Type 1 diabetes and celiac disease: The effects of gluten free diet on metabolic control

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Abstract
Type 1 diabetes mellitus is associated with celiac disease, with a prevalence that varies between 0.6% and 16.4%, according to different studies. After a diagnosis of celiac disease is confirmed by small bowel biopsy, patients are advised to commence a gluten-free diet (GFD). This dietary restriction may be particularly difficult for the child with diabetes, but in Europe (and in Italy) many food stores have targeted this section of the market with better labeling of products and more availability of specific GFD products. Treatment with a GFD in symptomatic patients has been shown to improve the symptoms, signs and complications of celiac disease. However, the effects of a GFD on diabetic control are less well established. Initial reports of improved hypoglycemic control were based on children who were diagnosed with celiac disease associated with malabsorption, but there have subsequently been reports of improvement in patients with type 1 diabetes with subclinical celiac disease. There are other studies reporting no effect, improved control and an improvement of hypoglycemic episodes. Moreover, in this review we wish to focus on low glycemic index foods, often suggested in people with type 1 diabetes, since they might reduce postprandial glycemic excursion and enhance long-term glycemic control. In contrast, GFD may be rich in high glycemic index foods that can increase the risk of obesity, insulin resistance and cardiovascular disease, worsening the metabolic control of the child with diabetes. Hence, it is important to evaluate the impact of a GFD on metabolic control, growth and nutritional status in children with type 1 diabetes.

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Key words: Adolescents; Celiac disease; Children; Glycemic control; Type 1 diabetes

Core tip: It is important to evaluate the impact of a gluten-free diet (GFD) on metabolic control, growth and nutritional status in children with type 1 diabetes and celiac disease. Since compliance with a strict GFD and a safe choice of food for diabetes is not easy, these patients require extra education and dietary intervention. A specialized follow-up and dietary counseling are essential in the management of patients affected by both type 1 diabetes and celiac disease.

INTRODUCTION
Type 1 diabetes is an immune-mediated disorder characterized by a deficit or absence of insulin resulting from T cell-mediated destruction of beta cells of the pancreas.

Children with type 1 diabetes have an increased risk of developing other autoimmune disorders like Hashi-
moto’s thyroiditis, Addison disease, vitiligo and celiac disease\(^5\). The relation between type 1 diabetes and these pathologies is a common genetic background. All of these diseases are associated with organ-specific autoantibodies that can be detected before the development of clinical diseases; consequently, patients affected by type 1 diabetes usually undergo a scheduled (usually once a year) screening for these pathologies.

Celiac disease is one of the most common autoimmune disease-based disorders; it is elicited by a failure of oral tolerance towards wheat, gluten and related cereals, which results in a multisystem inflammation of the intestinal tract. It usually develops in HLA-DQ2/8 positive individuals. The first association between type 1 diabetes and celiac disease was suggested in 1969\(^5\). The genetic risk factors associated with both diseases include human leukocyte antigen (HLA) genes and non-HLA genes.

The increased prevalence of celiac disease in patients with type 1 diabetes is due to an overlap in the genetic susceptibility to both diseases conferred by the HLA-DR3/DQ2\(^4\). This haplotype is present in over 90% of patients with celiac disease and 55% of those with type 1 diabetes, compared with only 20%-25% of the general population of European ancestry. HLA-DQ8 also confers a risk of type 1 diabetes\(^4\).

Celiac disease affects at least 10% of patients with type 1 diabetes at some point in their lives\(^9\), with a prevalence that varies between 0.6%-16.4%, according to different studies\(^6-8\). The prevalence of celiac disease among children with type 1 diabetes is significantly higher than in non-diabetic children (in Western countries celiac disease affects around 1%-2% of the non-diabetic population).

In Italy, the prevalence of celiac disease in children with type 1 diabetes is around 7%\(^10\), 3.6% of which at type 1 diabetes onset\(^10\), at a younger age\(^10\) and in boys\(^10\); moreover, according to a study by Salardi et al\(^11\), the prevalence of celiac disease has significantly increased since 1994 (10.6% vs 6.6%, \(P = 0.015\)), probably due to changes in environmental factors, namely, eating habits and viral infections.

