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Review Article

Is Celiac Disease (CD) Prevalent in Patients with Multiple Sclerosis (MS): A Systematic Review and Meta-Analysis

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Background. Celiac disease (CD) is an autoimmune disease, and its prevalence reported variously in different studies. The goal of this study is to evaluate the pooled prevalence of CD in subjects with MS. *Methods*. PubMed, Scopus, EMBASE, Web of Science, and Google Scholar along with gray literature were systematically searched. The search included all relevant studies which were published up to October 2022. Two researchers independently searched all databases and also references of included studies. *Results*. We found 8211 articles by literature search, and after deleting duplicates, 5594 remained. Fifteen articles remained for meta-analysis. Totally, 31418 patients were evaluated, and the total number of possible/confirmed cases was 124. Studies were published between 2004 and 2020, and the most published studies were from Italy. Five studies provided information regarding controls. The total number of controls was 22394, of whom 22 had CD. Mean age ranged from 35 to 55 years. The pooled prevalence of CD in MS patients was 0 ($I^2 = 88.2\%$, $p < 0.001$). The pooled odds of CD in subjects with MS are 0.46 (95% CI: 0.19-1.1) ($I^2 = 0$, $p = 0.9$). *Conclusion*. The pooled prevalence of this systematic review showed that CD is not prevalent in MS cases.

1. Introduction

Multiple sclerosis (MS) is an autoimmune disease of central nervous system (CNS) [1, 2], affecting youth all over the world. The exact etiology of the disease is unknown, but multiple putative etiologic factors have been considered to play a role in development of MS [3].

Accompanying with a wide range of autoimmune diseases, such as hypothyroidism, inflammatory bowel disease, rheumatoid arthritis, and diabetes, could highlight common genetic or environmental exposures between MS and other autoimmune diseases [3, 4]. Epidemiological studies showed an increased susceptibility for developing another autoimmune diseases in subjects with a single autoimmune disease [5–8].

Celiac disease (CD) is an autoimmune gluten-sensitive enteropathy, which results in small intestinal lesions and malabsorption in affected cases [9]. The pathogenesis of CD is based on genetic factors and mucosal immune response [10]. Almost all affected patients with CD have HLA DR3-

