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# Frequency of Celiac Disease in Type 1 Diabetic Children Presenting at Tertiary Care People Medical College Hospital Nawabshah Pakistan

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Author AAJ designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AL, NAM, BA, SAJ, Attiya Ayaz, DD and Arslan Ahmer managed the analyses of the study and managed the literature searches and data collection. Author FM managed the statistical analyses and review. All authors read and approved the final manuscript.*

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## ABSTRACT

**Objective:** The goal of this research has been to find out how common celiac disease is in type 1 children with type 1 diabetes who visit multispecialty hospitals.
**Methodology:** This was a cross-sectional research. This study was directed at Pediatric Medicine Department, Mother and Child Healthcare (M&CH) ⁄ People Medical College (PMC) Hospital Nawabshah Shaheed Benazeerabad. The length of research was from 07/09/2020 to 06/03/2021,

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(6 months) next to the authorization of synopsis. Current research included 124 children of together sex aged between 1 to 12 years diagnosed of Type-I diabetes mellitus who were assessed for concomitant presence of celiac disease which was labeled on duodenal biopsy revealing crypt hyperplasia and villous atrophy. Frequency of celiac disease was noted and compared across various subgroups of diabetic children based on age, gender, duration of diabetes, BMI and glycemic control. Each kid's parents signed written consent form.

**Results:** The average ages of the children were 8.6±2.6 years. The majority of the children (n=68, 54.8 %) were aged 10 and over, preceded by kids aged 6-9 years (36.3 %), and children aged less than 5 years (08.9%). There were 56 (45.2%) boys and 68 (54.8%) girls with boys to girls ratio of 1.1.2. The average lengths of diabetes were 03.2±1.4 year. 51 (41.1%) children had poor glycemic control (HbA1c ≥8.0%). Celiac disease were established in 14 (11.3%) youngsters having Type-I diabetes. Statistically no substantial variance in the frequency of celiac disease across various subgroups of Type-I diabetic children based on age (p =0.966), sex (p =0.854), length of diabetes (p-value=0.985), BMI (p =0.835) & status of glycemic control (p =0.889).

**Conclusion:** A significant number of children with Type I diabetes had celiac disease in the current study, indicating that regular screening of diabetic children is necessary for prompt detection and management of celiac disease in upcoming clinical settings.

*Keywords: Celiac disease; Type-I diabetes; autoimmune disorders.*

## 1. INTRODUCTION

Gluten-induced inflammation and structural destruction of the small intestinal mucosa in genetically sensitive individuals define Celiac disease, which is a life-long immune-mediated condition [1,2]. With a current estimated frequency of 1–2% in Western nations, the condition is one of the most frequent nutrition associated diseases [3]. Furthermore, it is strongly represented in type 1 diabetes (DM1), that has a genetic link with Celiac Disease [4]. Even though this relationship is widely recognised, especially in children, the impact of simultaneous DM1 on the clinicopathologic manifestations of celiac disease in adults is unknown. In contrary to autoimmune mediated type 1 diabetes (DM1), non-autoimmune mediated type 2 diabetes (DM2) is not thought to be better represented in celiac disease [5].

Histological assessment of small intestinal samples is used to diagnose celiac disease clinically. Serologic tests such immunoglobulin (Ig)-A tissue transglutaminase and endomysial antibody (EMA; IgA) might help confirm the diagnoses [6].

DM 1 develops once the pancreatic β cells are destroyed by the immune system, leading to hyperglycemia due to inadequate production of insulin. Type 1 diabetes is a chronic condition that requires a lot of work from the diabetic and their care providers, even with insulin substitution. The goal is to reduce hyperglycemia whereas limiting the hypoglycemic risk. Diet, insulin dosages, bodily stressors, activity, and a slew of other variables all play a role in glucose homeostasis [7]. The genetic and environmental contributions lead to immune-mediated loss of beta cell function resulting in hyperglycemia and life-long insulin dependence. Hyperglycemia, hyper-glucagonemia, glucosuria, and, without therapy, ketosis, acidosis, dehydration, and mortality results from a lack of endogenous insulin [8].