Less than 10% of patients with type 1 diabetes who develop celiac disease show gastrointestinal symptoms, while most of the children are either asymptomatic or only mildly symptomatic. Therefore, children affected by type 1 diabetes undergo screening for celiac disease. Usually, celiac autoantibodies are tested at the time of diabetes onset and yearly during follow-up, but debate exists about timing and frequency for screening\(^12,13\). When celiac antibodies are detected (ideally confirmed at least twice), it is mandatory to perform esophagogastroduodenoscopy with bowel biopsies to confirm diagnosis\(^14\).

**TREATMENT OF CELIAC DISEASE FOR PATIENTS WITH TYPE 1 DIABETES**

The presence of mucosal atrophy is an indication to start a gluten-free diet (GFD), which is the standard therapy for celiac disease, avoiding all foods containing wheat, rye, barley and oats.

Patients affected by celiac disease must follow a strict GFD for their entire life to prevent acute (malabsorption, diarrhea, folate deficiency, failure to thrive, iron deficiency) and chronic (intestinal lymphoma, osteoporosis, autoimmune diseases, infertility, mortality) complications\(^12,13,14\).

Gluten restriction added to a diabetic dietary regimen imposes practical limitations and leads to considerable restrictions in the lifestyle of a child or adolescent. Unfortunately, as a result, non-adherence to GFD among patients with type 1 diabetes and celiac disease is very common. A study by Valerio et al\(^15\) found that only 59% of patients with type 1 diabetes and celiac disease were compliant to a strict GFD, while compliance in patients with celiac disease only is around 78%\(^18\). This is an important factor to consider when treating a child or adolescent with type 1 diabetes. It is well established that an accurate diet is one of the cornerstones of the management in patients with type 1 diabetes\(^19\). Combining a GFD may raise major challenges and even some doubts. Dietary intervention aims to achieve and maintain blood glucose and blood pressure in the normal range, to attain normal lipid profile, to achieve normal body weight\(^19\).

Preserving a steady glycemic control is essential to reduce both micro and macrovascular complications of type 1 diabetes\(^24\). For this reason, it is important to give patients advice on carbohydrate amount, type and distribution throughout the day, and to educate them about carbohydrate counting. In this context, the choice of low glycemic index food may be important\(^25\). In this respect, a GFD could be an obstacle as many of the gluten-free foods have a high glycemic index. This might influence glycemic values, HbA1c, insulin requirement, lipid profile, and possibly the development of long-term diabetic complications. Moreover, GFD could modify both anthropometric measures, such as height, weight, body mass index (BMI), growth velocity, even if not all researchers agree on the final effects of GFD.

**BODY MASS INDEX IN CHILDREN WITH TYPE 1 DIABETES AND CELIAC DISEASE**

While, in patients with celiac disease alone, concern has been raised about gaining weight when on a GFD\(^24\), recent data show normal growth patterns in children and adolescents with type 1 diabetes and celiac disease\(^23,26\), with body mass index and height standard deviation scores only marginally but not significantly higher in the control (non-celiac) than the study group, and similar to subjects with celiac disease with good or fair/poor adherence to a GFD throughout the follow-up period. Among the reasons for increased BMI, the macronutrient composition of gluten-free foods, a high percentage of saturated fat and carbohydrates with high glycemic index, and a low percentage of proteins and fiber can be included.

After clearing gluten, as villous atrophy resolves, intestinal absorption is certainly improved, but an excessive weight gain may increase the risk of morbidity and may
lead to higher risk of cardiovascular disease especially in type 1 diabetes patients. However, data on weight gain (and BMI increasing) in patients with celiac disease are inconsistent. Dickey et al. showed that nearly 80% of patients gained some weight after 2 years on GFD, and about 51% were even overweight or obese. On the contrary, a recent study reported a weight loss in obese or overweight patients while on GFD, with a similar improvement in screen- and symptom-detected celiac disease patients on a GFD.

