies as being associated with CD, but the available evidence is not strong enough to assume that association.

4. Discussion

This focused review highlights that CD has important associations with other autoimmune conditions, namely: type 1 diabetes mellitus, autoimmune thyroid disorders, systemic lupus erythematosus, arthritis rheumatoid, autoimmune hepatitis, primary biliary cholangitis, inflammatory bowel diseases (including microscopic colitis), IgA nephropathy and psoriasis.

Naturally, this work has some limitations. The most important is that it is a narrative review and only a database was used for literature search. However, PubMed is probably the largest database out there and data for analysis was mainly extracted from systematic reviews, meta-analysis, cohort and case-control studies. These facts strengths our findings and become our conclusions reliable.

It is estimated that approximately 15% of patients with type 1 diabetes mellitus may develop another autoimmune disease.[7, 40] The association between CD and type 1 diabetes mellitus is well-established and has strong scientific evidence.[7-10] Due to this close association, the presence of CD or type 1 diabetes mellitus should lead to screen the other disease.[7, 9] Moreover, diet is a cornerstone in the treatment of both diseases and a GFD may have a positive impact on glycemic control.[9]

The association between autoimmune thyroid diseases and CD has been demonstrated and may justify that patients with autoimmune thyroid disease (mainly, Hashimoto's thyroiditis) should be primary candidates for CD screening.[11-13] Although there is no evidence to support the reverse (the screening for autoimmune thyroid disease in patients with CD), it might be prudent to check regularly the thyroid function in CD patients.

The association between CD and systemic lupus erythematosus has been advocated in the literature. Despite of CD harbors an increased risk of lupus when compared to the general population, that risk is low and do not justify the screening for systemic lupus erythematosus in asymptomatic patients with CD.[15, 16] Nevertheless, clinicians should be aware of that possible association, even because CD can be a very tricky diagnosis in patients with lupus.[16]

Concerning rheumatoid arthritis, CD patients may present an increased risk for developing this rheumatic disease. However, that risk seems to be mild.[18, 20] Physicians should keep in mind the described association between these conditions, but there is not enough data to support screening for rheumatoid arthritis in cases of CD.[18, 20]

Several studies have shown that patients with autoimmune hepatitis may have or develop concomitant CD.[21-23] Curiously, CD by itself can be the cause of abnormal liver tests (mainly increased transaminases) in the absence of any primary liver disease.[22]

Indeed, it was calculated that approximately 40% of adult patients with CD may course with increased liver transaminases.[22] Taking into account the revised literature, screening for CD in patients with autoimmune hepatitis is advisable. More, CD screening should be part of the investigation of abnormal liver tests, mainly in youth and young adults. On the other hand, it is important to monitor serum liver enzymes during the follow-up of patients with CD and to be aware that CD and autoimmune hepatitis can coexist.[21, 41]

The association between CD and primary biliary cholangitis has been reported, but the prevalence of CD in primary biliary cholangitis patients seems to be much higher than the opposite.[24, 26] Based on the revised literature, screening for CD in patients with primary biliary cholangitis diagnosis should be encouraged. The reverse cannot be recommended. However, as in any patient with cholestasis (namely increased alkaline phosphatases and gamma-glutamyl transferase) and imaging excluding extrahepatic biliary obstruction, primary biliary cholangitis should be considered as part of the differential diagnosis in CD patients as in general population.

Notably, inflammatory bowel disease and CD present a relevant association. According to the available data, the risk of a patient with CD for developing an inflammatory bowel disease is much higher than the opposite, and CD has been more frequently associated with Crohn's disease than with ulcerative colitis.[27, 28] In addition, we found that CD has a significant prevalence in both types of microscopic colitis.[29] CD diagnosis may be tricky in patients with inflammatory bowel disease, because of the similar gastrointestinal signs and symptoms and the possible effect of the immunosuppressants treatments. Therefore, it is important to keep in mind that CD and inflammatory bowel disease can coexist in the same patient. Indeed, all patients with inflammatory bowel disease should be screen for CD at the time of the diagnosis, or, during the follow-up when the initial CD screening was negative.

Another association that has been described is between CD and IgA nephropathy.[30, 31] Studies support this association and the need to monitor renal function in patients with CD.[30, 31, 42] The adoption of GFD is crucial to avoid mesangial deposition of IgA and may reduce the risk of developing this renal condition in CD patients.[42]

A proven dermatologic disease that can affect patients with CD is psoriasis.[32-34, 43, 44] It has been demonstrated that CD patients are more prone to develop psoriasis, and, patients with psoriasis may also be at risk for developing CD.[32-34] Considering the risk of coexistence of these two conditions, when a patient has confirmation of one it is important to rule out the other.[32, 44, 45] CD patients who adopted a GFD might have a lower probability for developing psoriasis. In patients with both conditions, a GFD might help to control skin lesions.[45]

In spite of there is weak data reporting a possible association between CD and other autoimmune disorders, such as autoimmune gastritis, Addison's disease and Sjogren's syndrome, physicians should keep in mind that these conditions may occur simultaneously in the same patient.