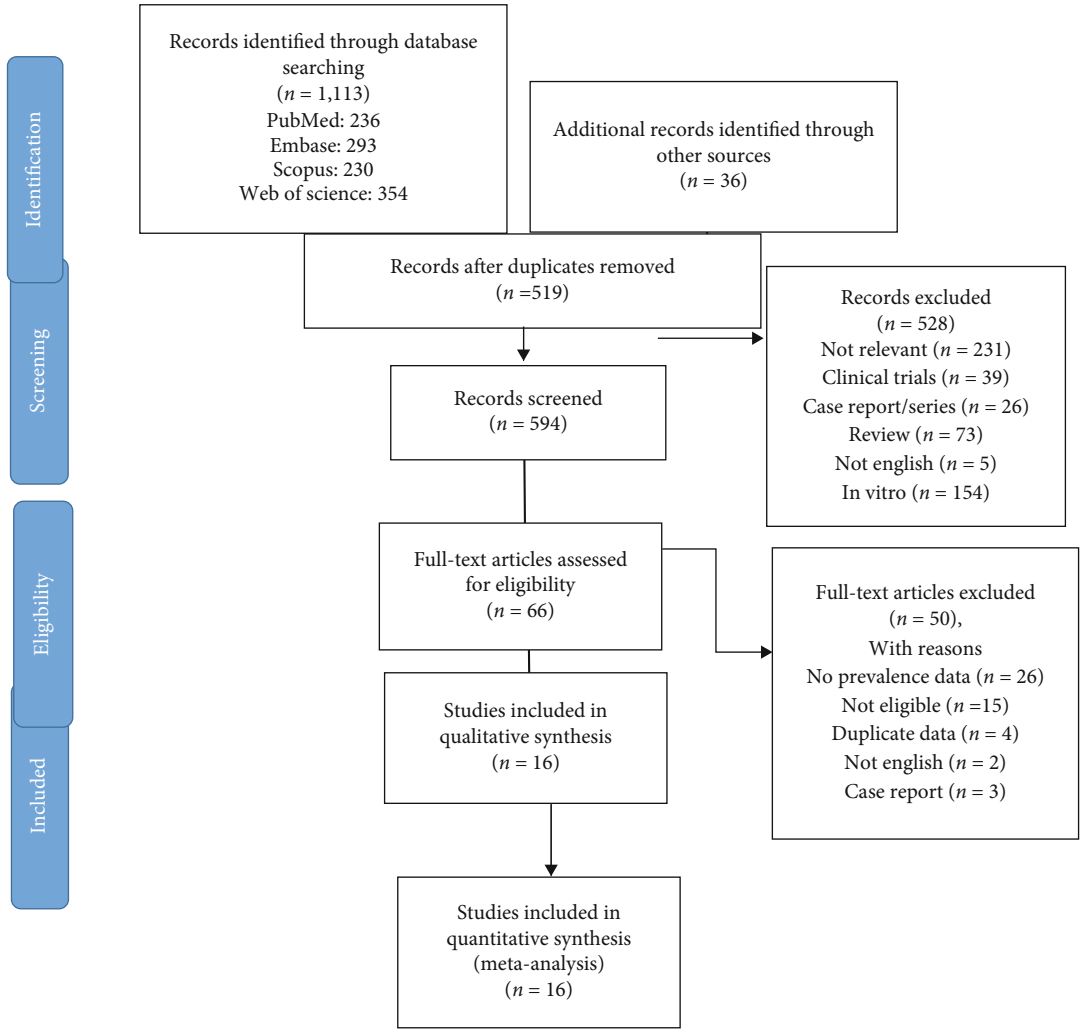

Figure 1: PRISMA flow diagram: the PRISMA diagram explains the intricacies of the search of systematic review and selection procedures.

DQ2 and/or the DR4-DQ8 [11–13]. These HLA class II haplotypes show strong association with MS [14, 15].

On the other hand, CD is associated with neurological manifestations and diseases such as ataxia, epilepsy, neuropathy, and multiple sclerosis (MS) [16].

In some previous studies, the increased levels of antigliadin and gluten antibodies were detected in MS cases while another study failed to confirm this finding [9, 17, 18].

As there is no systematic review and meta-analysis regarding the prevalence of CD in MS cases, we designed this study to evaluate the prevalence of CD in MS cases.

2. Methods

2.1. Search Strategy. PubMed, Scopus, EMBASE, Web of Science, and Google Scholar along with gray literature were systematically searched. The search included all relevant studies which were published up to October 2022.

Two researchers independently searched all databases and also references of included studies.

2.2. The Syntax Which Was Used in MeSH Is as Follows. ((Sclerosis AND multiple) OR (sclerosis AND disseminated) OR "disseminated sclerosis" OR "multiple sclerosis" OR "acute fulminating") AND ("Celiac Disease" OR (Disease AND Celiac) OR "Gluten Enteropathy" OR (Enteropathies AND Gluten) OR (Enteropathy AND Gluten) OR "Gluten Enteropathies" OR "Gluten-Sensitive Enteropathy" OR (Enteropathies AND Gluten-Sensitive) OR (Enteropathy AND Gluten-Sensitive) OR "Gluten Sensitive Enteropathy" OR "Gluten-Sensitive Enteropathies" OR (Sprue AND Celiac) OR (Sprue AND Nontropical) OR "Nontropical Sprue" OR "Celiac Sprue" OR Sprue).

Inclusion criteria were cross-sectional studies/case, articles which had been published in the English language.

We included studies only studies in which the diagnostic criteria were biopsy of duodenum.

Exclusion criteria are letter to editors, case reports, and RCT studies.

2.3. Data Extraction. Two independent researchers extracted data. In the case of discrepancies, they asked another

Table 1: Data extracted from included studies.

