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Celiac disease autoimmunity among Nigerian children and adolescents with type 1 diabetes mellitus

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Abstract

Background Celiac disease (CD) affects the small intestine and can hinder nutrient absorption. It is found worldwide and common in certain groups of people including individuals with Type 1 Diabetes Mellitus (T1DM). However, the prevalence of CD in the West African region is not documented. This study aimed to investigate the prevalence and pattern of CD autoimmunity in Nigerian children and adolescents diagnosed with T1DM.

Methods This was a cross-sectional descriptive study of children and adolescents with T1DM at the Paediatric Endocrinology Clinic of seven selected tertiary health facilities in Nigeria. Information was collected on socio-demographics, clinical characteristics and anthropometrics. The subjects were screened for markers of CD autoimmunity using anti-tissue transglutaminase antibody (tTG) and anti-endomysial antibody (EMA). Endoscopy and duodenal biopsy were recommended for participants with elevated CD-specific antibodies.

Results The study recruited a total of 104 children and adolescents with TIDM, out of which six participants (5.8%) had CD autoimmunity. All six participants were females, aged between 3 and 12 years, with a mean age of 9.2 ± 3.7 years. Participants with CD autoimmunity were more likely to have DM diagnosed before the age of 10 years compared to those without CD autoimmunity (83.3% vs. 37.7%, $p = 0.149$). Except for two participants, all individuals with CD autoimmunity experienced gastrointestinal symptoms such as nausea, vomiting, diarrhoea, and bloating.

Conclusion This study highlights the occurrence of CD autoimmunity in Nigerian children and adolescents with TIDM. Healthcare providers should consider screening for celiac disease in children and adolescents with T1DM, particularly in females and when gastrointestinal symptoms are present. Additionally, the findings from this study suggest that there is a high probability of a significant burden of CD, even within the general population in Nigeria. Therefore, it's important to maintain a high level of suspicion and to actively screen at-risk groups in clinical settings to ensure early diagnosis of CD.

Keywords Celiac disease, Type I diabetes mellitus, Children, Adolescents, Nigeria

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Introduction

Celiac disease (CD) is an autoimmune disorder that is triggered by the consumption of gluten, a protein found in wheat, rye, and barley [1]. It primarily affects the small intestine, causing villous atrophy, flattening of the duodenal folds, and impairment in nutrient absorption [1]. Symptoms of celiac disease include chronic diarrhea, constipation, failure to thrive, wasting, abdominal pain and abdominal distention [2, 3]. However, the disease may also be asymptomatic or present with atypical symptoms such as dental enamel hypoplasia, and psychiatric disorders [2–4].

The prevalence of celiac disease in the general population is about 1%. However, it is more common in specific groups, such as first-degree relatives of affected persons, individuals with Type 1 Diabetes Mellitus (T1DM), chronic diarrhea, failure to thrive, Down syndrome, Turner syndrome, autoimmune thyroiditis, selective IgA deficiency, and William syndrome. In these specific groups, the prevalence ranges from 5 to 20% [2, 3, 5]. The association between celiac disease (CD) and type 1 diabetes mellitus (T1DM) is largely due to overlapping genetic risk loci in the Human Leucocyte Antigen (HLA) system [6]. The HLA-DQ2 and DQ8 genes play important roles in determining susceptibility to both conditions. Furthermore, numerous studies have demonstrated a strong correlation between gluten consumption and a significant rise in insulin antibodies, which contributes to the development of T1DM [7, 8].

Celiac disease was initially thought to be common only in Europe and North America, where initial studies were conducted [5]. Recently, due to the availability of simple, sensitive and specific tests for rapid screening of large populations, similar incidences have been obtained for countries in Latin America, the Middle East, and parts of India where the disease was initially thought to be rare [9]. The varied presentations and similarity of symptoms with other common disorders in developing countries suggest the need for a high index of suspicion to diagnose CD.