Albatayneh et al. [9] (2018) conducted a study and found that the frequency of celiac disease in children with type-I diabetes was 6.5% in in South Jordan population. Joshi et al. [10] (2015) observed CD frequency to be 7.04% at the Tertiary Care Referral Centre in Western India. In Iranian population, Moayeri et al. [11] (2014) reported this frequency to be 3.4 %. Zamanfar et al. [12] (2014) observed frequency of CD to 6.8% among Iranian Population. While Araújo et al. [13] (2006) and Dogan [14] (2015) reported the frequency celiac disease 10.5% and 2.3% in Brosil and Istanbul respectively. In Pakistani population, Mahmood et al. [15] (2017) reported Celiac disease was present in 6 (8.8%) out of 68 such patients at JAIDE (Jinnah Allama Iqbal Institute of Diabetes and Endocrinology), Lahore. In another local study, a much higher frequency of 26.3% has been reported by Abbas et al. [16] (2018) at Foundation University Medical College, Islamabad.

In the light of above review, reported frequency of CD varies among different studies among different populations from as high as 26.3% [16]

in Pakistan to 2.5% [14] in Brosil population. The demographic variations that cause disagreement might be one explanation for these conflicts. There is also controversy in the frequency of CD in the mentioned studies from 8.8% [15] to 26.3% [16] while both the studies are addressing same populations of Pakistan. So to confirm the extent of this difference, we want to re-conduct this study in local population. Therefore the purpose of current study is to conclude the incidence of celiac disease in type-I diabetic kids presenting at tertiary care hospital in Sindh. The results of the present study will give an insight into the magnitude of problem and may deliver local standard statistical statistics for auxiliary researches in this regard.

The aims of the research were to determine the frequency of celiac disease in type 1 diabetic children presenting at a tertiary care hospital.

## 2. OPERATIONAL DEFINITIONS

1. **Celiac Disease:** Patients having diarrhea >3 weeks (non-responsive to antibiotics), with or without abdominal distention >3 weeks having tissue transglutaminase levels above the normal (>10 U/ml), underwent duodenal biopsy. Cases having crypt hyperplasia and villous atrophy in the duodenal mucosa on histopathology were labeled to have celiac disease.

2. **Type 1 Diabetes Mellitus:** Children having weight loss, abdominal pain, along with polydipsia and polyuria >2 weeks underwent blood sugar levels monitoring. Subjects with

    a. Fasting serum Glucose >126 mg/dl or
    b. Random blood sugar >200 mg/dl
    Were labeled to have type I diabetes

## 3. METHODOLOGY

### Study design

Current research was a cross-sectional in nature.

### Setting

Study was carried out at Pediatric Medicine Department Mother and Child Healthcare (M&CH) ⁄ People Medical College (PMC) Hospital Nawabshah Shaheed Benazeerabad.

### Duration of study

The length of current research after approval of synopsis was 06 months i.e. from 07/09/2020 to 06/03/2021.

### Sample size

With a 95% confidence level and a 5% margin of error, a sample size of 124 cases was recruited, with a predicted frequency of celiac disease of 8.8% 15 among Pakistani individuals with type I diabetes.

### Sampling technique

Non-Probability, Sequential Sampling were used for selection of subjects.

### Inclusion criteria

Youngsters from either sex groups with ages in the range of 1-12 years suffering type-I diabetes >6 months as per operational definition

### Exclusion criteria

1. Patients with other than type-I diabetes.
2. Patients with other malabsorptive disorders on basis of history and previous records were excluded from the study.

### Data collection

124 participants who fulfilled the inclusion criteria were included in the research from the outpatient department of Pediatric medicine, Mother and Child Healthcare, Nawabshah, after receiving clearance from the hospital ethics council. Each participant's family gave informed written permission and a full medical history. A systematic questionnaire was used to record all of the pertinent data.

A blood specimen was obtained from each type 1 diabetic and submitted to the lab to determine Anti-tTG (IgA) antibodies using an available commercially Enzyme linked immunosorbent test (ELISA) technology (Pharmacia Upjohn, Sweden) depending on human recombinant tTG as antigens. The children with positive results underwent duodenal biopsy and histopathological examination of the biopsy specimen. The presence of celiac disease was labeled as per operational definition. Another blood sample was supplied for HbA1C

measurement during the same appointment. Patients who were diagnosed with celiac disease were encouraged to follow a gluten-free food.

To eliminate bias, all biopsies, tests, and ELISA were obtained from the same (hospital) laboratory. Exclusion was used to adjust for confounding factors.

**Data analysis**

1. SPSS version 21.0 was used to input and evaluate all of the gathered data.
2. Mean±SD was used to provide Quantitative factors such as age, BMI, HbA1c levels, and diabetes duration.
3. Categorical variable i-e gender and celiac disease have been presented by frequency and percentage.
4. To account for impact transformers, data was segregated by age, gender, BMI, HbA1c levels, and diabetes duration. Subsequent to segregation, the chi-square test was used, with p ≤0.05 being considered significance.

