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Research Article

**OCCURRENCE OF ADEQUATE GLYCEMIC CONTROL
AMONG PATIENTS OF TYPE 1 DIABETES MELLITUS (T1DM)
ALONE AND T1DM+ CELIAC DISEASE (CD)**Dr. Maryam Safdar¹, Dr. Rida Tahir², Dr. Mariam Nissa Ullah²¹ THQ Hospital Chishtian, Pakistan² Wah Medical College Wah Cantt, Pakistan

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Abstract:

Objective: To determine the frequency of celiac disease among type 1 diabetic patients and to compare the frequency of adequate glycemic control in patients having T1DM plus CD and T1DM alone.

Study Design: Cross-sectional study.

Place and Duration: The Study was conducted in department of medicine, Services hospital, Lahore for the duration of one year from September, 2018 to August, 2019.

Methodology: Patients were recruited through medical and diabetes OPDs and medical wards. All the relevant information was recorded on a Proforma. In all type 1 diabetics a sample of blood was sent to AFIP for the determination of Anti-tTG (IgA) antibodies; using a commercially available ELISA technique (Pharmacia Upjohn, Sweden) based on recombinant human tTG as antigen. The measuring range of this test is 0.1 - 100 U/ml. We used the cut-offs: anti-tTG IgA ≤ 10 U/ml were considered negative, > 10 U/ml was considered positive. The assay was a quantitative assay. On the same visit, another blood sample was sent for HbA1C estimation.

Results: Total 160 patients were included according to the inclusion criteria of the study. Mean age (years) in the study was 26.58 \pm 9.13. There were 83 (51.9) male and 77 (48.1) female patients who were included in the study according to the inclusion criteria. The frequency of celiac disease among type 1 diabetic patients was 42 (26.3) in the study whereas the frequency of adequate glycemic control in patients having T1DM plus CD and T1DM alone was 26 (61.9) and 31 (26.3) respectively.

Conclusion: The study concludes that the prevalence of celiac disease in type 1 diabetes mellitus in our own population is high. Furthermore, gluten-free diet effects on glycemic control of type 1 diabetic patients which in screening for celiac disease in type 1 diabetes mellitus patients and to decreased risk of complication of diabetes.

Keywords: Celiac Disease, Diabetes Mellitus, Diabetes Mellitus Type 1.

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INTRODUCTION:

Celiac Disease (CD) is the insusceptible intervened enteropathy influencing about 1% of the overall population [1]. Immune reaction happens when hereditarily vulnerable people ingest the gluten, which is the capacity protein in the wheat and its related grain species, and this response is totally reversible upon the gluten withdrawal, that's only current accessible treatment for the Celiac Disease [1]. Celiac disease is seen in nearly 1% of the general population but in type 1 diabetes, CD prevalence ranges from 3% to 16% [2]. In another study the prevalence of CD is 28.2% [3].

A study conducted by Amit Akirov and Orit Pinhas-Hamiel [1] shows that patients with T1DM and Celiac disease concurring with each other leads to worsening of T1DM. In T1DM who were diagnosed to have CD glycaemic control was worse than those with only T1DM 8.2% vs 7.5% [4,5]. This leads to more micro and macroangiopathic complications and so a worse prognosis is seen. Also, in children with both these diseases together, the growth rate is poor compared to those children who just suffer from T1DM and don't have CD [1]. See et al [2] in a study published in 2015 showed that if the patient is given natural gluten-free foods such as brown rice, the glycaemic control is much better and there is very lower risk of the developing complications of the T1DM [2]. Diabetes mellitus type I is the multisystem infection with both biochemical and anatomic/basic outcomes. Event of diabetes mellitus type I is the conceivable in age group [6].

