ORIGINAL ARTICLE

# Celiac Disease and Glycemic Control Among Patients with Type 1 Diabetes Mellitus

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[1,3]Conception, planning of research and writing of the manuscript, Discussion
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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:** Unit-II, Department of Medicine, Foundation University Medical College, Islamabad. from 16th June 2016 to 16th December 2016

**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+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

## 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.[9]

Pilia et al reported a big incidence of against GAD antibodies and islet cell antibodies (IA2) in cases having autoimmune thyroiditis.[10] 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.[11] 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.[12] 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.[23] Risk of the improvement in antibodies "anti-islet" in the patient's relative having DMTI diminishes with expanding age. This discovering bolsters yearly screening for antibodies in relatives more youthful than 10 years and 1 extra screening during youthfulness.[14] Diabetes mellitus TI most common in males as compare to females. In European population the male-to-female ratio is 1.5:1.[15] In diabetic and non-diabetic cases, coronary vasodilator dysfunction is the indicator of cardiovascular mortality.[16] Epidemiological reports carried out in CD free areas, including Middle East, South America, Asia, and Africa, demonstrate that the illness was underdiagnosed previously.[17]

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.[18] interestingly, there is expanded CD prevalence among ladies contrasted with men with male: female proportion of 1:2.8.[19] 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.[20] Diabetes mellitus type I linked to other autoimmune events frequently and these events may effects the clinical management. These disease 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.[21] In previous studies showed that 4.4 to 11.1% celiac disease occurs in cases having TID as compare to general population.[22] Youngers mostly associated with double disease on type I diabetes onset as compare to TID alone.[23]

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.[24]

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.[25] 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 have been underscored as the risk of impairment of bones.[25] For diabetes type I and celiac disease, diet is the basic treatment part, while GFD may develop the some problems as; Kupper et al[27] 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[28] 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.[29] 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 cases of “T1D + CD”, is very difficult to treat due to the absence of experience regarding CD symptoms. According to Wagner et al[30] “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[31] 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 Childs.

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, Foundation University Medical College, Islamabad. The duration of the study was 06 months after approval of synopsis i.e 16th June 2016 to 16th December 2016. 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%[7], 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 on the basis of a positive anti-TG antibody report. We will use the cut-offs: anti-tTGIgA ≤ 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 ≤ 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 I: Descriptive Statistics of Demographic Variables**

| | | **Mean±SD** |
|---|---|---|
| Age (years) | | 26.58±9.13 |
| Duration (years) of diabetes | | 2.0±0.72 |
| HbA1c | | 7.31±1.43 |
| | | **n (%)** |
| 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 II: Comparison of Celiac Disease with Adequate Glycemic Control**

| | | Celiac Disease | | P-value |
|---|---|---|---|---|
| | | CD+ | CD- | |
| Adequate glycemic control | yes | 26 (61.9) | 31 (26.3) | 0.000 |
| | no | 16 (38.1) | 87 (73.7) | |
| Total | | 42 | 118 | |

## Discussion

Celiac disease described by the occurrence of particular 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.[106] 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 particular 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.[32] 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 as 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.[32]

In our study, mean age (years) in the study was 26.58±9.13 with ranges from 05 to 40 years. Gomes et al[7]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[7] found that the mean duration of diabetes was 2.40 ± 2.21, which is similar to our study findings. Gomes et al[7]in their study found that the majority were the female patients 102 (54.3) and 95 (50.5) were males patients whereas our study findings showed the majority of 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%.[7] 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[4] 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.

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