In African populations, a high prevalence of CD, similar to what was obtained in Europe, has also been reported but mostly from the Northern part, affecting both the general population and the population at risk of CD [10]. In a hospital study in Sudan, out of 172 patients suspected to have CD, 74.4% were found to have the disease [11]. The commonest presenting symptom was chronic diarrhoea followed by weight loss [11]. In the general population of Libyan school children, the prevalence of CD was 0.79–1.13% [12]. In Egypt, prevalence among the general population was 0.53% while a prevalence of 4.7% was reported among children with diarrhoea or failure to thrive [13]. In Tunisia, the prevalence of CD among children was 1 in 157 with most of the screened children showing atypical and symptomatic forms of presentation [14]. The highest prevalence of CD in the world was found among a population in North Africa called the Sahrawi population, of which 5.6% have CD [15].In Durban, South Africa the prevalence of CD among children with T1DM was 5.9% while another study from Pretoria, South Africa reported a prevalence of 1.9% [16, 17]. In Egypt, the prevalence of CD among children with T1DM was 6.4% [13].

Reports from other parts of Africa especially West Africa are lacking. In Nigeria, where bread, a gluten-rich food, is a major staple food, there is a documented record of only one case in a population of over 200 million people [18]. There is a possibility that this disease exists in significant numbers in Nigeria, but is not being diagnosed. A major concern is that poorly controlled CD or misdiagnosed CD can predispose to malignancies such as small intestine lymphoma, esophageal cancer, and squamous cell carcinoma of the small intestine [2]. In addition, CD is known to negatively affect the clinical course of T1DM if undetected and untreated. Hence, when untreated in children with T1DM, celiac disease can contribute to disease burden, poor quality of life and increased rate of death. This study aimed to determine the prevalence and pattern of CD autoimmunity among children with T1DM in Nigeria.

Materials and methods

Study location

This study was part of a larger study on T1DM in Nigerian children. The study was carried out at seven tertiary hospitals in Nigeria that have pediatric endocrinologists and paediatric gastroenterologists and access to children with type 1 diabetes mellitus. These hospitals are located in the Southern and Northern parts of Nigeria, namely Lagos State University Teaching Hospital (LASUTH) and Lagos University Teaching Hospital (LUTH), both located in Lagos, Olabisi Onabanjo University Teaching Hospital (OOUTH) in Sagamu, University College Hospital (UCH) in Ibadan, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) in Ile-Ife, Aminu Kano University Teaching Hospital (AKUTH) in Kano, and Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH) in Bauchi.

Nigeria is the sixth most populous country in the world, with a population of over 227 million people [19]. Half of the population is under 19 years old. The country has a culturally diverse federation with over 250 ethnic groups. The three largest ethnic groups are the Hausa-Fulani in the north and the Igbo and Yoruba in the south. The country has distinct climate zones, with a tropical monsoon climate in the south and a hot, semi-arid Sahelian climate in the north. The uneven distribution of natural resources, differences in climate and physical

conditions, and unequal institutional policies result in varying economic opportunities for the population in different regions. Despite the differences in geographical location and environmental interactions, there is considerable homogeneity in the genetic composition among the Yoruba, Igbo and Hausa ethnic groups in Nigeria [20] There are about 27 Teaching Hospitals in Nigeria [21]. As of 2021, there were approximately 4,400 children and adolescents with Type 1 Diabetes (T1DM), including 3,800 new cases reported [22].

The details of study design, sampling technique, selection of study participants and data collection have been previously reported [23].

Instruments and data collection

Using the questionnaire specifically designed for the study, interviews were conducted with T1DM children and adolescents as well as parents/guardians of young children who were unable to answer study questions. Information regarding the socioeconomic, clinical, and demographic characteristics of the study subjects was obtained. The subjects were screened for CD autoimmunity by measuring the levels of total serum IgA, anti-tissue transglutaminase antibody (tTG) and anti-endomysial antibody (EMA). Endoscopy and duodenal biopsy were recommended for participants with positive markers of CD autoimmunity.