Pilia et al reported a big incidence of against GAD antibodies and islet cell antibodies (IA2) in cases having autoimmune thyroiditis [7]. In a study conducted by Philippe et al utilized CT scan, glucagon stimulation test results, and fecal elastase-1 assessments to affirm diminished the volume of pancreas people having DM [8]. This discovering, which was similarly present in both type 1 and II DM, may as well simplify the linked dysfunction of exocrine which happens in DM [9]. Disease Control and Prevention of United state stated that about 1 million Americans having DMTI. As well as Middle East, Europe and Australia, DMTI expanding by 2-5% every year [10]. Risk of the improvement in antibodies "anti-islet" in the patient's relative having DMTI diminishes with expanding age. These discovering bolsters yearly screening for antibodies in relatives more youthful than 10 years and 1 extra screening during youthfulness [11]. Diabetes mellitus TI most common in males as compare to females. In European population the male-to-female ratio is 1.5:1 [12]. In diabetic and non-diabetic cases, coronary vasodilator

dysfunction is the indicator of cardiovascular mortality [13]. Epidemiological reports carried out in CD free areas, including Middle East, South America, Asia, and Africa, demonstrate that the illness was underdiagnosed previously [14].

Previously, prevalence of CD had been underestimated, however it is currently respected a standout amongst the most widely recognized hereditary issue in the West with 1% prevalence [15]. interestingly, there is expanded CD prevalence among ladies contrasted with men with male: female proportion of 1:2.8 [16]. Prevalence of CD in In Europe and north America CD prevalence was found to be similar in symptomatic cases and not-at-risk subjects. Celiac disease prevalence believed to affect 0.5%-1.0% of the general population in United states [17]. Diabetes mellitus type I linked to other autoimmune events frequently and these events may affect the clinical management. These diseases also related to organ specific autoantibodies; celiac disease with EMA and transglutaminase autoantibodies, autoimmune thyroid with thyroglobulin autoantibodies and thyroid peroxidase and AD with the adrenal autoantibodies [18]. In previous studies showed that 4.4 to 11.1% celiac disease occurs in cases having TID as compare to general population [19]. Youngers mostly associated with double disease on type I diabetes onset as compare to TID alone [20].

Risk of celiac disease adversely and individually connected with the age at diabetes starting, with the high risk being found in kid's age less than 4 years as compare to those having age more than 9 years. Diabetes diagnosed first usually in cases having TID and CD developed 10-25% at diabetes onset. Accordingly, autoimmune disorder prevalence in CD, closely linked to age on diagnosis, or to period of the revelation to thyroid and gluten-associated antibodies incline to disappear through 12 months of the gluten-free diets, as CD linked antibodies. Though it is unidentified whether management of the CD decrease the chance of autoimmune disorder or altered the natural history of their and in fact others seen no association between of exposure of gluten in adults and autoimmune disorder risk [21].

In cases having CD event, recognizing and treating by gluten free diet confidently confer advantage in reducing or resolving the poor nutrition, malabsorption, impaired growth, infertility, risk of malignancy, osteoporosis and mortality. Likewise, children having T1D and symptomatic CD 'could be improved by GFD and diabetic metabolic control [22]. Concerning to patient's natural history with pot-CD, a

currents report stated that 30% these cases develops the overt CD in the follow-up of three years and highlights requirement of re-test. Although no adequate data found regarding follow-up of the cases having T1D and pot-CD. It may possible to show the structure and metabolism impairment of bones, particularly in association with duration or poor diabetes control in cases presented with T1D. Moreover, celiac disease also has been underscored as the risk of impairment of bones [23]. For diabetes type I and celiac disease, diet is the basic treatment part, while GFD may develop some problems as; Kupper et al [24] stated that GFD may cause of nutrients deficiency, particularly as vitamin B, D, magnesium, iron, zinc and calcium, but adequate information not documented accurately. Finally, Berti et al [25]. reported that greater fats amount in gluten-free bread than gluten, but fibers found equally.

Adherence to GFD in T1D-CD cases, in current experience, is for the most part great in cases those having clear experience of clinical indications of CD, though is infrequent in cases presented with asymptomatic or few symptoms. Inconsistently with T1D populace, dietary consistency in CD cases "without T1D" seems to be higher: about 73% of cases that followed diet strictly [26]. Possibly for the cases having T1D, already occupied a complex of disease day by day, the expansion of a moment "restricting" condition, is a significant distress. Subsequently a case of "T1D + CD", is very difficult to treat due to the absence of experience regarding CD symptoms. According to Wagner et al [27] "celiac adolescents non-compliant with GFD reported no differences between compliant patients with CD and adolescents without any chronic condition were found in all aspects" of the quality of life. Sud et al [28] reported that in children having T1D-CD double diagnosis seems to have the insignificant influence on the quality of life, even cases parents conveyed regarding important difficulties in the management. Moreover, parents of the children having "T1D-CD" did express higher concern regarding social functioning of their Children.