## 4. RESULTS

The ages of children were from 01 to 12 years, and average age as 8.6±2.6 years. The bulk of the youngsters (n=68, 54.8 %) ranged 10 years and over, preceded by kids aged 6-9 years (36.3 %), and kids aged less than five years (8.9 %).There were 56 (45.2%) boys and 68 (54.8%) girls with boys to girls ratio of 1.1.2. Diabetes lasted from around 1 to 5 years, with a mean of 3.2±1.4 year. The BMI of these children ranged from 21.3 Kg/$m^2$ to 33.5 Kg/$m^2$ with a mean of 27.0±3.4 Kg/$m^2$. 24 (19.4%) children were obese. Glycated hemoglobin level ranged from 6.6% to 9.5% with a mean of 7.9±0.89%. 51 (41.1%) children had poor glycemic control (HbA1c ≥8.0%) as shown in Table 1.

Table 2 shows that 14 (11.3%) of youngsters with Type I diabetes were diagnosed with Celiac disease. As shown in Table 3, there was no statistically significant variation in the frequency of celiac disease among several subcategories of children depending on age (p=0.966), gender (p=0.854), diabetes duration (p=0.985), BMI (p-value=0.835), and glycemic control level (p=0.889).

**Table 1. Demographic Characteristics of included Type-I Diabetic Children**

| Characteristics | Participants n=124 |
|---|---|
| Age (years) | 8.6±2.6 |
| • ≤5 years | 11 (8.9%) |
| • 6-9 years | 45 (36.3%) |
| • ≥10 years | 68 (54.8%) |
| Gender | |
| • Boys | 56 (45.2%) |
| • Girls | 68 (54.8%) |
| Duration of Diabetes (years) | 3.2±1.4 |
| • 1-3 years | 80 (64.5%) |
| • 4-5 years | 44 (35.5%) |
| BMI (Kg/$m^2$) | 27.0±3.4 |
| • Non-Obese | 100 (80.6%) |
| • Obese | 24 (19.4%) |
| HbA1c Level (%) | 7.9±0.89 |
| • Good Glycemic Control | 73 (58.9%) |
| • Poor Glycemic Control | 51 (41.1%) |

**Table 2. Frequency of Celiac Disease in Children with Type-I Diabetes n=124**

| Celiac Disease | Frequency | Percent (%) |
|---|---|---|
| Yes | 14 | 11.3% |
| No | 110 | 88.7% |
| Total | 124 | 100.0% |

**Table 3. Comparison of Celiac Disease across Various Subgroups of Children with Type-I Diabetes n=124**

| Subgroups | n | Celiac Disease n (%) | P-value |
|---|---|---|---|
| Age (years) | | | |
| • ≤5 years | 11 | 1 (9.1%) | 0.966 |
| • 6-9 years | 45 | 5 (11.1%) | |
| • ≥10 years | 68 | 8 (11.8%) | |
| Gender | | | |
| • Boys | 56 | 6 (10.7%) | 0.854 |
| • Girls | 68 | 8 (11.8%) | |
| Duration of Diabetes | | | |
| • 1-3 years | 80 | 9 (11.3%) | 0.985 |
| • 4-5 years | 44 | 5 (11.4%) | |
| BMI | | | |
| • Non-Obese | 100 | 11 (11.0%) | 0.835 |
| • Obese | 24 | 3 (12.5%) | |
| HbA1c Level | | | |
| • Good Glycemic Control | 73 | 8 (11.0%) | 0.889 |
| • Poor Glycemic Control | 51 | 6 (11.8%) | |

*Chi-square test, observed difference was statistically insignificant*

## 5. DISCUSSION

Celiac disease (CD) is often characterized by a set of other digestive symptoms, rendering it a widespread illness instead of just a gastrointestinal disorders [1]. Its is largely due to the fact that CD is classified as an autoimmune illness [1,2]. The merely unique thru a recognized cause is linked to a lifelong gluten sensitivity [2]. Due to an increased interest in the diagnosis of atypical and asymptomatic patients in recent years, significant advancements have been made [1-3]. The existence of various related disorders might help in the search for oligo symptomatic instances and also research done on parents of CD patients [1]. The origins of the start and appearance of linked diseases are varied; some, like type 1 diabetes mellitus, have a common genetic basis; some shared pathological processes; but many also are undetermined [1,3].