Author	Continent	Region	Year	Study design	Total MS cases	Female cases	Male cases	Age mean (SD)	MS stage	EDSS mean (SD) or median (range)	Total celiac case	Total control	Female control	Male control	Total celiac control	Quality assessment*
Lo et al. [22]	Australia	Australia	2021	Cohort	1518	1204	309	55.7 (11.2)	NR	NR	15	NA	NA	NA	NA	7/9
Lo et al. [23]	Australia	Australia	2021	Cross-sectional	902	709	193	55.8 (11.4)	NR	NR	10	NA	NA	NA	NA	7/10
Piccini et al. [24]	Europe	Italy	2020	Cohort	2050	1579	471	28.8 (10.8)	RRMS: 1251	NR	9	NA	NA	NA	NA	7/9
Lorefice et al. [25]	Europe	Italy	2018	Cross-sectional	286	205	81	42.4 (10.6)	NR	2.7 (1.8)	4	NA	NA	NA	NA	7/10
Laroni et al. [26]	Europe	Italy	2017	Cohort	1877	1218	659	35.3 (11.3)	NR	2.1 (1.1)	12	NA	NA	NA	NA	7/9
Zanchi et al. [27]	Europe	Italy	2017	Cross-sectional	601	403	198	43.9	RRMS: 487 SPMS: 103 PRMS: 11	2 (1.0-9.0)	47	NA	NA	NA	NA	8/10
de Oliveira et al. [28]	Latin America	Brazil	2016	Cross-sectional	249	176	73	NR	NR	NR	1	NA	NA	NA	NA	8/10
Farez et al. [29]	Latin America	Argentina	2014	Case control	211	163	48	40.4 (10)	NR	1 (0-8.5)	1	211	163	48	3	7/10
Levinthal et al. [30]	America	USA	2013	Cross-sectional	218	170	48	47.6 (1.0)	RRMS: 154 SPMS: 24 PRMS: 9 Undefined: 32	NR	2	NA	NA	NA	NA	7/10
Khoshbaten	Asia	Iran	2012	Cross-sectional	100	68	32	33.1 (8.8)	RRMS: 78 SPMS: 14	3.9 (1.9)	0	121	75	46	0	6/10
Rodrigo et al. [31]	Europe	Spain	2011	Cross-sectional	72	60	12	43 (10)	RRMS: 72	1.7 (1.1)	8	Check				7/10
Nicoletti et al. [16]	Europe	Italy	2008	Case control	217	130	87	40.2 (10.2)	RRMS: 193 SPMS: 21 PRMS: 3	NR	0	200	123	77	1	8/10
Nielsen et al. [32]	Europe	Denmark	2008	Cohort	12403	NR	NR	NR	NR	NR	1	20798	NR	NR	4	
Eaton et al. [33]	Europe	Denmark	2007	Cohort	9961	NR	NR	NR	NR	NR	6	NA	NA	NA	NA	
Edwards and Constantinescu [34]	Europe	UK	2004	Case control	658	454	204	45	NR	NR	3	1064	NR	NR	13	
Salvatore et al. [17]	Europe	Italy	2004	Cross-sectional	95	NR	NR	41.3 (21-63)	RRMS: 76 SPMS: 16 PRMS: 3	NR	0	NA	NA	NA	NA	6/10