Although many studies have shown that GFD, due to its high glycaemic index, has a negative impact on the T1DM and has led to more complications. As no local statistics were available on the prevalence of CD in T1DM and also the international studies show controversial results regarding the role of GFD in such cases we have decided to conduct a study to see the prevalence of CD in T1DM in our own population, how these diseases interact with each other and what is the effect of GFD on glycemic control of type 1

diabetic patients. It will help in emphasizing screening for Celiac Disease in T1DM patients and to decreased risk of complication of diabetes.

METHODOLOGY:

A cross-sectional study was conducted in Unit-II, Department of Medicine, Services hospital, Lahore. The duration of the study was 12 months after approval of synopsis i.e from September, 2018 to August, 2019. Non-probability consecutive sampling was used for the patient's data collection in the study. The researcher had collected data after taking permission from hospital Ethical Committee. The patient was explained about the whole procedure and informed written consent was taken. Total 160 patients were enrolled in the study by using WHO Sample size calculator; Confidence level = 95%, anticipated population proportion = 28.2%, absolute precision required = 7%. Diabetes mellitus type 1 was defined as FBS > 126 mg/dl or random blood sugar > 200 mg/dl on one occasion in a patient with diabetes onset before 40 years of age using insulin or already on insulin before inclusion into the study. Celiac disease was diagnosed based on a positive anti-tTG antibody report. We will use the cut-offs: anti-tTG IgA \leq 10 U/ml will be considered negative, > 10 U/ml will be considered positive whereas HbA1c level <7% was considered as Adequate glycemic control. Patients of either gender more the 5 years and less than 40 years of age, type 1 diabetes mellitus diagnosed for more than 6 months and patients with a regular (at least monthly) follow up in OPD for last 06 months were taken as inclusion criteria. Patients with poor compliance to insulin therapy, (missing more than two doses per week) and patients who were not on monthly follow-up for three months prior to enrollment were considered as the exclusion criteria of the study. The researcher had collected data after taking permission from hospital Ethical Committee. The patient was explained about the whole procedure and informed written consent was taken. Patients were recruited through medical and diabetes OPDs and medical wards. All the relevant information was recorded on a structured proforma.

In all type 1 diabetics a sample of blood was sent to AFIP for the determination of Anti-tTG (IgA) antibodies; using a commercially available ELISA technique (Pharmacia Upjohn, Sweden) based on recombinant human tTG as antigen. The measuring range of this test is 0.1 - 100 U/ml. We used the cut-offs: anti-tTG IgA \leq 10 U/ml were considered negative, > 10 U/ml was considered positive. The

assay was a quantitative assay. On the same visit, another blood sample was sent for HbA1C estimation.

Data was entered and analyzed using Statistical Package for Social Sciences (SPSS) version 17.0. Mean and the standard deviation was calculated for quantitative variables like age, duration of diabetes and HbA1C levels. Frequency and percentages were calculated for a qualitative variable like gender, presence celiac disease and control of diabetes. The frequency of adequate glycemic control was compared

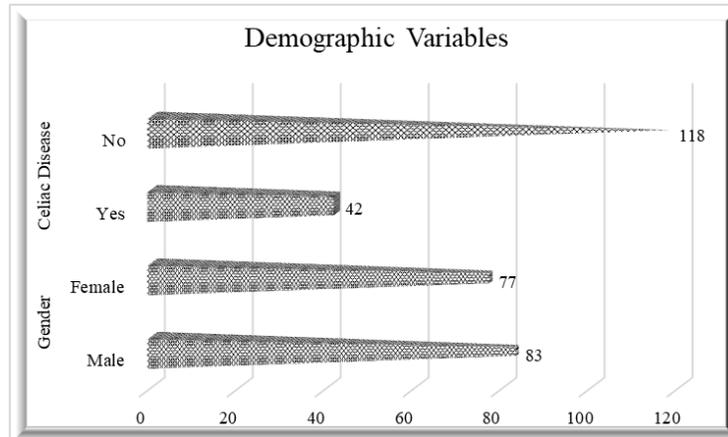
between CD+ group and CD- a group using chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS:

Data was entered and analyzed in SPSS version 17.0. Total 160 patients were included according to the inclusion criteria of the study. Table. No. I showed mean age (years) of the patents was 26.58 ± 9.13 whereas average duration (years) of diabetes in the study was 2.0 ± 0.72 . Mean HbA1c levels was observed 7.31 ± 1.43 .

