ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

THE PROBABILITY OF CELIAC DISEASE, INDICATED BY HIGH ANTI TTG TITER, IN OMANI PATIENTS WITH TYPE 1 DIABETES MELLITUS.

Internal Medicine

Dr Hamdi Saleh Al-Mutori Principal Investigator. Assistant Professor, National University for Science and Technology – College of Medicine and Health Sciences. Oman

Dr Mazin Saleh Al-Rudaini* Assistant Professor, National University for Science and Technology – College of Medicine and Health Sciences. Oman *Corresponding Author

Dr Ali Al Reesi Consultant Endocrinologist, Suhar Hospital, Oman.

Dr Salem Al Ghaithi Medical Officer Endocrine, Suhar Hospital, Oman.

Dr Hamed Al Reesi Head of Studies and Research Department, Directorate of Planning and Studies, Ministry of Health, North Batinah Governorate, Oman

ABSTRACT

The coexistence of autoimmune disorders is not uncommon in clinical practice. Giving that both Type 1 diabetes mellitus (T1DM) and celiac disease (CD) are common autoimmune disorders, the association between the two conditions often exist. Many literatures demonstrated such association; however this associated was not studied thoroughly in Oman.

Methods: Patients with T1DM who were included in the study were tested serologically for probable CD using Anti-TTG antibody. Other nutritional parameters were also assessed. Information regarding patients' age, sex, duration of diabetes, presence of any symptoms suggestive CD and any family history of CD were gathered. Statistical Package for the Social Science (SPSS) was used to collect and analyze data.

Results: A total of 34 patients with T1DM visited the diabetic outpatient clinic in Suhar Hospital / Oman were included in the study during the study period. The majority of the patients (70.6%) were females and 29.4% were males. Seven patients had significantly high Anti-TTG which accounting for an incidence of 21.2%. The probability of positive CD for females was 71.4% compared to 28.6% for males, however, the difference wasn't statistically significant. None of the celiac patients showed a weight change and the minority had diarrhea (14.3%). There was a significant association between BODY MASS INDEX and CD (p=0.036).The BMI level was lower among positive celiac patients compared to negative celiac patients. Nutritional indicators showed no significant differences between those who are suspected to have CD and those who were not.

These findings suggest that the probability of having CD in patients with T1DM is high in Oman and screening for CD for all T1DM patients might be important.

KEYWORDS

Type 1 diabetes mellitus (T1DM), Celiac disease (CD), Anti-TTG ant

INTRODUCTION:

The association between celiac disease (CD) and type 1 diabetes mellitus was first noted over 40 years ago[1,2] and since then has been established in numerous studies.[3-6]

It is now recognized that CD may be more common and of a more varied presentation than previously thought, especially in patients with type 1 diabetes mellitus.[7–13] Many cases appear to be atypical, silent or latent in their presentation and are at risk of remaining undetected and untreated. If such patients are not treated, they risk complications such as anemia, infertility, malabsorption, vitamin and mineral deficiencies, osteoporosis, osteomalacia, growth retardation and malignant disorders. In patients with type 1 diabetes mellitus, untreated CD may be particularly associated with growth retardation, poor glycemic control, recurrent hypoglycemic attacks and delayed puberty.[10,14]

Both CD and type 1 diabetes mellitus are associated with HLA class II genes on chromosome 6p21.[15] The prevalence of CD in North America is estimated to approach 1% of the general population[16] and has increased fourfold over the past 50 years.[17] CD occurs more frequently in type 1 diabetes mellitus than in the general population, with estimates varying from 2.4%[18] to 16.4%.[19] The prevalence of CD in patients with type 1 diabetes mellitus is on rising.[20] The risk of CD may vary by age of diagnosis of type 1 diabetes mellitus.[21]

Despite the higher prevalence of CD in type 1 diabetes mellitus, there is no consensus on screening patients with type 1 diabetes mellitus for CD.[22] The American Diabetes Association recommends screening select patients based on symptoms and treating patients with biopsy-confirmed CD with the gluten-free diet.[23]