GLYCEMIC CONTROL IN CHILDREN WITH TYPE 1 DIABETES AND CELIAC DISEASE

Regarding patients with type 1 diabetes and celiac disease, the most recent data show no difference between patients with and without celiac disease. However, a link between a change in body mass index and a possible improvement of metabolic control remains controversial. Acerni et al. observed an improvement both in body mass index and in HbA1c, while Nóvoa Medina et al., who studied only type 1 diabetes patients with symptomatic celiac disease, did not find any effects on metabolic control or on height or weight. Other studies evaluated the influence of a GFD on metabolic parameters, such as insulin dose, HbA1c, glucose excretion and hypoglycemic episodes. Saadah et al. observed that a GFD resulted in a significant improvement of growth and influenced diabetic control (more insulin in celiac disease patients when compared to baseline). Other authors did not find any significant difference in insulin dose, HbA1c, 24 h urinary glucose excretion, or number of hypoglycemic episodes. Similar findings have been observed in adult patients with type 1 diabetes and celiac disease. Abid et al. documented in type 1 diabetes children with celiac disease that a GFD showed short-term benefits by reducing gastrointestinal symptoms and, in particular, episodes of severe hypoglycemia, while there was no change in standard deviation score for height, weight, and BMI or the mean HbA1c before and after GFD. The mean insulin requirement significantly increased. More refined indexes of an altered or better metabolic control, like continuous glucose monitoring, glycemic variability indexes, and frequency of insulin dose changes are usually difficult to measure.

TYPE 1 DIABETES, CELIAC DISEASE AND MICRO OR MACROANGIOPATHIC COMPLICATIONS

Few studies have been published about this topic and almost all involved adult patients with type 1 and celiac disease. Bakker et al collected HbA1c before celiac disease diagnosis, at diagnosis and the most recent together with the presence of nephropathy and retinopathy. An interesting finding was that diabetes patients with celiac disease had a lower prevalence of retinopathy when compared to controls (diabetes patients without celiac disease), whereas no difference in the prevalence of nephropathy was found, suggesting that a GFD possibly favorably affects the development of vascular complications in diabetes patients.

Similar findings have also been observed about macrovascular complications. Picarelli et al. evaluated whether the presence of celiac disease in a group of type 1 diabetes patients is associated with different expression of some hemostatic factors and with a different manifestation/progression of complications. The authors claim a potential protective role of celiac disease in the prothrombotic state of type 1 diabetes (celiac disease patients had significantly lower HbA1c, total cholesterol, triglycerides, factor VII antigen, factor VIII coagulant activity, and prothrombin degradation fragments). In contrast, Pitocco et al. found that in type 1 diabetes patients with long duration of celiac disease, the carotid intima-media layer was thicker compared to diabetes patients without celiac disease. However, if GFD seems to have a protective role in the appearance of micro- and macroangiopathic complications, the misdiagnosis of celiac disease in adult patients with type 1 diabetes is associated with a higher prevalence of retinopathy, nephropathy and peripheral neuropathy. These findings raise the issue of regular celiac disease screening in order to detect type 1 diabetes patients at risk of developing celiac disease in a timely manner.

In this context, the case reported by Sildorf et al. of a 6-year-old boy who, after type 1 diagnosis, even without celiac disease, was started on a GFD, gradually suspending insulin therapy and remaining free of exogenous insulin after 20 mo seems very interesting. The GFD was reported to be safe and without side effects, and it is believed that the GFD acted to prolong the remission phase of diabetes.

TYPE 1 DIABETES, CELIAC DISEASE AND GLYCEMIC INDEX

As stated above, the most difficult factor to handle for a child/adolescent with type 1 diabetes and celiac disease is that most GFD foods have a high glycemic index. Indeed, in 2002 the American Society for Clinical Nutrition compared many foods regarding their glycemic index. What they discovered was that gluten-free foods have a higher glycemic index than gluten-containing equivalents. Since glycemic index represents a direct measure of carbohydrate absorption, it is obvious that high glycemic index foods determine a rise in rapid blood glucose values. Hyperglycemia causes an increase in free fatty acids that induce oxidative stress and promote atherosclerosis. On the other hand, the subsequent rapid fall in glucose removal is associated with a sensation of hunger and excessive calorie intake. Thus, a diet with low glycemic index is suggested either because of a lack of normal insulin response to high glycemic index foods in diabetes patients, or because of the aim of reducing micro and macrovascular complications. Indeed, we have seen that GFD seems to have a protective role rather than a
deteriorating one,[12,33] even in pediatric age[34]. The means by which the presence of celiac disease might prevent micro- and macrovascular complications of diabetes asks further investigations. Hypothetically, a greater dietary vigilance, an increased awareness of food intake and several consultations by a skilled dietitian might result in a better controlled carbohydrate intake and could lead to healthier eating habits. Finally, gluten free foods have a reduced content of many micronutrients: B and D vitamins, calcium, iron, magnesium and zinc. In particular, calcium content in a GFD should be appropriate, since an impairment of bone metabolism and structure has been found both in type 1 diabetes and celiac disease.

**CONCLUSION**

Hence, it is important to evaluate the impact of a GFD on metabolic control, growth and nutritional status in children with type 1 diabetes and celiac disease.