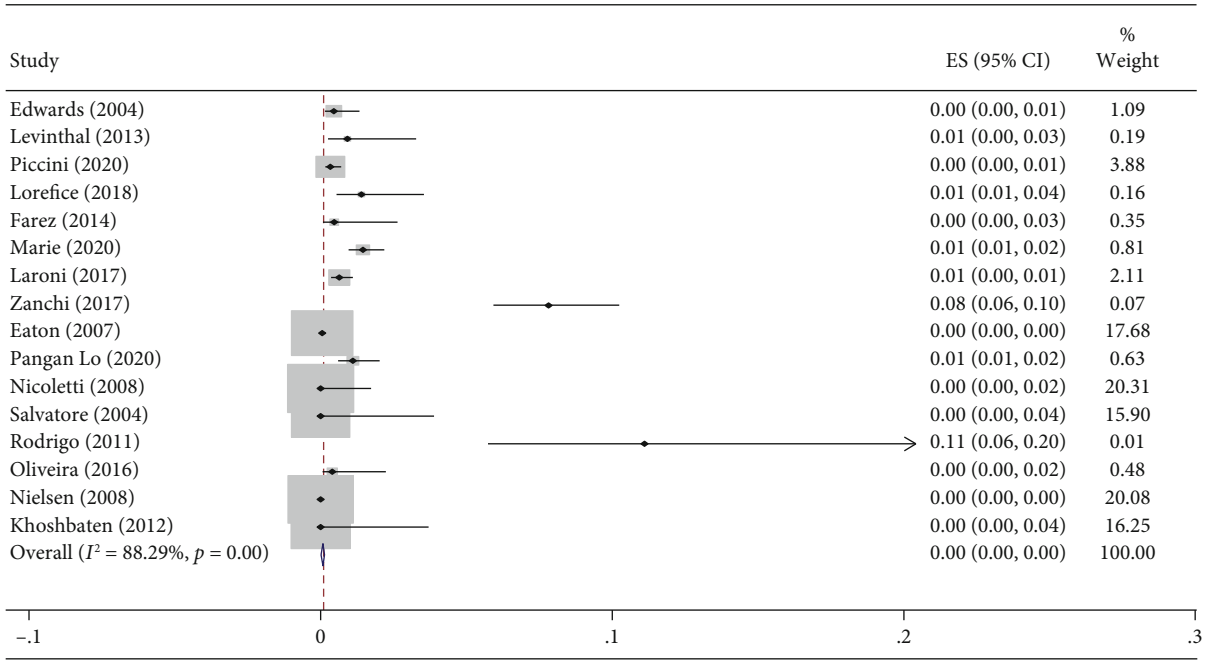

Figure 2: The pooled prevalence of CD in MS patients.

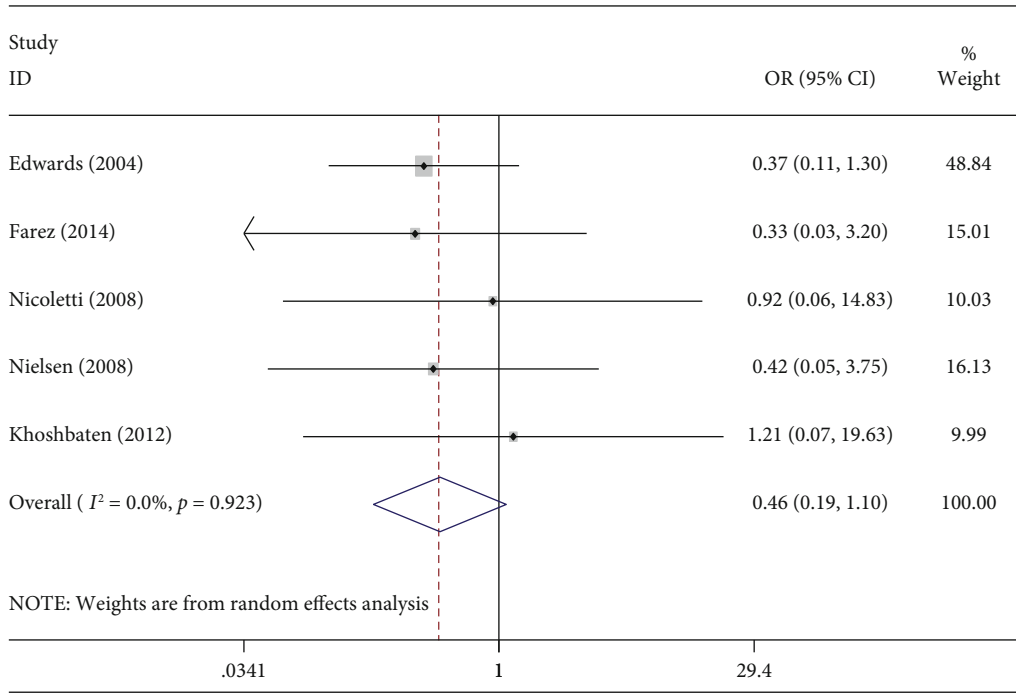

Figure 3: The pooled odds of CD in subjects with MS.

researcher. Each one entered data in an Excel sheet and data regarding the first author, country of origin, number of enrolled patients, number of CD cases, mean age, male and female numbers, mean EDSS, mean duration of the disease, number of controls, and number of CD in controls were extracted.