One of the most well-studied associations seems to be between celiac disease and autoimmune insulin-dependent diabetic mellitus [1]. The occurrence of celiac disease amongst people with type 1 diabetes is believed to be around 04%, with the risk being higher when diabetes is diagnosed in infancy. Type 1 diabetes and CD are indeed recognised to have immunological etiology [9]. Both illnesses also have been linked to the major histocompatibility complex class-II antigen DQ2, which is expressed by the alleles DQA1501 and DQB1201, providing a genetic foundation for their manifestation [6] The prevalence rate of celiac diseases among children with type I diabetes, though, differed not just among diverse communities [14,16] but even in the same group [15,16], necessitating the current investigation.

The focus of this research has been to find out how common celiac disease is in type 1 children with type 1 diabetes who visit a referral hospital. The average age of the subjects having type I diabetes in this research was 8.6±2.6 year. The bulk (54.80%) of the kids aged 10 and more years, trailed by kids aged 06-09 years (36.30%) and kids aged below 05 years were 08.90%. At the National Institute of Child Health in Karachi, Qayyum et al. [17] (2010) observed a similar average age of 09.9±6.5 years amongst kids with type I diabetes mellitus. Lone et al. [18] (2010) found that 55.60 percent of kids presented with type-I diabetes at Aga Khan University Hospital, Karachi, were aged 10 and more years of age, trailed by 36.80% of kids aged between 06-09 years, and only 07.70% of children were younger than five years. Laitinen et al. [19] (2017) found a comparable average age of 7.8±3.1 years amongst Finnish kids with Type I diabetics, whereas Cerutti et al. [20] (2004) found a similar mean age of 7.2±4.3 years among Italian kids with Type I diabetes. In Iran, Moayeria et al. [21] (2004) found that type 1 diabetic children had a comparable mean age of 7.2±2.1 years.

With a male to female ratio of 1:1.2, we found a modest female dominance amongst type I children with type 1 diabetes. Our findings are consistent with those of Qayyum et al. [17] (2010), who found a male to female ratio of 1:1.2 amongst type I diabetes kids reporting at the National Institute of Child Health in Karachi. In Kids with type I diabetes, Singh et al. [22] (2017) found a similar female preponderance, with a male to female ratio of 1:1.1.

Laitinen et al. [19] found a male to female ratio of 1:1.7 in Finland, whereas Honar et al. [23] recorded a ratio of 1:1.4 in Iran. The average period of diabetes mellitus in this research was 3.2±1.40 year. Our findings are consistent with those of two other studies including Iranian children with type 1 DM, Honar et al. [23] found that the mean duration of diabetes at diagnosis was 3.4±0.8 years, while Moayeria et al. [11] found it to be 3.5±1.8 year. Celiac disease was revealed in 11.30 percent of kids with Type I DM in the current analysis. Here would be no statistical significance alteration in the incidence of CD amongst sub groups of kids depending on age (p=0.966), sex (p=0.854), diabetes length (p=0.985), BMI (p=0.835), or glycemic control level (p=0.889).

Our findings match that of Frolich-Reiterer et al. [24] (2008), who found an incidence of 11.1 percent in Germany, and Larsson et al. [25] (2008), who found an incidence of 11.1 percent in Sweden. According to Arajo et al. [13] (2006), celiac disease affects 10.5 percent of type I diabetes kids in Brosil. In kids with type 1 diabetes mellitus, Bhadada et al. [25] (2011) in India and Al-Hussaini et al. [26] (2012) in Saudi Arabia found an incidence of 11.10 percent and 11.30 percent, correspondingly, for celiac disease. The current study contributed to the existing of studies on the matter that has already been publicized. The current research revealed that a significant number of kids with Type I DM too had asymptomatic or minimally symptomatic celiac disease, that could be frequently overlooked if not aggressively sought for.

In view of this findings, we recommend regular celiac disease screening in diabetic children, because as earlier diagnosis and care of celiac disease can enhance the prognosis of such patients in the future.

The current survey's features were its large sample size (124 cases) and tight exclusion criteria. Researchers also divided the outcomes into groups to account for different influence factors. The lack of consideration of the therapeutic intervention of celiac diseases among children having or not having DM, that may have aided in the management strategy of these kind of youngsters, was a significant drawback of the current study. In upcoming clinical trials, such a research is strongly suggested.

## 6. CONCLUSION

A significant number of children with Type I DM have celiac disease in the current research, indicating that regular screening of children with type 1 DM is necessary for prompt detection and managing of celiac disease in upcoming medical care.

## CONSENT

Written consent was obtained from the parents.

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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