Since compliance with a strict GFD and a safe choice of food for diabetes is not easy, these patients require extra education and dietary intervention.

A specialized follow-up and dietary counseling are essential in the management of patients affected by both type 1 diabetes and celiac disease.

**REFERENCES**

1. Atkinson MA, Maclaren NR. The pathogenesis of insulin-dependent diabetes mellitus. *N Engl J Med* 1994; 331: 1248-1436 [PMID: 7969282 DOI: 10.1056/NEJM1994112331432107]

2. Barker JM. Clinical review: Type 1 diabetes-associated autoimmunity: natural history, genetic associations, and screening. *J Clin Endocrinol Metab* 2006; 91: 1210-1217 [PMID: 16403820 DOI: 10.1210/jc.2005-1679]

3. Walker-Smith JA. Grigor W. Coeliac disease in a diabetic child. *Lancet* 1969; 1: 1021 [PMID: 4811787 DOI: 10.1016/S0140-6736(69)91817-0]

4. Rewers M, Eisenbarth GS. Autoimmunity: Celiac disease in T1DM-the need to look long term. *Nat Rev Endocrinol* 2012; 8: 7-8 [PMID: 22065402 DOI: 10.1038/nrendo.2011.193]

5. Rewers M, Liu E, Simmons J, Redondo MJ, Hoffenberg EJ. Celiac disease associated with type 1 diabetes mellitus. *Endocrinol Metab Clin North Am* 2004; 33: 197-214 [PMID: 15053903 DOI: 10.1016/j.ecl.2003.12.007]

6. Marchese A, Lovati E, Biagi F, Corazza GR. Coeliac disease and type 1 diabetes mellitus: epidemiology, clinical implications and effects of gluten-free diet. *Endocrine* 2013; 43: 1-2 [PMID: 22820894 DOI: 10.1007/s12020-012-9758-0]

7. Camarca ME, Mozillo E, Nugnes R, Zito E, Falco M, Fantinuolo V, Mobilia S, Buono P, Valerio G, Troncone R, Franzese A. Celiac disease in type 1 diabetes mellitus. *Ital J Pediatr* 2012; 38: 10 [PMID: 22449104 DOI: 10.1186/1824-7288-38-10]

8. Lohi S, Mustalähi K, Kaukinen K, Laurila K, Collin P, Risvanen H, Lohi O, Bravi E, Gasparin M, Reunanen A, Mäki M. Increasing prevalence of coeliac disease over time. *Aliment Pharmacol Ther* 2007; 26: 1217-1225 [PMID: 17944736 DOI: 10.1111/j.1365-2036.2007.03502.x]

9. Barera G, Bonfanti R, Viscardi M, Bazzigaluppi E, Calori G, Meschi F, Bianchi C, Chiurullo G. Occurrence of celiac disease after onset of type 1 diabetes: a 6-year prospective longitudinal study. *Pediatrics* 2002; 109: 833-838 [PMID: 11986449 DOI: 10.1542/peds.109.5.833]

10. Cerutti F, Bruno G, Chiarelli F, Lorini R, Meschi F, Sacchetti C. Younger age at onset and sex predict celiac disease in children and adolescents with type 1 diabetes: an Italian multicenter study. *Diabetes Care* 2004; 27: 1294-1298 [PMID: 15161778 DOI: 10.2337/diacare.27.6.1294]

11. Salardi S, Volta U, Zucchiini S, Fiorini E, Maltoni G, Vaira B, Cicognani A. Prevalence of celiac disease in children with type 1 diabetes mellitus increased in the mid-1990 s: an 18-year longitudinal study based on anti-endomysial antibodies. *J Pediatr Gastroenterol Nutr* 2008; 46: 612-614 [PMID: 18493223 DOI: 10.1097/MPG.0b013e31815d9e76]

12. Freemark M, Levitsky LL. Screening for celiac disease in children with type 1 diabetes: two views of the controversy. *Diabetes Care* 2015; 38: 1952-1959 [PMID: 25766138 DOI: 10.2337/diabetes.26.6.1932]

13. Sud S, Marcon M, Assor E, Palmet MR, Daneman D, Mahmoud FH. Celiac disease and pediatric type 1 diabetes: diagnostical and treatment dilemmas. *Int J Pediatr Endocrinol* 2010; 2010: 161285 [PMID: 20652072 DOI: 10.1155/2010/161285]