2.4. Risk of Bias Assessment. We evaluated the risk of potential bias by the Newcastle-Ottawa Quality Assessment Scale (adapted for cross-sectional studies, cohort, and case control studies) [19–21].

2.5. Statistical Analysis. We used STATA (version 14.0; StataCorp LP, College Station, TX, USA) for data analysis. To determine heterogeneity, inconsistency (I^2) was calculated. As the I^2 was more than 50%, we used random effects for pooling the data. We reported pooled prevalence with 95% CI.

3. Results

We found 1113 articles by literature search, and after deleting duplicates, 519 remained. Sixteen articles remained for meta-analysis (Figure 1).

Totally, 31418 patients were evaluated and total number of possible/confirmed cases was 124. Studies were published between 2004 and 2020, and the most published studies were form Italy. Five studies provided information regarding controls. The total number of controls was 22394, of whom 22 had CD.

Mean age ranged from 35-55 years. The quality assessment score ranged between 4 and 10 (table 1).

The pooled prevalence of CD in MS patients was 0 ($I^2 = 88.2\%$, $p < 0.001$) (Figure 2). The pooled odds of CD in subjects with MS are 0.46 (95% CI: 0.19-1.1) ($I^2 = 0$, $p = 0.9$) (Figure 3).

4. Discussion

This is the first systematic review and meta-analysis evaluating the prevalence of celiac disease in MS patients.

The results show that the prevalence is near zero in MS, and the odds of CD in subjects with MS are not high.

Patients with MS suffer from a wide range of gastrointestinal manifestations such as dysphagia, constipation, and/or fecal incontinence [35–38]. Dyspeptic symptoms and pain are also common in MS cases which impair quality of life and interfere with daily activities [30].

de Oliveira et al. assessed 249 MS patients and reported CD in only one [28] which was along with findings of Nielsen et al. who evaluated gluten-sensitive enteropathy in 12403 MS cases and found it in only one (RR = 0.6, 95% CI: 0.1-4.6) [32].

Rodrigo et al. included 72 MS cases and 123 healthy controls and found the antibodies (IgA-anti-transglutaminase-2) in 10% of MS cases and 2.4% ($p < 0.05$) (OR = 5.3) while HLA-DQ2 markers did not significantly differ between patients and healthy subjects [31]. In their study, 32% of first degree had CD.

In Germany in 2001, 75 children with CD were evaluated by electroencephalogram, computed tomography (CT scan), and magnetic resonance imaging (MRI) of the brain and reported white matter lesions in 15 cases [39].

CD has a clear etiology which is autoimmunity and is the consequence of gluten intolerance. Genetics play an important role [31] and mostly occurs at adolescence [40]. The relationship between MS and CD is considered in some studies while the pathogenesis of both diseases' T-cells plays an important role, and Matheson found that patients with MS benefit from gluten free diet [41]. Shor et al. and Reichelt and Jensen reported the decrease in number of demyelinating lesions in MS cases who were treated with gluten free diet [42, 43]. They also share common HLAs [14, 15]. The prevalence of CD in different general populations is estimated between 0.2% and 0.7% [44–47].

It has been shown that CD is related with other neurological diseases such as peripheral neuropathies, seizure, ataxia, and cognitive impairment. One suggestion is that antibodies to gliadin or a peptide sequence of gliadin are neurotoxic and precede neurological manifestation in CD [48].

This systematic review had some limitations. There were studies that used serologic evaluation for CD diagnosis which were excluded. There were no reports from some countries. The control groups were different; as in some studies, the control group was healthy subjects, and in others, the control group was patients with other diseases except MS. Larger multicentric studies from lots of countries are reported.

5. Conclusion

The pooled prevalence of this systematic review showed that CD is not prevalent in MS cases.

Conflicts of Interest

The authors declare that they had no conflict of interest.

References

[1] A. Azimi, M. Ghajarzadeh, M. A. Sahraian et al., "Effects of vitamin D supplements on IL-10 and INFγ levels in patients with multiple sclerosis: a systematic review and meta-analysis," *Maedica*, vol. 14, no. 4, pp. 413–417, 2019.