In conclusion, this review provides another perspective about CD and its potential associations with other autoimmune diseases. We found that type 1 diabetes mellitus, Hashimoto's thyroiditis, autoimmune hepatitis, primary biliary cholangitis, Crohn's disease, ulcerative colitis, microscopic colitis and psoriasis can coexist frequently with CD. Physicians who manage patients with any of these conditions must be aware of that possible associations. This knowledge will allow early diagnosis and treatment of patients with concomitant diseases and consequently the improvement of outcomes.

5. References

1. van der Windt DA, Jellema P, Mulder CJ, Kneepkens CM, van der Horst HE. Diagnostic testing for celiac disease among patients with abdominal symptoms: a systematic review. JAMA. 2010;303(17):1738-46.

2. Hindryckx P, Levesque BG, Holvoet T, Durand S, Tang CM, Parker C, et al. Disease activity indices in coeliac disease: systematic review and recommendations for clinical trials. Gut. 2018;67(1):61-9.

3. Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, et al. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2018;16(6):823-36 e2.

4. Calado J, Verdelho Machado M. Celiac Disease Revisited. GE Port J Gastroenterol. 2022;29(2):111-24.

5. Aljada B, Zohni A, El-Matary W. The Gluten-Free Diet for Celiac Disease and Beyond. Nutrients. 2021;13(11).

6. Haines ML, Anderson RP, Gibson PR. Systematic review: The evidence base for long-term management of coeliac disease. Aliment Pharmacol Ther. 2008;28(9):1042-66.

7. Nederstigt C, Uitbeijerse BS, Janssen LGM, Corssmit EPM, de Koning EJP, Dekkers OM. Associated auto-immune disease in type 1 diabetes patients: a systematic review and meta-analysis. Eur J Endocrinol. 2019;180(2):135-44.

8. Prieto J, Singh KB, Nnadozie MC, Abdal M, Shrestha N, Abe RAM, et al. New Evidence in the Pathogenesis of Celiac Disease and Type 1 Diabetes Mellitus: A Systematic Review. Cureus. 2021;13(7):e16721.

9. Elfstrom P, Sundstrom J, Ludvigsson JF. Systematic review with meta-analysis: associations between coeliac disease and type 1 diabetes. Aliment Pharmacol Ther. 2014;40(10):1123-32.

10. Pham-Short A, Donaghue KC, Ambler G, Phelan H, Twigg S, Craig ME. Screening for Celiac Disease in Type 1 Diabetes: A Systematic Review. Pediatrics. 2015;136(1):e170-6.

11. Ashok T, Patni N, Fatima M, Lamis A, Siddiqui SW. Celiac Disease and Autoimmune Thyroid Disease: The Two Peas in a Pod. Cureus. 2022;14(6):e26243.

12. Roy A, Laszkowska M, Sundstrom J, Lebwohl B, Green PH, Kampe O, et al. Prevalence of Celiac Disease in Patients with Autoimmune Thyroid Disease: A Meta-Analysis. Thyroid. 2016;26(7):880-90.

13. Kahaly GJ, Schuppan D. Celiac disease and endocrine autoimmunity. Dig Dis. 2015;33(2):155-61.

14. Kahaly GJ, Frommer L, Schuppan D. Celiac Disease and Glandular Autoimmunity. Nutrients. 2018;10(7).

15. Ludvigsson JF, Rubio-Tapia A, Chowdhary V, Murray JA, Simard JF. Increased risk of systemic lupus erythematosus in 29,000 patients with biopsy-verified celiac disease. J Rheumatol. 2012;39(10):1964-70.

16. Dahan S, Shor DB, Comaneshter D, Tekes-Manova D, Shovman O, Amital H, et al. All disease begins in the gut: Celiac disease co-existence with SLE. Autoimmun Rev. 2016;15(8):848-53.

17. Zhernakova A, Stahl EA, Trynka G, Raychaudhuri S, Festen EA, Franke L, et al. Meta-analysis of genome-wide association studies in celiac disease and rheumatoid arthritis identifies fourteen non-HLA shared loci. PLoS Genet. 2011;7(2):e1002004.

18. Zylberberg HM, Lebwohl B, Green PHR. Celiac Disease-Musculoskeletal Manifestations and Mechanisms in Children to Adults. Curr Osteoporos Rep. 2018;16(6):754-62.

19. Lerner A, Matthias T. Rheumatoid arthritis-celiac disease relationship: joints get that gut feeling. Autoimmun Rev. 2015;14(11):1038-47.

20. Hua L, Xiang S, Xu R, Xu X, Liu T, Shi Y, et al. Causal association between rheumatoid arthritis and celiac disease: A bidirectional two-sample mendelian randomization study. Front Genet. 2022;13:976579.

21. Haggard L, Glimberg I, Lebwohl B, Sharma R, Verna EC, Green PHR, et al. High prevalence of celiac disease in autoimmune hepatitis: Systematic review and meta-analysis. Liver Int. 2021;41(11):2693-702.

22. Mirzaagha F, Azali SH, Islami F, Zamani F, Khalilipour E, Khatibian M, et al. Coeliac disease in autoimmune liver disease: a cross-sectional study and a systematic review. Dig Liver Dis. 2010;42(9):620-3.