The study used standard procedures for anthropometric measurements and periodically checked weighing scales and height boards. Participants' nutritional status was determined using weight-for-height for children under five years old and Body mass index-for-age for children over five years old and interpreted using WHO Child Growth Standards [24]. Families were assigned a socio-economic class based on parents' occupations and education, with mean scores falling within the 1–5 range. Those with 1 and 2 scores were classified as upper class, those with a score of 3 were middle class while those with 4 and 5 scores were lower class [25].

Estimation of CD specific antibodies and diagnosis of celiac disease

The serum IgA-tissue transglutaminase antibody (anti-tTG) and the total serum immunoglobulin A (IgA) were measured in all study participants. Serum IgA-endomysial antibody (EMA) was determined if serum total IgA was low or if the participant tested positive for serum IgA anti-tTG. This is because patients with IgA deficiency would have normal IgA anti-tTG levels, which could be false negative. The enzyme-linked immunosorbent assay method was used to measure serum anti-tTG using test kits from EUROIMMUN, Lübeck, Germany. The serum samples were analyzed for total serum IgA using BNII nephelometry according to the manufacturer's recommendations (Siemens BNII, Oststeinbek, Germany) while EMA was estimated using the test kits from Inova Diagnostics, San Diego, USA. Based on the manufacturer's instructions, the standard reference ranges used in this study for IgA anti-tTG and EMA were 0–12 U/mL and 0–20 U/mL, respectively. For serum IgA, the standard reference range for children varies with age but it is generally between 0.27 and 3.56 g/L. The reference ranges of the lower limit of normality for total IgA are lower for smaller children than for older ones.

Upper gastrointestinal endoscopy and small intestinal biopsy were recommended for study participants positive for serum IgA anti-tTg or serum EMA. This procedure was performed on a single participant by the lead author, assisted by adult physicians and nurse assistants. The Olympus video endoscope (EVIS EXERA II CV-180 Model) with a 9.2 mm diameter oesophagogastroduodenoscope was used for the procedure. The endoscope was inserted into the mouth and passed down to the small intestine. Biopsy specimens from four different areas in the descending duodenum and 2 different areas from the bulb were sent to the laboratory for histological examination.

The diagnosis of celiac autoimmunity was established in individuals with a positive serum IgA anti-tTG test. The diagnosis of celiac disease (CD) was confirmed in individuals with a serum IgA anti-tTG level that is equal to or greater than 10 times the upper limit of normal, along with a positive serum IgA-EMA in a separate blood sample, or with CD enteropathy of variable severity (ranging from Marsh stage 2 to Marsh stage 3).

Data analysis and presentation

Data analysis was by descriptive and inferential statistics using the Statistical Package for the Social Sciences version 25.0 (IBM SPSS Statistics, IBM Corporation, Armonk, New York, USA). Univariate analyses were carried out for all major variables of interest like demographic and socio-economic factors. The means and standard deviations (SD) were calculated for continuous variables while ratios and proportions were calculated for categorical variables. Prevalence estimates were reported as percent proportion. Proportions and ratios were compared using Fisher's exact test. A P value of less than 0.05 was accepted as statistically significant.

Results

Socio-demographic characteristics and frequency of gluten-containing food consumption among study participants

The study recruited 104 participants with T1DM out of 161 eligible individuals, resulting in a response rate of 64.6%. Table 1 shows the socio-demographic characteristics of the subjects, whose ages ranged from 3 to 19 years

Table 1 Socio-demographic characteristics and frequency of gluten-containing food consumption in relation to serum anti-tTG among study participants