Table No 01: Descriptive Statistics of Demographic Variables

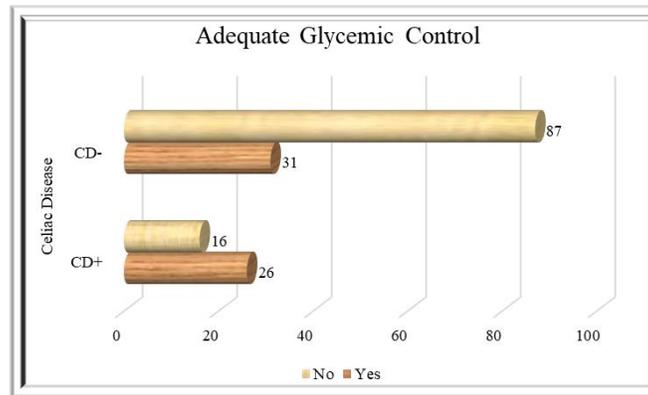
| Statistics | | Qty | %age |
|------------------------------|---------|------------|-------|
| Age (years) | Mean±SD | 26.58±9.13 | |
| Duration of diabetes (years) | Mean±SD | 2.0±0.72 | |
| HbA1c | Mean±SD | 7.31±1.43 | |
| Gender | Male | 83 | 51.9% |
| | Female | 77 | 48.1% |
| Celiac Disease | Yes | 42 | 26.3% |
| | No | 118 | 73.8% |



There were 83 (51.9) male and 77 (48.1) female patients who were included in the study. Out of 160 patients, the frequency of celiac disease among type 1 diabetic patients was 42 (26.3) whereas the frequency of adequate glycemic control in patients having T1DM plus CD and T1DM alone was 26 (61.9) and 31 (26.3) respectively which was statistically significant (p-value 0.000), as shown in Table. No. II.

Table No 02: Comparison of Celiac Disease with Adequate Glycemic Control

| Adequate glycemic control | Celiac Disease | | | | P-value |
|---------------------------|----------------|-------|-----|-------|---------|
| | CD+ | | CD- | | |
| | Qty | %age | Qty | %age | |
| Yes | 26 | 61.9% | 31 | 26.3% | 0.000 |
| No | 16 | 38.1% | 87 | 73.7% | |
| Total | 42 | 100% | 118 | 100% | |



DISCUSSION:

Celiac disease described by the occurrence of antibodies, enteropathy, and the wide clinical range going from shapes with gastrointestinal and additionally extra intestinal manifestations to salient, potential structures and dormant which might be spoken to as an iceberg [28]. The part of gluten in different conditions is progressively stressed, as several diseases, the immune system ones specifically, are related with CD, including diabetes mellitus type I and the chromosomal variations like as down syndrome (DS). In many nations “including Brazil” celiac disease prevalence in DMT1 raised from 3.0% to 16.0% and down syndrome from 4.0% to 17.0%, being impressively higher contrasted and the general populace “0.5– 1.0%”. From clinical perspective, most people having DMT1 and Down syndrome are accepted to show the quiet type of celiac disease. Although, finding in view of more delicate and serologic screening has permitted the retrospective identification of signs and symptoms that were earlier not considered, in this manner pointing out the development of other clinical profiles [29]. GI and additionally extra intestinal symptoms showed through cases with DM1 and down syndrome might be viewed as suitable to those conditions and accordingly

not considered in the diagnosis of celiac disease, which is along these lines deferred, therefore debilitating the quality of life in cases and upsetting the anticipation of disease complications. Inside the present situation, the clinical pattern of celiac diseases in diabetes mellitus type I and down syndrome is focal point of abundant interest, requiring studies stated that survey associatively clinical side effects, more than one serological marker, small intestinal histopathology and their relationship to distinguish CD in the previously mentioned high-risk group. Brazilian Health Ministry in 2009 published a national convention for exploring the celiac disease. Though the proposals made are yet not palatably met on account of the trouble of their usage by Public Health System of the Brazilian. Therefore, CD screening has not yet been incorporated into the observing routine of cases having DMT1 and Down syndrome in most general wellbeing administrations, and subsequently, the signs and side effects presence should fill in as a notice for the need to CD diagnosis [29].