The Canadian Diabetes Association recommends screening patients with symptoms and notes that for those with no symptoms, treatment is controversial.[24]

Those that advocate routine screening of type 1 diabetes mellitus patients for CD[25-27] emphasize that patients with type 1 diabetes mellitus may have no symptoms, unrecognized symptoms[5,27], or symptoms that are only recognized retrospectively[28] and that there are complications of untreated CD.[29]

Published studies on the prevalence of CD in type 1 diabetes mellitus from the Arab World are scant. The prevalence of CD in Omani children and adolescents with type 1 diabetes mellitus is similar to the World's reported prevalence, but is less than that reported for Middle Eastern Arab children. To our knowledge, this is the first reported study on the prevalence of CD in Omani children with type 1 diabetes mellitus.[30]

Although a definite association between type 1 diabetes mellitus and CD exists, it is controversial as to whether a screening program should be instituted to detect clinically unrecognized CD, particularly whether implementation of a gluten free diet (GFD) in these patients may be practical as well as cost-effective.

The research question investigated was whether diabetes centers screen for CD in patients with type 1 diabetes mellitus more frequently than other facilities.

METHODS:

This is a cross sectional study included adult patients with type 1 diabetes mellitus who attended diabetes outpatient clinic at Suhar Hospital for regular follow up in the period between August 2016 and August 2017. All patients were explained the possible relation between the CD and type 1 diabetes mellitus and the nature of the study. A comprehensive consent form was taken from those who agreed to be part of the study.

The following information was collected from each patient: Age, sex, duration of diabetes, mode of presentation at time of diagnosis, presence of any symptoms suggestive CD (diarrhea, weight loss,

abdominal cramps or bloating, etc.) and any family history of CD.

Blood samples from all participants were collected for serum Anti-tissue Transglutaminase Antibodies (Anti-TTG) using Enzyme Linked Immunosorbent Assay (ELISA) quantitative assay for human autoantibodies of IgA class against tissue transglutaminase. Patients with Anti-TTG antibody titer of 20 u/ml or above were considered as possible positive cases for CD. Additionally, serum level of vitamin B12, folic acid, hemoglobin, calcium, vitamin D, ferritin and glycosylated hemoglobin (HbA1c) were also assessed.

Statistical Package for the Social Science (SPSS) was used to collect and analyze data. Data analysis started by describing each of the study variables in terms of frequency and statistical summaries. The difference between patients with and without CD was compared by all other risk factors using non-parametric tests (chi-square, Mann-Whitney U and Kruskal-Wallis H) due to the small sample size.

RESULTS:

A total of 34 patients with type 1 diabetes mellitus visited the diabetic outpatient clinic in Suhar Hospital during the study period. The majority of the patients (70.6%) were females and 29.4% were males. Of the patients, 85.3% were present with hyperglycemia and 44.1% with hypoglycemia. Just 11.8% of the patients showed increase in their weight, 5.9% presented with diarrhea and 20.6% presented with family history of type 1 diabetes mellitus. The average age of the patients was 21.0 years (SD=7.2 years) and ranged between 9 and 39 years. The body mass index (BMI) was ranged from 14.0 to 42.4 with an average of 23.42 (SD=5.51). In average, patients hold diabetes mellitus for 8.41 years (SD=6.39 years) with a range 0.30 to 26.0 years.

Table 1: Characteristics of Type 1 diabetes patients participated in the study.