Parameters	Normal serum anti-tTG (*n* = 98) No (%)	Elevated serum anti-tTG (*n* = 6) No (%)	*P* value
Age (years)			0.202
< 5	6 (6.1)	1 (16.7)	
5–9	13 (13.3)	2 (33.3)	
10–14	45 (45.9)	3 (50.0)	
15–19	34 (34.7)	0 (0.0)	
Sex			0.042
Male	41 (41.8)	0 (0.0)	
Female	57 (58.2)	6 (100)	
Tribe			0.207
Hausa	39 (39.8)	5 (83.3)	
Ibo	9 (9.2)	0 (0.0)	
Yoruba	38 (38.8)	1 (16.7)	
Others	12 (12.2)	0 (0.0)	
Child level of education			0.422
Pre-school	7 (7.1)	1 (16.7)	
Not schooling	4 (4.1)	0 (0.0)	
Primary	23 (23.5)	1 (16.7)	
Secondary	61 (62.2)	3 (50.0)	
Tertiary	3 (3.1)	1 (16.7)	
Social class			0.852
Upper	26 (23.9)	2 (33.3)	0.713
Middle	26 (27.5)	1 (16.7)	
Lower	46 (48.6)	3 (50.0)	
Frequency of gluten-containing food consumption			
Once a day	22	0	
Twice a week	24	2	
Thrice a week	23	2	
Once a month	9	1	
Others	20	1	

anti-tTG = serum IgA-tissue transglutaminase antibody

Table 2 Serum level of CD-specific antibodies, total IgA, and the histology report of duodenal biopsy for the six study participants with CD autoimmunity

Patients	*Serum IgA (g/L)	Anti-tTG (0–12 U/L	Anti-EMA (0–20 U/L)	Histology of the duodenal biopsy
1	1.47 (0.42–2.95)	> 300	4.9	Findings consistent with celiac disease, Marsh stage 1
2	6.76 (0.34–2.74)	40.2	53.9	Not done
3	1.65 (0.34–2.74)	79.1	8.92	Not done
4	2.41 (0.34–2.74)	137	197	Not done
5	1.40 (0.42–2.95)	47.7	40.7	Not done
6	0.77 (0.27–2.46)	35.2	2.49	Not done

*Figures in parenthesis are the laboratory reference values for each participant; anti-tTG = IgA-tissue transglutaminase antibody; IgA = immunoglobulin A; EMA = IgA-endomysial antibody

with a mean age of 12.3±4.1 years. Most of the participants (82; 78.8%) were aged 10 years and above, with a male-to-female ratio of 1:1.5. The study found that four participants (4.1%) were not currently attending school, and about three-quarters of the participants (76; 73.1%) were from the middle and lower socioeconomic class. All study participants agreed to consuming gluten-containing foods.

Prevalence of CD autoimmunity in children with T1DM

Table 2 shows the pattern of serology results for CD-specific antibodies and the histopathology report. Six (5.8%) participants had elevated serum anti-tTG levels. Three of these participants had rather low titers of tTG, one had a moderate elevation and two had titers greater than 10 times the upper limit of normal. Only three (50.0%) of the six participants with elevated serum anti-tTG levels had elevated serum EMA. Low serum total IgA was found in

4 (3.8%) of the 104 children with TIDM. None of the children with low total serum IgA had elevated EMA. Only one of the six participants with elevated serum anti-tTG levels had an endoscopy and biopsy of the duodenum. The histology revealed villi lined by uniform columnar epithelial cells interspersed with numerous goblet cells and underlying hyperplastic Brunner's glands. Additionally, there were abundant lymphoplasmacytic aggregates within the lamina propria (Fig. 1).

Clinical characteristics of study participants with or without CD autoimmunity

Table 3 shows the clinical characteristics of the study participants. The age at diagnosis of T1DM ranged from 4 months-18 years with a mean of 9.7±4.2 years. A higher percentage of the study participants with elevated serum tTG presented with features of DM at age below 10 years compared to those with normal serum tTG levels, although this was not statistically significant (83.3% vs. 37.7%, $p=0.149$). Eight (12.5%) participants had packed cell volume less than 30%. The random blood glucose level was above 100 mg/dL in 82.7% of the participants while the range for HbA1c was 5.5–15.6% with a mean of 9.2±3.2%. Among the participants that had laboratory results for HbA1c, 52 (83.9%) children had HbA1c concentrations equal to or greater than 7.0%. The nutritional status of the participants showed that 11 (10.6%) were undernourished while 16 (15.4%) were either overweight or obese. There was no significant difference in the nutritional status between participants with and without elevated serum tTG ($\chi^2=2.23$, $p=0.526$).