14. Hufty S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, Troncone R, Giersiepen K, Braneski D, Cattani C, Lelegman M, Mäki M, Ribe-Köninkx C, Ventura A, Zimmer KP. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr* 2012; 54: 136-160 [PMID: 22197856 DOI: 10.1097/MPG.0b013e318212a23d0]

15. Hill ID, Dirks MH, Liptak GS, Colletti RB, Fasan A, Guandalini S, Hoffenberg EJ, Horvath K, Murray JA, Pivov M, Seidman EG. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr* 2005; 40: 1-19 [PMID: 15625418 DOI: 10.1097/00005051-200501000-00001]

16. Rubino-Tapia A, Kyle RA, Kaplan EL, Johnson DR, Page W, Erdtmann F, Brantner TL, Kim WR, Phelps TK, Lahr BD, Zinsmeister AR, Melton LJ, Murray JA. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology* 2009; 137: 88-93 [PMID: 19562553 DOI: 10.1053/j.gastro.2009.03.059]

17. Valerio G, Mauri I, Troncone R, Buono P, Lombardi F, Palmieri R, Franzese A. Severe clinical onset of diabetes and increased prevalence of other autoimmune diseases in children with coeliac disease diagnosed before diabetes mellitus. *Diabetologia* 2002; 45: 1719-1722 [PMID: 12488963 DOI: 10.1007/s00125-002-0923-5]

18. Errichelli S, Esposito O, Di Mase R, Camarca ME, Natale C, Limongelli MG, Marano C, Corazza G, Lombardo M, Strisciuglio P, Greco L. Celiac disease: predictors of compliance with a gluten-free diet in adolescents and young adults. *J Pediatr Gastroenterol Nutr* 2010; 50: 54-60 [PMID: 19644397 DOI: 10.1097/MPG.0b013e3181e9d62a]

19. Smart C, Aslander-van Vliet E, Waldron S. Nutritional Management. Global IDF/ISPAD guidelines for Diabetes in Childhood and Adolescence 2011:66-69

20. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *N Engl J Med* 1993; 329: 977-986 [PMID: 8566922 DOI: 10.1056/NEJM199309033290301]

21. Marsh K, Barclay A, Colagiuiri S, Brand-Miller J. Glycemic index and glycemic load of carbohydrates in the diabetes diet. *Curr Diab Rep* 2011; 11: 120-127 [PMID: 21222056 DOI: 10.1007/s11892-010-0173-8]

22. Dickey W, Koarny N. Overweight in celiac disease: prevalence, clinical characteristics, and effect of a gluten-free diet. *Am J Gastroenterol* 2006; 101: 2356-2359 [PMID: 17032202]

23. Taler I, Phillip M, Lebenthal Y, de Vries L, Shamir R, Shalitin S. Growth and metabolic control in patients with type 1 diabetes and celiac disease: a longitudinal observational case-control study. *Pediatr Diabetes* 2012; 13: 597-606 [PMID: ]
22564209 DOI: 10.1111/j.1399-5448.2012.00878.x

24 **Berrington de Gonzalez A**, Hartge P, Cerhan JR, Flint AJ, Hannan L, Machnius RJ, Moore SC, Tobias GS, Anton-Culver H, Freeman LB, Beeson WL, Clipp SL, English DR, Folsom AR, Freedman DM, Giles G, Hakansson N, Henderson KD, Hoffman-Bolton J, Hoppin JA, Koenig KL, Lee IM, Linet MS, Park Y, Pocobelli G, Schatzkin A, Sesso HD, Weiderpass E, Wilcoxon BJ, Wolk A, Zeleniuch-Jacquotte A, Willett WC, Thun MJ. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010; 363: 2211-2219 [PMID: 21212834 DOI: 10.1056/NEJMoa1000367]

25 **Ukkola A**, Mäki M, Kurppa K, Collin P, Huhtala H, Kekkonen L, Kaukinen K. Changes in body mass index on a gluten-free diet in coeliac disease: a nationwide study. *Eur J Intern Med* 2012; 23: 384-388 [PMID: 22560391 DOI: 10.1016/j.ejim.2011.12.012]

26 **Acerini CL**, Ahmed ML, Ross KM, Sullivan PB, Bird G, Dunger DB. Coeliac disease in children and adolescents with IDDM: clinical characteristics and response to gluten-free diet. *Diabet Med* 1998; 15: 38-44 [PMID: 9472862]