[2] M. Ghajarzadeh, A. R. Foroushani, P. Ghezelbash et al., "Prevalence of multiple sclerosis (MS) in Zanjan province of Iran," *International journal of Preventive Medicine*, vol. 11, no. 1, p. 116, 2020.

[3] R. A. Marrie, N. Reider, J. Cohen et al., "A systematic review of the incidence and prevalence of autoimmune disease in multiple sclerosis," *Multiple sclerosis journal*, vol. 21, no. 3, pp. 282–293, 2015.

[4] E. Benjaminsen, K. M. Myhr, N. Grytten, and K. B. Alstadhaug, "Comorbidity in multiple sclerosis patients from Nordland County, Norway - validated data from the Norwegian Patient Registry," *Multiple sclerosis and related disorders*, vol. 48, article 102691, 2021.

[5] S. Broadley, J. Deans, S. Sawcer, D. Clayton, and D. Compston, "Autoimmune disease in first-degree relatives of patients with multiple sclerosis," *Brain*, vol. 123, no. 6, pp. 1102–1111, 2000.

[6] S. Sloka, "Observations on recent studies showing increased co-occurrence of autoimmune diseases," *Journal of autoimmunity*, vol. 18, no. 3, pp. 251–257, 2002.

[7] A. Karni and O. Abramsky, "Association of MS with thyroid disorders," *Neurology*, vol. 53, no. 4, p. 883, 1999.

[8] J. Sloka, P.-W. Phillips, M. Stefanelli, and C. Joyce, "Co-occurrence of autoimmune thyroid disease in a multiple sclerosis cohort," *Journal of Autoimmune Diseases*, vol. 2, no. 1, pp. 1–6, 2005.

[9] M. Khoshbaten, M. Farhoudi, M. Nikanfar et al., "Celiac disease and multiple sclerosis in the northwest of Iran," *Bratislavske lekarske listy*, vol. 113, no. 8, pp. 495–497, 2012.

[10] J. Carreras, "Artificial intelligence analysis of celiac disease using an autoimmune discovery transcriptomic panel highlighted pathogenic genes including BTLA," *Healthcare*, vol. 10, no. 8, 2022.

[11] A. Al–Toma, M. S. Goerres, J. W. Meijer, A. S. Peña, J. B. Crusius, and C. J. Mulder, "Human leukocyte antigen-DQ2 homozygosity and the development of refractory celiac disease and enteropathy-associated T-cell lymphoma," *Clinical Gastroenterology and Hepatology*, vol. 4, no. 3, pp. 315–319, 2006.

[12] M. M. Pietzak, T. C. Schofield, M. J. McGinniss, and R. M. Nakamura, "Stratifying risk for celiac disease in a large at-risk United States population by using HLA alleles," *Clinical Gastroenterology and Hepatology*, vol. 7, no. 9, pp. 966–971, 2009.

[13] E. Liu, H.-S. Lee, C. A. Aronsson et al., "Risk of pediatric celiac disease according to HLA haplotype and country," *New England Journal of Medicine*, vol. 371, no. 1, pp. 42–49, 2014.

[14] D. Luckey, D. Bastakoty, and A. K. Mangalam, "Role of HLA class II genes in susceptibility and resistance to multiple sclerosis: studies using HLA transgenic mice," *Journal of autoimmunity*, vol. 37, no. 2, pp. 122–128, 2011.

[15] S. Ouadghiri, K. El Alaoui Toussi, C. Brick et al., "Facteurs genetiques et sclerose en plaque dans la population marocaine : role du HLA de classe II," *Pathologie Biologie*, vol. 61, no. 6, pp. 259–263, 2013.

[16] A. Nicoletti, F. Patti, S. Lo Fermo et al., "Frequency of celiac disease is not increased among multiple sclerosis patients," *Multiple Sclerosis Journal*, vol. 14, no. 5, pp. 698–700, 2008.

[17] S. Salvatore, S. Finazzi, A. Ghezzi et al., "Multiple sclerosis and celiac disease: is there an increased risk?," *Multiple Sclerosis Journal*, vol. 10, no. 6, pp. 711-712, 2004.