The clinical profile of the six participants diagnosed with CD autoimmunity is shown in Table 4. Their ages ranged from 3 to 12 years with a mean age of 9.2±3.7 years. Their mean age at diagnosis of TIDM was 6.7±2.7 years. All were of the female gender.

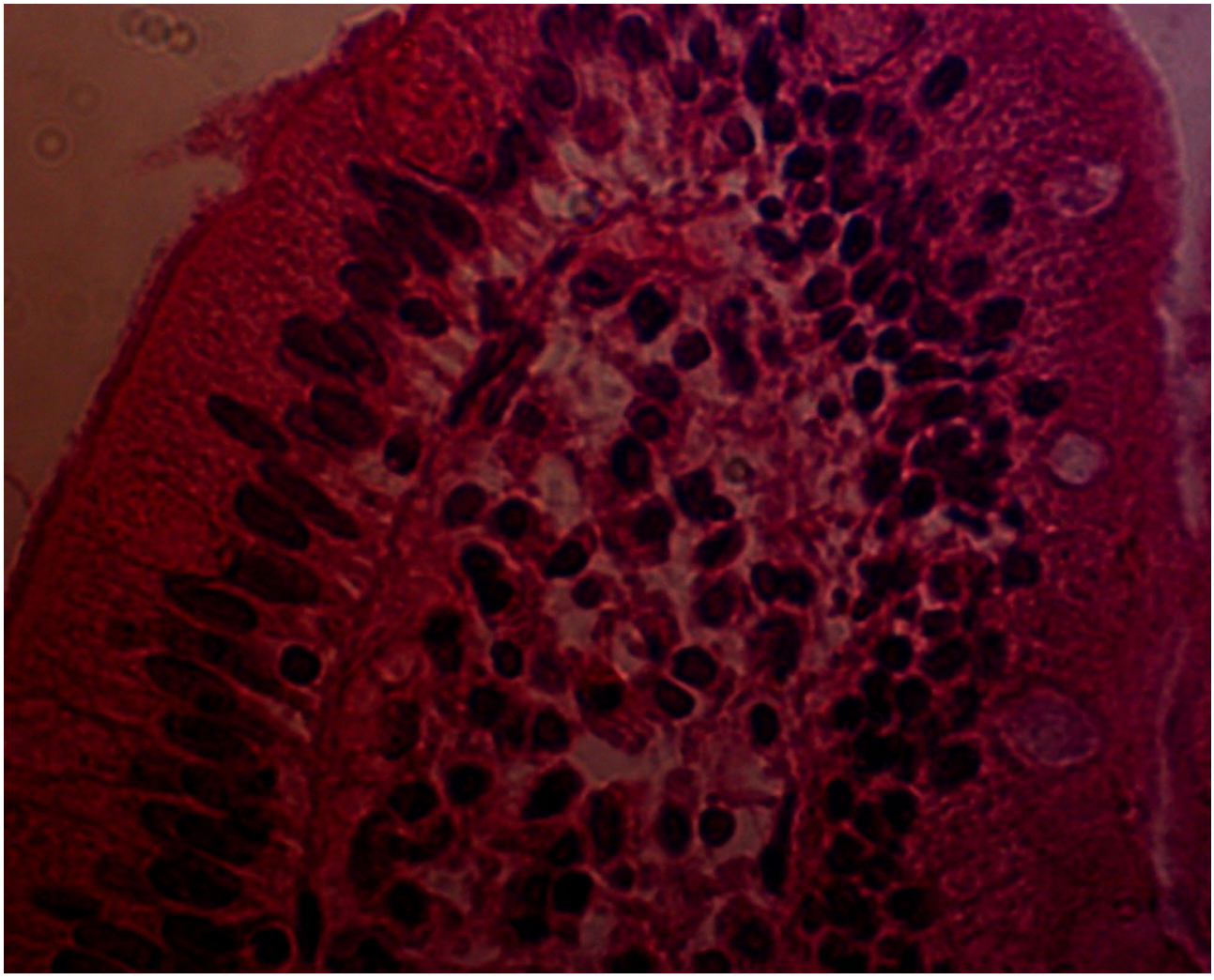

Fig. 1 Histology of duodenal biopsy of one of the study participants seropositive for CD. The photomicrograph showed intraepithelial lymphocytes and lymphocytes within the lamina propria at 400x magnification. More than 40 intraepithelial lymphocytes were seen per 100 epithelial cells (Marsh stage 1)

Table 3 Association between CD autoimmunity and clinical characteristics among study participants

Parameters	Normal serum anti-tTG (*n* = 98) No (%)	Elevated serum anti-tTG (*n* = 6) No (%)	*P* value
Age of the child when DM was diagnosed			0.149
< 5	11 (11.2)	1 (16.7)	
5–9	26 (26.5)	4 (66.6)	
10–14	50 (51.0)	1 (16.7)	
15–19	11 (11.2)	0 (0.0)	
Packed cell volume (*n* = 64)[#]			0.400
Less than 30%	8 (12.5)	0 (0.0) [&]	
≥ 30%	56 (87.5)	5 (83.3)	
Random blood glucose			0.029
≤ 100 mg/dL	15 (15.3)	3 (50.0)	
> 100 mg/dL	83 (84.7)	3 (50.0)	
Glycosylated haemoglobin (*n* = 58)[#]	9 (15.5)	1 (25.0) [$]	0.618
Less than 7.0%	49 (84.5)	3 (75.0)	
≥ 7.0%			
Nutritional Status			0.526
Undernourished	11 (11.2)	0 (0.0)	
Normal	71 (72.4)	6 (100.0)	
Overweight	9 (9.2)	0 (0.0)	
Obesity	7 (7.1)	0 (0.0)	

[#]Laboratory results were available only for the stated number of participants

[&]PCV value available for 5 of the six patients with positive serum tTG

[$]Glycosylated haemoglobin value available for four of the six patients with positive serum tTG

anti-tTG = IgA-tissue transglutaminase antibody