Type 1 Patients Characteristics		Frequency	Percent
Gender	Male	10	29.4
	Female	24	70.6
	Total	**34**	**100**
Presentation	Hyperglycemia	29	85.3
	DKA	5	14.7
	Total	**34**	**100**
Hypoglycemia	Yes	15	44.1
	No	19	55.9
	Total	**34**	**100**
Weight Change	No	30	88.2
	Increase	4	11.8
	Total	**34**	**100**
Diarrhea	Yes	2	5.9
	No	32	94.1
	Total	**34**	**100**
FH.type1	Yes	7	20.6
	No	27	79.4
	Total	**34**	**100**
Celiac Disease	Positive	7	21.2
	Negative	26	78.8
	Total	**33**	**100**

Table 2: Descriptive Statistics of Some of the Type 1 diabetes Patients Characteristics

	Valid Cases	Mean	Standard Deviation	Minimum	Maximum
Age (years)	34	21.00	7.24	9.00	39.00
BMI*	33	23.42	5.51	14.00	42.10
Duration (years)	34	8.41	6.39	0.30	26.00
Calcium (mmole)	34	2.35	0.07	2.19	2.50
Serum Ferritin (ng/ml)	34	67.96	91.22	2.12	489.20
Serum B12 (pg/ml)	34	528.51	213.87	247.00	1272.00
Folic Acid (nmole)*	33	24.32	9.40	3.28	38.80
Vitamin D (nmole)*	29	38.41	18.85	10.78	95.70
HbA1c	34	9.52	3.07	5.25	18.85
AntiTTG*	33	40.36	82.16	2.00	300.00
IgA*	33	2.57	1.11	1.15	5.30
**** Missing values***					

Patients Suspected of Celiac Disease (CD):

Anti-tissue Transglutaminase Antibodies (Anti-TTG) in patients with type 1 diabetes mellitus was carried out as an indicator of possible CD. Patients with Anti-TTG of 20 u/ml and above were suspected to have celiac disease and required further investigation for confirmation. The Anti-TTG values ranged between 2.0 and 300.0 with an average of 40.4 u/ml (SD=82.2 u/ml).

Table 3 shows that seven patients were diagnosed, through Anti-TTG, to be suspected of CD accounting for an incidence of 21.2%. The probability of positive CD for females was 71.4% compared to 28.6% for males, however, the difference wasn't statistically significant. The majority of celiac patients (71.4%) were present with hyperglycemia and 57.1% were present with hypoglycemia. None of the celiac patients showed a weight change. The minority have diarrhea (14.3%) and family history of type 1 diabetes mellitus (14.3%).

Table 3: The Association between Celiac Disease and patient characteristics (Categorical data)

		Celiac Disease				Total	Fisher's Exact Test
		Positive		Negative			
		No.	%	No.	%		(P-value)
Gender	male	2	28.6	8	30.8	10	0.648
	female	5	71.4	18	69.2	23	
	Total	7	100.0	26	100.0	33	
Presentation	hyperglycemia	5	71.4	23	88.5	28	0.282
	DKA	2	28.6	3	11.5	5	
	Total	7	100.0	26	100.0	33	
Hypoglycemia	yes	4	57.1	10	38.5	14	0.422
	no	3	42.9	16	61.5	19	
	Total	7	100.0	26	100.0	33	
Weight Change	no	7	100.0	22	84.6	29	0.555
	increase	0	0.0	4	15.4	4	
	Total	7	100.0	26	100.0	33	
Diarrhea	yes	1	14.3	1	3.8	2	0.384
	no	6	85.7	25	96.2	31	
	Total	7	100.0	26	100.0	33	
FH Type1	yes	1	14.3	6	23.1	7	1.00
	no	6	85.7	20	76.9	26	
	Total	7	100.0	26	100.0	33	

Table 4 shows that positive celiac patients (Mean=19.6 years) were younger than negative celiac patients (Mean=21.6 years), however, the difference wasn't significant. There was a significant association between BMI and CD (Z=-2.10, p=0.036). The BMI level was lower among positive celiac patients (Mean=19.3) compared to negative celiac patients (Mean=24.5 years). Although, the level of serum ferritin was lower among positive celiac patients (Mean=41.7 ng/ml) than among negative celiac patients (Mean=75.1 ng/ml), however, the difference wasn't significant. Similarly, the level of serum vitamin B12 was lower among positive celiac patients (Mean=426.3 pg/ml) than among negative celiac patients (Mean=553.3 pg/ml), however, the difference wasn't significant. The average diabetes mellitus duration, calcium level, folic acid level, vitamin D level, HbA1c and IgA were almost similar between positive and negative celiac patients and statistically the differences were not significant.