23. Villalta D, Girolami D, Bidoli E, Bizzaro N, Tampoia M, Liguori M, et al. High prevalence of celiac disease in autoimmune hepatitis detected by anti-tissue tranglutaminase autoantibodies. J Clin Lab Anal. 2005;19(1):6-10.

24. Volta U, Caio G, Tovoli F, De Giorgio R. Gut-liver axis: an immune link between celiac disease and primary biliary cirrhosis. Expert Rev Gastroenterol Hepatol. 2013;7(3):253-61.

25. Jena A, Kumar MP, Kumar A, Birda CL, Choudhury A, Kumar N, et al. Liver abnormalities in celiac disease and response to gluten free diet: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2023;38(1):11-22.

26. Callichurn K, Cvetkovic L, Therrien A, Vincent C, Hetu PO, Bouin M. Prevalence of Celiac Disease in Patients with Primary Biliary Cholangitis. J Can Assoc Gastroenterol. 2021;4(1):44-7.

27. Shah A, Walker M, Burger D, Martin N, von Wulffen M, Koloski N, et al. Link Between Celiac Disease and Inflammatory Bowel Disease. J Clin Gastroenterol. 2019;53(7):514-22.
28. Pinto-Sanchez MI, Seiler CL, Santesso N, Alaedini A, Semrad C, Lee AR, et al. Association Between Inflammatory Bowel Diseases and Celiac Disease: A Systematic Review and Meta-Analysis. Gastroenterology. 2020;159(3):884-903 e31.
29. Nimri FM, Muhanna A, Almomani Z, Khazaaleh S, Alomari M, Almomani L, et al. The association between microscopic colitis and celiac disease: a systematic review and meta-analysis. Ann Gastroenterol. 2022;35(3):281-9.
30. Welander A, Sundelin B, Fored M, Ludvigsson JF. Increased risk of IgA nephropathy among individuals with celiac disease. J Clin Gastroenterol. 2013;47(8):678-83.
31. Wijarnpreecha K, Thongprayoon C, Panjawatanan P, Thamcharoen N, Pachariyanon P, Nakkala K, et al. Celiac disease and the risk of kidney diseases: A systematic review and meta-analysis. Dig Liver Dis. 2016;48(12):1418-24.
32. Acharya P, Mathur M. Association between psoriasis and celiac disease: A systematic review and meta-analysis. J Am Acad Dermatol. 2020;82(6):1376-85.
33. Ungprasert P, Wijarnpreecha K, Kittanamongkolchai W. Psoriasis and Risk of Celiac Disease: A Systematic Review and Meta-analysis. Indian J Dermatol. 2017;62(1):41-6.
34. Birkenfeld S, Dreiher J, Weitzman D, Cohen AD. Coeliac disease associated with psoriasis. Br J Dermatol. 2009;161(6):1331-4.
35. Conti L, Galli G, Ligato C, Carabotti M, Annibale B, Lahner E. Autoimmune atrophic gastritis and coeliac disease: A case-control study. Dig Liver Dis. 2023;55(1):69-74.
36. Zingone F, Marsilio I, Fassan M, Pilotto V, Maddalo G, Lorenzon G, et al. Duodenal Histological Findings and Risk of Coeliac Disease in Subjects with Autoimmune Atrophic Gastritis: A Retrospective Evaluation. Digestion. 2021;102(4):615-21.
37. Freeman HJ. Endocrine manifestations in celiac disease. World J Gastroenterol. 2016;22(38):8472-9.
38. Joltikov KA, Lobo-Chan AM. Epidemiology and Risk Factors in Non-infectious Uveitis: A Systematic Review. Front Med (Lausanne). 2021;8:695904.
39. Fousekis FS, Katsanos A, Katsanos KH, Christodoulou DK. Ocular manifestations in celiac disease: an overview. Int Ophthalmol. 2020;40(4):1049-54.

40. Kaur N, Bhadada SK, Minz RW, Dayal D, Kochhar R. Interplay between Type 1 Diabetes Mellitus and Celiac Disease: Implications in Treatment. Dig Dis. 2018;36(6):399-408.

41. Davison S. Coeliac disease and liver dysfunction. Arch Dis Child. 2002;87(4):293-6.

42. Stanley JC, Deng H. Progress in Pathogenesis of Immunoglobin A Nephropathy. Cureus. 2020;12(6):e8789.

43. Rodrigo L, Beteta-Gorriti V, Alvarez N, Gomez de Castro C, de Dios A, Palacios L, et al. Cutaneous and Mucosal Manifestations Associated with Celiac Disease. Nutrients. 2018;10(7).

44. Pietrzak D, Pietrzak A, Krasowska D, Borzecki A, Franciszkiewicz-Pietrzak K, Polkowska-Pruszynska B, et al. Digestive system in psoriasis: an update. Arch Dermatol Res. 2017;309(9):679-93.

45. Bhatia BK, Millsop JW, Debbaneh M, Koo J, Linos E, Liao W. Diet and psoriasis, part II: celiac disease and role of a gluten-free diet. J Am Acad Dermatol. 2014;71(2):350-8.