Table 4 Clinical profile of the six children with CD autoimmunity

Patients	Age (years)	Age at diagnosis of DM (years)	Location of participants	GIT symptoms	BMI-z-score	PCV	Hb1Ac
1	12	9	Southern Nigeria	Nausea, vomiting and bloating	1.14	42	NA
2	7	5	Northern Nigeria	Nausea	0.10	34	8.0
3	12	10	Northern Nigeria	No	1.35	46	5.50
4	9	5	Northern Nigeria	Nausea, vomiting	-0.05	39	NA
5	12	8	Northern Nigeria	Diarrhoea, bloating, foul-smelling stool	-0.62	36	7.60
6	3	3	Northern Nigeria	No	-0.22*	NA	10.2

NA – not available; *weight-for age z-score; DM = Diabetes Mellitus; GIT = Gastrointestinal; BMI = Body Mass Index; PCV = Packed Cell Volume; HbA1c = Glycated haemoglobin

Discussion

The study found that the prevalence of CD autoimmunity among Nigerian children and adolescents with TIDM was 5.8%. This prevalence is low compared with the prevalence of 9.1% obtained in the Moroccan population [26], 11.5% from the district General Hospital in Riyadh, Saudi Arabia [27], and 10.2% from a tertiary diabetic clinic in Pretoria, South Africa [17]. The study in the Moroccan population was hospital-based and multicentric, similar to this study, but different because it included adults. The difference in prevalence reported by the Riyadh study may be attributed to their methodology, which involved a retrospective chart review and focused on adolescents and adults. On the other hand, the Pretoria study included individuals of various races, such as blacks, whites, and those of mixed race. It's worth noting that HLA-DQ2-associated celiac disease is commonly found in white populations, which could explain the high prevalence observed in the Pretoria study [10].