Table 4: The Association between Celiac Disease and patient characteristics (Continuous data)

	Celiac Disease	N	Mean Rank	Mann-Whitney U	Z	Sig
Age	Positive	7	13.36	65.5	-1.124	0.261
	Negative	26	17.98			
BMI	Positive	7	9.93	41.5	-2.098	0.036
	Negative	25	18.34			
DM duration (years)	Positive	7	18.07	83.5	-0.331	0.74
	Negative	26	16.71			
Calcium (mmole)	Positive	7	17.07	90.5	-0.022	0.982
	Negative	26	16.98			

Serum ferritin (ng/ml)	Positive	7	14.64	74.5	-0.727	0.467
	Negative	26	17.63			
Serum B12 (pg.ml)	Positive	7	12	56	-1.541	0.123
	Negative	26	18.35			
Folic Acid (nmole)	Positive	7	16.79	89.5	-0.066	0.947
	Negative	26	17.06			
Vitamin D (nmole)	Positive	6	11.83	50	-0.896	0.37
	Negative	22	15.23			
HbA1c	Positive	7	14.71	75	-0.705	0.481
	Negative	26	17.62			
IgA	Positive	7	13.36	65.5	-1.123	0.261
	Negative	26	17.98			

DISCUSSION:

The link between CD and type 1 diabetes mellitus as autoimmune diseases that affect genetically susceptible individuals was established. Such well documented association in young people is vary in its prevalence from 1.6% to 16.4% wordwide.[19,31-34]

We have found that the prevalence rate of CD in type 1 diabetes mellitus patients was high (21.2%) compared to other studies. The highest prevalence was reported in Algeria (16.4%)[19] while the lowest was reported in Germany and Switzerland (1.6%)[35, 36]. Another example of geographical variation was shown by Newton et al study where they found the highest prevalence rates in the Sahrawi population comparing to Japanese population. [37]

It remains to be established whether the variation in the prevalence of CD in patients with type 1 diabetes mellitus can be attributed to variations in genetic susceptibility, dietary habit of the population, other environmental factors or to a combination of all these.[38]

Gender wise, CD is a female predominant disease, and is 2-3 times more common among females.[39] Consistently, our study shows that the probability of positive CD for females is 71.4% compared to 28.6% for males, with no statistical difference between both genders. Although there was no gender difference in the prevalence rates of type 1 diabetes mellitus, CD was reported to be more prevalent in females than in males with type 1 diabetes mellitus.[40-42]

None of the CD patients which were included in our study showed any weight change. Nevertheless, 14.3% complained of diarrhea. This is comparable to Scaramuzza et. al study where about 10% of patients with type 1 diabetes mellitus and CD show gastrointestinal symptoms.[43] Although the classical presentations of CD cases (diarrhea, weight loss, anemia, etc.) are known features, several reports in the literature stated that many cases of CD are asymptomatic or only associated with mild symptoms.[44-46]

We could not find a significant statistical difference in HbA1c level between diabetes mellitus and CD on one hand and diabetes mellitus only on the other hand. Such finding is consistent with similar study in children, where HbA1c levels at baseline did not differ significantly between patients with type 1 diabetes mellitus and CD, and between those with type 1 diabetes mellitus alone.[47] Yet, among adult type 1 diabetes mellitus patients who were newly diagnosed with CD, glycemic control was significantly worse than for those with type 1 diabetes mellitus alone, 8.2% *vs* 7.5%, $P = 0.05$.[48] Amin et al. noted that HbA1c level was lower in diabetes mellitus patients with CD disease before gluten free diet.[49]

Thus data remain inconsistent regarding glycemic control in patients with dual diagnosis of CD and type 1 diabetes mellitus and the difference between these studies most probably reflect the impact of delayed diagnosis of CD or the variability in disease severity.