In our study, mean age (years) in the study was 26.58+9.13 with ranges from 05 to 40 years. Gomes et al [30] in their study observed that the mean age in years was 8.95 ± 4.74. In our study mean duration

(years) of diabetes was 2.0 ± 0.72 with ranges from 01 to 03 years. A study in 2016 found that the mean duration of diabetes was 2.40 ± 2.21 , which is like our study findings. Gomes et al [30] in their study found that the majority were the female patients 102 (54.3) and 95 (50.5) were male patients whereas our study findings showed most female patients 77 (48.1%) then male patients 83 (51.9%).

In our study, frequency of celiac disease among type 1 diabetic patients was 26.3%. Whereas, in another study conducted in 2016, the prevalence of celiac disease is 28.2% [30]. In our study, frequency of adequate glycemic control in patients having T1DM plus CD and T1DM alone was 61.9% and 26.3% respectively. Similarly, in a study by Pinhas-Hamie et al [11] found that the T1DM with CD glycaemic control were 8.2% than those with only T1DM were 7.5%.

CONCLUSION:

The study concluded that the prevalence of celiac disease in type 1 diabetes mellitus in our own population is high. Furthermore, gluten free diet effects on glycemic control of type 1 diabetic patients which in screening for celiac disease in type 1 diabetes mellitus patients and to decreased risk of complication of diabetes.

REFERENCES:

1. Lauret E, Rodrigo L. Celiac disease and autoimmune-associated conditions. *Biomed Res Int*. 2013; 2013:127589.
2. See JA, Kaukinen K, Makharia GK, Gibson PR, Murray JA. Practical insights into gluten-free diets. *Nature Reviews Gastroenterology & Hepatology*. 2015; 12:580-91.
3. Mahmud FH, DeMelo EN, Noordn K, Assor E, Sahota K, Davies- Shaw J. The Celiac Disease and Diabetes-Dietary Intervention and Evaluation Trial (CD-DIET) protocol: a randomised controlled study to evaluate treatment of asymptomatic coeliac disease in type 1 diabetes. *Pediatr Diabetes*. 2012; 13:597-606.
4. Akirov A, Pinhas-Hamiel O. Co-occurrence of type 1 diabetes mellitus and celiac disease. *World J Diabetes*. 2015; 6(5):707-14.
5. Simmons KM, McFann K, Taki I, Liu E, Klingensmith GJ, Rewers MJ, Frohnert BI. Reduced Bone Mineral Density Is Associated with Celiac Disease Autoimmunity in Children with Type 1 Diabetes. *J Pediatr*. 2016; 169:44-8.
6. Tao B, Pietropaolo M, Atkinson M, Schatz D, Taylor D. Estimating the cost of type 1 diabetes in the U.S.: a propensity scores matching method. *PLoS One*. 2010 ;9. 5(7): e11501.
7. Pilia S, Casini MR, Cambuli VM, Ibba A, Civolani P, Zavattari P et al. Prevalence of Type 1 diabetes autoantibodies (GAD and IA2) in Sardinian children and adolescents with autoimmune thyroiditis. *Diabet Med*. 2011;28(8):896-9
8. Philippe MF, Benabadji S, Barbot-Trystram L, Vadrot D, Boitard C, Larger E. Pancreatic volume and endocrine and exocrine functions in patients with diabetes. *Pancreas*. 2011;40(3):359- 63.
9. Noble JA, Valdes AM. Genetics of the HLA region in the prediction of type 1 diabetes. *Curr Diab Rep*. 2011;11(6):533-42.
10. Imkampe AK, Gulliford MC. Trends in Type 1 diabetes incidence in the UK in 0- to 14-year-olds and in 15- to 34-year-olds, 1991- 2008. *Diabet Med*. 2011; 28(7):811-4.
11. Vehik K, Beam CA, Mahon JL, Schatz DA, Haller MJ, Sosenko JM et al. Development of Autoantibodies in the TrialNet Natural History Study. *Diabetes Care*. 2011;34(9):1897-1901.
12. Harjutsalo V, Maric C, Forsblom C, Thorn L, Wadén J, Groop PH et al. Sex-related differences in the long-term risk of microvascular complications by age at onset of type 1 diabetes. *Diabetologia*. 2011; 54(8):1992-1999.
13. Murthy VL, Naya M, Foster CR, Gaber M, Hainer J, Klein J, et al. Association Between Coronary Vascular Dysfunction and Cardiac Mortality in Patients with and without Diabetes Mellitus. *Circulation*. 2012 Aug 23.
14. Catassi C, Yachha SK. The global village of celiac disease. In: Fasano A, Troncone R, Branski D, editors. *Frontiers in celiac disease*. Basel: Switzerland Karger; 2008. pp. 23-31
15. Rostom A, Murray JA, Kagnoff MF. American Gastroenterological Association (AGA) Institute technical review on the diagnosis and management of celiac disease. *Gastroenterology*. 2006; 131:1981-2002
16. Thomas HJ, Ahmad T, Rajaguru C, Barnardo M, Warren BF, Jewell DP. Contribution of histological, serological, and genetic factors to the clinical heterogeneity of adult-onset coeliac