However, the prevalence of CD autoimmunity in the present study is similar to the 4.1% reported from Bristol Royal Hospital in England and 3.8% from Tampere

University Hospital, in Finland [28, 29]. Based on the positive serum CD-specific antibodies, it can be inferred that this index study has established the occurrence of CD autoimmunity among Nigerian children with TIDM and this is in tandem with the global incidence of 5% among diabetic children [5]. It is possible that a significant proportion of the general population of Nigerian children may also be affected by CD. Nigeria is one of the most populous countries in the world with possibilities of a large burden of CD which needs to be explored.

It is worthy of note that out of the six participants with CD autoimmunity, five were from the Northern region of Nigeria, indicating a higher prevalence of the disease in that area. The Northern region shares its borders with North African countries where the Sahrawi people, who have the highest incidence of CD in the world, are found [15]. Trans-migration in the North African population and the mixing of genetic profiles may be contributory factors to this observation.

The confirmation of diagnosis of CD is by histology of biopsied duodenal tissue [30]. However, according to the European Society of Paediatric Gastroenterology and Hepatology and Nutrition and American Gastroenterology Association clinical practice guidelines, high tTG IgA values equal to or greater than 10 times the upper limit of normal can be considered a reliable and accurate test for diagnosing active CD in children, while those with positive tTG-IgA but with titers less than ten times the upper limit of normal should undergo biopsies to decrease the risk of false positive diagnosis [31]. In addition, the positive predictive value for CD diagnosis is almost 100% in children with strongly positive tTG IgA values combined with a positive EMA. In this study, only two of the six children with positive tTG IgA antibodies had values higher than 10 times the upper limit of normal. However, the child with the highest tTG IgA titer had a negative EMA, and the histology of the biopsied duodenal tissue showed Marsh stage 1, which is not confirmatory of the presence of active CD in the child. The second child with tTG IgA antibody values higher than 10 times the upper limit of normal. had positive serum EMA, indicating active CD. However, we were unable to perform an upper gastrointestinal endoscopy and biopsy of the duodenum to confirm CD in the child. Also, the other children with CD autoimmunity did not have a duodenal biopsy done because of the non-availability of paediatric endoscopy service and difficulties encountered in transferring the patients to where the service can be accessed. In most low- and middle-income countries, paediatric gastroenterology practice is poorly developed and paediatric gastroenterologists and other paediatricians often struggle to cope with available resources, which may result in underdiagnosis. In such settings, the tTG IgA antibody and IgA-Ema thus have primary importance in the diagnosis of CD.

Celiac disease has a varied presentation of clinical signs and symptoms which may cause misdiagnosis and underdiagnosis [2, 3]. All the participants with elevated tTG IgA antibodies except two had gastrointestinal symptoms such as nausea, vomiting and bloating. This is similar to the findings in the Moroccan population where frequencies of constipation, abdominal pain and bloating were significantly higher among T1DM patients with CD autoimmunity [26]. It is also similar to the findings in a study of Turkish children with T1DM, where five out of the 12 patients diagnosed with biopsy-proven CD were symptomatic [32]. Three of the symptomatic patients had failure to thrive, one had chronic constipation, and one had anemia. However, these findings contrast with other studies that reported most children with T1DM are asymptomatic for CD [17, 27]. Therefore, healthcare professionals in the country must be aware that the disease exists and must exhibit a high index of suspicion to make a diagnosis.