[18] C. D. P. Tengah, R. J. Lock, D. J. Unsworth, and A. J. Wills, "Multiple sclerosis and occult gluten sensitivity," *Neurology*, vol. 62, no. 12, pp. 2326-2327, 2004.

[19] P. A. Modesti, G. Reboldi, F. P. Cappuccio et al., "Panethnic differences in blood pressure in Europe: a systematic review and meta-analysis," *PLoS One*, vol. 11, no. 1, article e0147601, 2016.

[20] G. Wells, B. Shea, D. O'Connell et al., *Newcastle-Ottawa Quality Assessment Scale Cohort Studies*, University of Ottawa, 2014.

[21] Y. B. Lv, Y. Wang, W. G. Ma et al., "Association of renalase SNPs rs2296545 and rs2576178 with the risk of hypertension: a meta-analysis," *PLoS One*, vol. 11, no. 7, article e0158880, 2016.

[22] L. M. P. Lo, B. V. Taylor, T. Winzenberg, A. J. Palmer, L. Blizzard, and I. van der Mei, "Change and onset-type differences in the prevalence of comorbidities in people with multiple sclerosis," *Journal of Neurology*, vol. 268, no. 2, pp. 602–612, 2021.

[23] L. M. P. Lo, B. V. Taylor, T. Winzenberg et al., "Estimating the relative contribution of comorbidities in predicting health-related quality of life of people with multiple sclerosis," *Journal of Neurology*, vol. 268, no. 2, pp. 569–581, 2021.

[24] B. Piccini, M. Ulivelli, M. P. Amato et al., "Association of celiac disease in patients with multiple sclerosis in Tuscany," *Revista Española de Enfermedades Digestivas*, vol. 112, no. 6, pp. 474–476, 2020.

[25] L. Lorefice, G. Fenu, R. Pitzalis et al., "Autoimmune comorbidities in multiple sclerosis: what is the influence on brain volumes? A case–control MRI study," *Journal of Neurology*, vol. 265, no. 5, pp. 1096–1101, 2018.

[26] A. Laroni, A. Signori, G. T. Maniscalco et al., "Assessing association of comorbidities with treatment choice and persistence in MS: a real-life multicenter study," *Neurology*, vol. 89, no. 22, pp. 2222–2229, 2017.

[27] C. Zanchi, S. La Gioia, V. Barcella et al., "Comorbidity prevalence in a multiple sclerosis center," in *MULTIPLE SCLEROSIS JOURNAL 2017 Oct 1 (Vol. 23, pp. 713-713). 1 OLIVERS YARD, 55 CITY ROAD, LONDON EC1Y 1SP*SAGE PUBLICATIONS LTD, ENGLAND.

[28] P. de Oliveira, D. R. de Carvalho, I. V. Brandi, and R. Pratesi, "Serological prevalence of celiac disease in Brazilian population of multiple sclerosis, neuromyelitis optica and myelitis," *Multiple sclerosis and related disorders*, vol. 9, pp. 125–128, 2016.

[29] M. F. Farez, M. E. Balbuena Aguirre, F. Varela, A. A. Köhler, and J. Correale, "Autoimmune disease prevalence in a multiple sclerosis cohort in Argentina," *Multiple sclerosis international*, vol. 2014, Article ID 828162, 3 pages, 2014.

[30] D. J. Levinthal, A. Rahman, S. Nusrat, M. O'Leary, R. Heyman, and K. Bielefeldt, "Adding to the burden: gastrointestinal symptoms and syndromes in multiple sclerosis," *Multiple sclerosis international*, vol. 2013, Article ID 319201, 9 pages, 2013.

[31] L. Rodrigo, C. Hernández-Lahoz, D. Fuentes, N. Alvarez, A. López-Vázquez, and S. González, "Prevalence of celiac disease in multiple sclerosis," *BMC Neurology*, vol. 11, no. 1, pp. 1–7, 2011.

[32] N. M. Nielsen, M. Frisch, K. Rostgaard et al., "Autoimmune diseases in patients with multiple sclerosis and their first-degree relatives: a nationwide cohort study in Denmark," *Multiple Sclerosis Journal*, vol. 14, no. 6, pp. 823–829, 2008.