- disease. *Scand J Gastroenterol.* 2009; 44:1076–1083
27. Cataldo F, Montalto G. Celiac disease in the developing countries: a new and challenging public health problem. *World J Gastroenterol.* 2007; 13:2153–2159
 18. Smyth DJ, Plagnol V, Walker NM, Cooper JD, Downes K, Yang JH et al. Shared and distinct genetic variant in Type 1 diabetes and celiac disease. *N Eng J Med.*2008;359(0028-4793):2837– 2838.
 19. Goh C, Banerjee K. Prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus in a clinic-based population. *Postgrad Med J.* 2007; 83:132–136
 20. Gabriel S, Mihaela I, Angela B, Mariana A, Doru D. Prevalence of IgA antitissue transglutaminase antibodies in children with type 1 diabetes mellitus. *J Clin Lab Anal.* 2011;25(3):156–161
 21. Viljamaa M, Kaukinen K, Huhtala H, Kyronpalo S, Rasmussen M, Collin P. Coeliac disease, autoimmune diseases and gluten exposure. *Scand J Gastroenterol.* 2005;40(4):437–443
 22. Artz E, Warren-Ulanch J, Becker D, Greenspan S, Freemark M. Seropositivity to celiac antigens in asymptomatic children with type 1 diabetes mellitus: association with weight, height, and bone mineralization. *Pediatr Diabetes.* 2008;9(4):277–284.
 23. Tosco A, Salvati VM, Auricchio R, Maglio M, Borrelli M, Coruzzo A et al. Natural history of potential celiac disease in children. *Clin Gastroenterol Hepatol.* 2011;9(4):320–325.
 24. Kupper C. Dietary guidelines and implementation for celiac disease. *Gastroenterology.* 2005;128: S121–S127
 25. Berti C, Riso P, Monti L, 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
 26. Errichiello S, Esposito O, Di Mase R, Camarca ME, Natale C, Limongelli MG et al. Celiac disease: predictors of compliance with a gluten-free diet in adolescents and young adults. *J Pediatr Gastroenterol Nutr.* 2010;50(1):54–60
 27. Wagner G, Berger G, Sinnreich U, Grylli V, Schober E, Huber WD et al. Quality of life in adolescents with treated coeliac disease: influence of compliance and age at diagnosis. *J Pediatr Gastroenterol Nutr.* 2008;47(5):555–561
 28. Sud S, Marcon M, Assor E, Daneman D, Mahmud FH. Quality of life in children with diabetes and celiac disease: minimal impact of the 'double diagnosis'. *Pediatric Diabetes.* 2011;13(2):163-169.
 29. Narula P, Porter L, Langton J, Rao V, Davies P, Cummins C, et al. Gastrointestinal symptoms in children with type1 diabetes screened for celiac disease. *Pediatrics* 2009;124: e489–e495.
 30. Gomes RC, Cerqueira MJ, Femando AR, Andre NC, Auxiliadora CR, Edinilma FM, et al. The celiac iceberg: from the clinical spectrum to serology and histopathology in children and adolescents with type 1 diabetes mellitus and Down syndrome. *Scand J Gastroenterol.* 2016;51(2):178-85.