There are conflicting reports on the relationship between the age of diagnosis of TIDM and the frequency of CD. While some studies reported a significantly higher frequency of CD in patients with an earlier age of T1DM diagnosis [27, 33, 34], other studies revealed no such relationship [26, 35]. The mean age of onset of T1DM in this study was about 10 years which is similar to the mean age of about 13 years reported in children from two cities in the South-Western part of Nigeria [36, 37]. However, the mean age of the participants with elevated anti-tTG IgA was about 7 years supporting the evidence of a higher frequency of CD in those with earlier onset of T1DM [27, 33, 34]. Recently, some studies have reported the normalization of celiac serology in patients with T1DM, even with no gluten-free dietary intervention [38, 39]. Unal et al. showed that about a quarter of CD cases diagnosed within the first five years of T1DM had spontaneous resolution of their positive tTG IgA antibody [39]. It is recommended that screening for CD is done at the time.

of T1DM diagnosis and serological follow-up of patients done for about five years, especially for those that are asymptomatic and have a mild elevation of anti-tTG IgA.

Since celiac disease is an autoimmune disorder, it is expected to be more common in females than in males. In this study, all the participants with CD autoimmunity were females. This is consistent with numerous other studies that indicate that CD predominantly affects females [3, 27].

This study has some limitations. Due to various constraints, most of the children with CD autoimmunity could not undergo duodenal biopsies to confirm the diagnosis. However, we included EMA as a serological

marker for CD to increase the accuracy of diagnosis. The combined use of both serological tests, EMA and anti-tTG, is expected to improve the diagnosis. The measurement of IgA-EMA in IgA-deficient patients in this study could lead to a high risk of false negative results. Additionally, the study had a small sample size, which may have caused an underestimation of the prevalence of CD autoimmunity. Since the study was cross-sectional and the prevalence of CD autoimmunity was low, it is difficult to establish a cause-and-effect relationship and draw any firm conclusions between CD autoimmunity and the demographics and clinical symptoms that were found to be significantly related. The cross-sectional design also means that we were unable to analyze CD-specific antibody levels at multiple time points to track any changes over time.

We suggest that longitudinal research with a larger sample size is necessary to have a better understanding of the burden and impact of CD on the clinical progression of T1DM in children and adolescents, including the effect of CD on diabetic control as well as its effect on their quality of life. The implication of markers of CD autoimmunity for diagnosing or ruling out CD in this environment requires further investigation.

In conclusion, this study revealed that CD may be quite common among Nigerian children and adolescents with TIDM; hence, screening for the disease should be recommended for children and adolescents with T1DM, especially females and those with gastrointestinal symptoms. Furthermore, the findings from this study indicate that there is a high likelihood of a large number of children in the general population of Nigeria having celiac disease. Therefore, it is recommended that programs for active screening of at-risk populations as well as proactive efforts to diagnose the disease in clinical settings should be supported in the country.

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Author contributions
IOS conceived the idea of the study. OOA and AOA contributed to the design of the study and writing of the manuscript. IJA, CHA, OFA, AAA, OOA, GDG, MFB, UIU, OEO, OJU, SS and DAS participated in data collection, analysis of data and interpretation of the results. IOS drafted the original manuscript. MBF and AOO supervised the conduct of the study. All the authors reviewed the manuscript draft and approved the final version for submission.

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Data availability
The data analyzed in the study are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate
Ethical approval was obtained from the ethics committees of all the involved hospitals – Health Research and Ethics Committee of LASUTH (LREC/06/10/1121); Health Research and Ethics Committee of LUTH (ADM/DCST/HREC/2682); Ethics and Research Committee of OAUTHC (ERC/2019/07/05); Health Research Ethics Committee of OOUTH (OOUTH/HREC/377/2020AP); Research Ethics Committee of AKUTH (AKTH/MAC/SUB/12A/P-3/VI/2108); Research and Ethics Committee of ATBUTH (ATBUTH/ADM/42/VOL.1) and Research Ethics Committee of UI/UCH (UI/EC/24/0362). Written informed consent was obtained from all parents or guardians and assent from all subjects.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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