Due to impaired absorption of dietary nutrients, low levels of nutritional elements (folic acid, vitamin D, ferritin, vitamin B12, calcium) were expected. However, we could not find statistically different figures between both groups of diabetes mellitus with CD and diabetes mellitus alone regarding Levels Of Those Elements elements. Such finding was in contrary to other studies which documented the impact of nutrients malabsorption caused by CD in both children and adults that included B vitamins, iron, folic acid and minerals.[50-52]This discrepancy might be attributed to mild form of CD cases included in our study. Jameson et. al study reported that the more pronounced the lesion, the lower the levels are seen for iron, copper, folate and vitamin B-12.[51]

In conclusion, the prevalence of CD in patients with type 1 diabetes mellitus is high; however additional studies are required to prove this relationship. Giving that, it seems worthy to consider screening for CD in all patients with type 1 diabetes mellitus on regular bases.

REFERENCES:

1. Walker-Smith JA, Grigor W. Coeliac disease in a diabetic child. Lancet. 1969;1(7603):1021.
2. Thain ME, Hamilton JR, Ehrlich RM. Coexistence of diabetes mellitus and celiac disease. J Pediatr. 1974;85(4):527-529.
3. Crone J, Rami B, Huber WD, Granditsch G, Schober E. Prevalence of celiac disease and follow-up of EMA in children and adolescents with type 1 diabetes mellitus. J Pediatr Gastroenterol Nutr. 2003;37(1):67-71.
4. Franzese A, Iafusco D, Spadaro R, et al. Potential celiac disease in type 1 diabetes: a multicenter study. Diabetes Res Clin Pract. 2011;92:53-56.
5. Freemark M, Levitsky LL. Screening for celiac disease in chil¬dren with type 1 diabetes: two views of the controversy. Diabetes Care. 2003;26(6):1932-1939.
6. Holmes GK. Screening for coeliac disease in type 1 diabetes. Arch Dis Child. 2002;87:495-498.
7. Bottaro G, Cataldo F, Rotolo N et al. The clinical pattern of subclinical/silent celiac disease: an analysis on 1026 consecutive cases. Am J Gastroenterol 1999; 94:691–6.
8. Nuti R, Martini G, Valenti R et al. Prevalence of undiagnosed celiac syndrome in osteoporotic women. J Intern Med 2001; 250:361–6.
9. Pocecco M, Ventura A. Coeliac disease and insulindependent diabetes mellitus: a causal association? Acta Paediatr 1995; 84:1432–3.
10. Lorini R, Scaramuzza A, Vitali L et al. Clinical aspects of coeliac disease in children with insulin-dependent diabetes mellitus. J Pediatr Endocrinol Metab 1996; 9(Suppl 1):101–11.
11. Bottaro G, Failla P, Rotlo N et al. Changes in coeliac disease behaviour over the years. Acta Paedatr 1993;82:566–8.
12. Cronin CC, Shanahan F, Liddy G et al. High prevalence of coeliac disease in patients with insulin-dependent (type I) diabetes mellitus. Irish J Med Sci 1996; 165(Suppl 4):2.
13. Catassi C, Ratsch IM, Fabiani E et al. Coeliac disease in the year 2000: exploring the iceberg. Lancet 1994; 343:200–3.
14. Lorini R, Scotta MS, Cortona L et al. Celiac disease and type 1 (insulin-dependent) diabetes mellitus in childhood: follow-up study. J Diabetes Comp 1996; 10:154–9.
15. Smyth DJ, Plagnol V, Walker NM, et al. Shared and distinct genetic variants in type 1 diabetes and celiac disease. N Engl J Med. 2008;359(26):2767-2777.
16. Fasano A, Berti I, Gerarduzzi T, et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large mul¬ticenter study. Arch Intern Med. 2003;163(3):286-292.
17. Rubio-Tapia A, Kyle RA, Kaplan EL, et al. Increased prevalence and mortality in undiagnosed celiac disease. Gastroenterology. 2009;137(1):88-93.
18. Saukkonen T, Savilahti E, Reijonen H, Ilonen J, Tuomilehto-Wolf E, Akerblom HK. Coeliac disease: frequent occurrence after clinical onset of insulin-dependent diabetes mellitus. Childhood Diabetes in Finland Study Group. Diabet Med. 1996;13(5):464-470.