27 **Nóvoa Medina Y**, López-Capapé M, Lara Orejas E, Alonso Blanco M, Camarero Salces C, Barrio Castellanos R. Impact of diagnosis of celiac disease on metabolic control of type 1 diabetes. *An Pediatr* (Barc) 2008; 68: 13-17 [PMID: 18194622 DOI: 10.1157/13114465]

28 **Saadah OI**, Zacharin M, O’Callaghan A, Oliver MR, Catto-Smith AG. Effect of gluten-free diet and adherence on growth and diabetic control in diabetes with coeliac disease. *Arch Dis Child* 2004; 89: 871-876 [PMID: 15321869 DOI: 10.1136/adc.2002.012799]

29 **Savilahti E**, Simell O, Koskimies S, Silva A, Akerblom HK. Celiac disease in insulin-dependent diabetes mellitus. *J Pediatr* 1986; 108: 690-693 [PMID: 3701514 DOI: 10.1016/S0022-3476(86)81042-3]

30 **Kaukinen K**, Salmi J, Lahtela J, Siljamäki-Ojansuu U, Koivistö AM, Oksa H, Collin P. No effect of gluten-free diet on the metabolic control of type 1 diabetes in patients with diabetes and celiac disease. Retrospective and controlled prospective survey. *Diabetes Care* 1999; 22: 1747-1748 [PMID: 10526749 DOI: 10.2337/diacare.22.10.1747a]

31 **Abid N**, McGlone O, Cardwell C, McCallion W, Carson D. Clinical and metabolic effects of gluten free diet in children with type 1 diabetes and coeliac disease. *Pediatr Diabetes* 2011; 12: 322-325 [PMID: 21616561 DOI: 10.1111/j.1399-5448.2010.00700.x]

32 **Bakker SF**, Tushuien ME, von Blomberg ME, Mulder CJ, Simsek S. Type 1 diabetes and celiac disease in adults: glycemic control and diabetic complications. *Acta Diabetol* 2013; 50: 319-324 [PMID: 22539236]

33 **Picarelli A**, Di Tola M, Sabbatella L, Mercuri V, Pietrobono D, Bassotti G, D’Amico T, Donato G, Picarelli G, Marino M, Borghini R, Contanni M, Gargiulo P. Type 1 diabetes mellitus and celiac disease: endothelial dysfunction. *Acta Diabetol* 2011 Jun 21; [Epub ahead of print] [PMID: 21691748]

34 **Pitocco D**, Giubilato S, Martini F, Zaccardi F, Pazzano V, Manto A, Cammarota G, Di Stasio E, Pedicino D, Liuzzo G, Crea F, Ghirlanda G. Combined atherogenic effects of celiac disease and type 1 diabetes mellitus. *Atherosclerosis* 2011; 217: 531-535 [PMID: 21601206 DOI: 10.1016/j.atherosclerosis.2011.04.042]

35 **Leeds JS**, Hopper AD, Hadijvasiliou M, Tesfaye S, Sanders DS. High prevalence of microvascular complications in adults with type 1 diabetes and newly diagnosed celiac disease. *Diabetes Care* 2011; 34: 2158-2163 [PMID: 21911773 DOI: 10.2337/dc10-1949]

36 **Sildorf SM**, Fredheim S, Svensson J, Buschard K. Remission without insulin therapy on gluten-free diet in a 6-year-old boy with type 1 diabetes mellitus. *BMJ Case Rep* 2012; 2012: DOI: 22729336 DOI: 10.1136/bcr.02.2012.5878

37 **Ceriello A**. Postprandial hyperglycemia and diabetes complications: is it time to treat? *Diabetes* 2005; 54: 1-7 [PMID: 15616004 DOI: 10.2337/diabetes.54.1.1]

38 **Berti C**, Riso P, Monti LD, Porrini M. In vitro starch digestibility and in vivo glucose response of gluten-free foods and their gluten counterparts. *Eur J Nutr* 2004; 43: 198-204 [PMID: 15309439 DOI: 10.1007/s00394-004-0459-1]

39 **Brand-Miller J**, Hayne S, Petocz P, Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care* 2003; 26: 2261-2267 [PMID: 12882846 DOI: 10.2337/diacare.266.8.2261]

40 **Malasekera V**, Cameron F, Gristi E, Thomas MC. Potential reno-protective effects of a gluten-free diet in type 1 diabetes. *Diabetologia* 2009; 52: 798-800 [PMID: 19219421 DOI: 10.1007/s00125-009-1277-z]