[33] W. W. Eaton, N. R. Rose, A. Kalaydjian, M. G. Pedersen, and P. B. Mortensen, "Epidemiology of autoimmune diseases in Denmark," *Journal of autoimmunity*, vol. 29, no. 1, pp. 1–9, 2007.

[34] L. Edwards and C. Constantinescu, "A prospective study of conditions associated with multiple sclerosis in a cohort of 658 consecutive outpatients attending a multiple sclerosis clinic," *Multiple Sclerosis Journal*, vol. 10, no. 5, pp. 575–581, 2004.

[35] M. Sørensen, M. Lorentzen, J. Petersen, and J. Christiansen, "Anorectal dysfunction in patients with urologic disturbance

due to multiple sclerosis," *Diseases of the colon & rectum*, vol. 34, no. 2, pp. 136–139, 1991.

[36] J. Weber, P. Grise, M. Roquebert et al., "Radiopaque markers transit and anorectal manometry in 16 patients with multiple sclerosis and urinary bladder dysfunction," *Diseases of the colon & rectum*, vol. 30, no. 2, pp. 95–100, 1987.

[37] Y.-W. Chia, C. J. Fowler, M. A. Kamm, M. M. Henry, M.-C. Lemieux, and M. Swash, "Prevalence of bowel dysfunction in patients with multiple sclerosis and bladder dysfunction," *Journal of Neurology*, vol. 242, no. 2, pp. 105–108, 1995.

[38] A. De Pauw, E. Dejaeger, B. D'hooghe, and H. Carton, "Dysphagia in multiple sclerosis," *Clinical neurology and neurosurgery*, vol. 104, no. 4, pp. 345–351, 2002.

[39] M. Kieslich, G. Errázuriz, H. G. Posselt, W. Moeller-Hartmann, F. Zanella, and H. Boehles, "Brain white-matter lesions in celiac disease: a prospective study of 75 diet-treated patients," *Pediatrics*, vol. 108, no. 2, p. e21, 2001.

[40] L. Rodrigo-Sáez, D. Fuentes-Álvarez, I. Pérez-Martínez, N. Álvarez-Mieres, and P. Niño-García, "Differences between pediatric and adult celiac disease," *Revista espanola de enfermedades digestivas*, vol. 103, no. 5, pp. 238–244, 2011.

[41] N. Matheson, "Multiple sclerosis and diet," *The Lancet*, vol. 304, no. 7884, p. 831, 1974.

[42] D. B. A. Shor, O. Barzilai, M. Ram et al., "Gluten sensitivity in multiple sclerosis," *Annals of the New York Academy of Sciences*, vol. 1173, no. 1, pp. 343–349, 2009.

[43] K. L. Reichelt and D. Jensen, "IgA antibodies against gliadin and gluten in multiple sclerosis," *Acta neurologica scandinavica*, vol. 110, no. 4, pp. 239–241, 2004.

[44] S. Riestra, E. Fernandez, L. Rodrigo, S. Garcia, and G. Ocio, "Prevalence of coeliac disease in the general population of northern Spain: strategies of serologic screening," *Scandinavian journal of gastroenterology*, vol. 35, no. 4, pp. 398–402, 2000.

[45] A. Rubio-Tapia, J. F. Ludvigsson, T. L. Brantner, J. A. Murray, and J. E. Everhart, "The prevalence of celiac disease in the United States," *Official journal of the American College of Gastroenterology| ACG*, vol. 107, no. 10, pp. 1538–1544, 2012.

[46] J. C. Gomez, G. S. Selvaggio, M. Viola et al., "Prevalence of celiac disease in Argentina: screening of an adult population in the La Plata area," *The American journal of gastroenterology*, vol. 96, no. 9, pp. 2700–2704, 2001.

[47] U. Volta, S. Bellentani, F. B. Bianchi et al., "High prevalence of celiac disease in Italian general population," *Digestive diseases and sciences*, vol. 46, no. 7, pp. 1500–1505, 2001.

[48] H. J. Freeman, "Neurological disorders in adult celiac disease," *Journal canadien de gastroenterologie*, vol. 22, no. 11, pp. 909–911, 2008.