19. Boudraa G, Hachelaf W, Benbouabdellah M, Belkadi M, Benmansour FZ, Touhami M. Prevalence of coeliac disease in diabetic children and their first-degree relatives in west Algeria: screening with serological markers. Acta Paediatr Suppl. 1996;412:58-60.
20. Salardi S, Volta U, Zucchini S, et al. 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(5):612-614.
21. Cerutti F, Bruno G, Chiarelli F, et al. 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(6):1294-1298.
22. Sud S, Marcon M, Assor E, Palmert MR, Daneman D, Mahmud FH. Celiac disease and pediatric type 1 diabetes: diagnostic and treatment dilemmas [published online June 23, 2010]. Int J Pediatr Endocrinol. doi: 10.1155/2010/161285.
23. Executive summary: standards of medical care in diabetes—2011. Diabetes Care. 2011;34(suppl 1):S4-10.24. Canadian Diabetes Association 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Canadian J Diabetes. 2008;32(suppl 1):22-35.
25. Holmes GK. Coeliac disease and type 1 diabetes mellitus-the case for screening. Diabet Med. 2001;18(3):169-177.
26. Franzese A, Spagnuolo MI, Valerio G. Diabetic children with asymptomatic celiac disease: is it necessary to stress gluten-free diet? Clin Nutr. 2004;23(2):281-282.
27. O'Connor TM, Cronin CC, Loane JF, et al. Type 1 diabetes mel¬litus, coeliac disease, and lymphoma: a report of four cases. Diabet Med. 1999;16(7):614-617.
28. Spiekerkoetter U, Seissler J, Wendel U. General screening for celiac disease is advisable in children with type 1 diabetes. Horm Metab Res. 2002;34(4):192-195.
29. Hansen D, Bennedbaek FN, Hansen LK, et al. High prevalence of coeliac disease in Danish children with type I diabetes mellitus. Acta Paediatr. 2001;90(11):1238-1243
30. Al-Sinani S1, Sharef SW, Al-Yaarubi S, Al-Zakwani I, Al-Naamani K, Al-Hajri A, Al-Hasani S. Prevalence of celiac disease in omani children with type 1 diabetes mellitus: a cross sectional study. Oman Med J. 2013 Jul;28(4):260-3. doi: 10.5001/omj.2013.73.
31. Poulain C, Johanet C, Delcroix C, Lévy-Marchal C, Tubiana-Rufi N. Prevalence and clinical features of celiac disease in 950 children with type 1 diabetes in France. Diabetes Metab. 2007;33(6):453–458
32. Al-Hussaini A, Sulaiman N, Al-Zahrani M, Alenizi A, El Haj I. High prevalence of celiac disease among Saudi children with type 1 diabetes: a prospective cross-sectional study. BMC Gastroenterol. 2012;12:180
33. Baptista ML, Koda YKL, Mitsunori R, Nisihara , Ioshii SO. Prevalence of celiac disease in Brazilian children and adolescents with type 1 diabetes mellitus. J Pediatr Gastroenterol Nutr. 2005;41(5):621–624
34. Djuri_c Z, Stamenkovi_c H, Stankovi_c T, et al. Celiac disease prevalence in children and adolescents with type 1 diabetes from Serbia. Pediatr Int. 2010;52(4):579–583
35. Koletzko S, Burgin-Wolff A, Koletzko B et al. Prevelance of coeliac disease in diabetic children and adolescents. A multicentre study. Eur J Paediat 1988;148:113–17.
36. Seissler J, Schott M, Boms S et al. Autoantibodies to human tissue transglutaminase identify silent coeliac disease in type I Diabetes. Diabetologia 1999; 42:1440–1.
37. K. P. Newton and S. A. Singer, "Celiac disease in children and adolescents: special considerations," Seminars in Immunopathology, vol. 34, no. 4, pp. 479–496, 2012.
38. H. Soran, G. Gill, N. Younis. Type 1 Diabetes and Coeliac disease. J R Coll Physicians Edinb 2002; 32:178-188.
39. Bai D, Brar P, Holleran S, Ramakrishnan R, Green PH. Effect of gender on the manifestations of celiac disease: evidence for greater malabsorption in men. Scand J Gastroenterol 2005; 40: 183-187 [PMID: 15764149 DOI:10.1080/00365520510011498]
40. Picarelli A, Sabbatella L, Di Tola M, Vetrano S, Casale C, Anania MC, Porowska B, Vergari M, Schiaffini R, Gargiulo P. Antiendomysial antibody of IgG1 isotype detection

strongly increases the prevalence of coeliac disease in patients affected by type I diabetes mellitus. Clin Exp Immunol 2005; 142: 111-115 [PMID:16178863 DOI: 10.1111/j.1365-2249.2005.02866.x]
41. Kaspers S, Kordonouri O, Schober E, Grabert M, Hauffa BP, Holl RW. Anthropometry, metabolic control, and thyroid autoimmunity in type 1 diabetes with celiac disease: A multicenter survey. J Pediatr 2004; 145: 790-795 [PMID: 15580203 DOI: 10.1016/j.jpeds.2004.07.031]
42. Greco D, Pisciotta M, Gambina F, Maggio F. Celiac disease in subjects with type 1 diabetes mellitus: a prevalence study in western Sicily (Italy). Endocrine 2013; 43: 108-111 [PMID:22707396 DOI: 10.1007/s12020-012-9718-8]
43. Scaramuzza AE, Mantegazza C, Bosetti A, Zuccotti GV. Type 1 diabetes and celiac disease: The effects of gluten free diet onmetabolic control. World J Diabetes 2013; 4: 130-134 [PMID:23961323 DOI: 10.4239/wjd.v4.i4.130]
44. Valerio G, Maiuri L, 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]
45. Ventura A, Neri E, Ughi C, Leopaldi A, Città A, Not T. Glutendependent diabetes-related and thyroid-related autoantibodies in patients with celiac disease. J Pediatr 2000; 137: 263-265 [PMID:10931424]
46. Holmes GK. Potential and latent coeliac disease. Eur J Gastroenterol Hepatol 2001; 13: 1057-1060 [PMID: 11564955]
47. Simmons JH, Klingensmith GJ, McFann K, Rewers M, Ide LM, Taki I, Liu E, Hoffenberg EJ. Celiac autoimmunity in children with type 1 diabetes: a two-year follow-up. J Pediatr 2011; 158: 276-81. e1 [PMID: 20817171 DOI: 10.1016/j.jpeds.2010.07.025.Celiac]
48. Leeds JS, Hopper AD, Hadjivassiliou 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/dc11-0149]
49. Amin R, Murphy N, Edge J, et al. A longitudinal study of effect of a gluten-free diet on glycemic control and weight gain in subjects with type 1 diabetes and celiac disease. Diabetes Care 2002;25:1117-1122.
50. Bona G, Marinello D, Oderda G. Mechanisms of abnormal puberty in coeliac disease. Horm Res 2002;57(Suppl 2):63–65.
51. Jameson S. Coeliac disease, insulin-like growth factor, bone mineral density, and zinc. Scand J Gastroenterol 2000;35:894–896.
52. Hallert C, Grant C, Grehn S, Grännö C, Hultén S, Midhagen G, Ström M, Svensson H, Valdimarsson T. Evidence of poor vitamin status in coeliac patients on a gluten-free diet for 10 years. Aliment Pharmacol Ther 2002;16:1333–1339.