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Original Research Article

To Determine the Prevalence of Celiac Disease in a Group of First-Degree Relatives of Our Patients with Celiac Disease

Dr Mahender Kumar Meena[1], Dr Mamta Rani[2], Dr Dinesh Yadav[3], Dr Anand Bhatia[4*]

[1]GDMO Paediatrics, North DMC Medical College and Hindu Rao Hospital, Delhi, India
[2]Senior Medical officer Paediatrics, North DMC Medical College and Hindu Rao Hospital, Delhi, India
[3]Chief Medical officer Paediatrics, North DMC Medical College and Hindu Rao Hospital, Delhi, India
[4]Assistant Professor Paediatrics, North DMC Medical College and Hindu Rao Hospital, Delhi, India

*Corresponding Author: Dr. Anand Bhatia

Abstract

Aim: The aim of the present study was to determine the prevalence of celiac disease in a group of first-degree relatives of our patients with celiac disease.

Materials and methods: The present study included first-degree relatives of 100 subjects being studied with a diagnosis of celiac disease at Hindu Rao Hospital, Delhi. Parents and siblings of these subjects were invited to celiac disease clinic via telephone to participate in the study. Informed written consent in local language was taken from parents of these children willing to participate in the study and they were explained about the purpose of study. The study has been approved by the ethical and scientific committee of the Hindu Rao Hospital, Delhi.

Results: There were 48% males and 52% females. Majority of the subjects belonged to 31-40 years of age. Out of 100, 10% were TTG +ve. The prevalence of TTG Ab positive association was highly significant. TTG was raised up to less than 5 times in 2 subjects of FDR TTG positive group whereas it was 6 subjects in index cases. The value is raised >5 times in 8 subjects of the FDR TTG+VE group and 43 subjects of the index cases. TTG was normal in 1 subject of the index cases. The association was statistically significant (p=<0.001).

Conclusion: The prevalence of Celiac disease was more common in siblings than parents of first degree relatives of index cases. Extra intestinal symptoms were more common in FDR TTG+ve CDs than intestinal symptoms. Diarrhoea, abdominal distension, pain abdomen, poor weight gain, failure to gain height, generalized weakness and anaemia specially iron deficiency anaemia and rickets were more common.

Keywords: Celiac Disease, First-Degree Relatives, Prevalence, Tissue Transglutaminase Immunoglobulin A.

1. Introduction

Celiac disease (CD) is an immune-mediated enteropathy triggered by ingestion of gluten present in wheat and related prolamines present in rye and barley in genetically susceptible individuals carrying HLA-DQ2 and/or HLA-DQ8 haplotype.[1] Once thought to be

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uncommon, CD affects approximately 1% of the world's population.[2-4] Even in Asian countries, where CD was thought to be a rare disease, recent studies including one from our centre suggest a prevalence of 1 in 330 to 1 in 96 in the general population in Northern India.[5,6] CD is now being observed in other Asian countries including China, Malaysia and Pakistan.[7-10]

Since CD is a genetic disease, first-degree relatives (FDRs) of patients with CD are at higher risk of developing CD due to close genetic repertoire, which leads to higher genetic susceptibility.[4] Advent of celiac-specific antibodies (a reflection of adaptive immune response to gluten peptide) has revolutionized the case detection rate and has led to recognition of CD as a public health problem world over.[11] With the help of celiac-specific serologic tests, it is now possible to screen and detect CD not only the clinically apparent patients but also those who still have not developed any symptoms. With increasing use of screening and diagnostic tests along with increase in the awareness, CD has become one of the most common genetic disease.

Because of the genetic susceptibility, both FDRs and second- degree relatives are at a higher risk of developing CD than the general population. The prevalence of CD in FDRs vary widely from 5% to 38%.[12-15] The three studies from Asia, all from the Northern part of India have also reported a prevalence of CD in FDRs to vary from 8.2% to 22%.[16-18] The risk of having CD in FDRs varies with the individual relationship with the index patient with CD. Several studies have suggested that siblings are at a higher risk of developing CD in comparison to parents and children.[19,20]

The aim of the present study was to determine the prevalence of celiac disease in a group of first-degree relatives of our patients with celiac disease.

2. Materials and Methods

The present study included first-degree relatives of 100 subjects being studied with a diagnosis of celiac disease at Hindu Rao Hospital, Delhi. Parents and siblings of these subjects were invited to celiac disease clinic via telephone to participate in the study. Informed written consent in local language was taken from parents of these children willing to participate in the study and they were explained about the purpose of study. The study has been approved by the ethical and scientific committee of the Hindu Rao Hospital, Delhi.

Inclusion Criteria:

1. Siblings of celiac disease patient above the age of 8 months who are on gluten diet for at least 6 weeks.
2. Parents of celiac disease patient.

Exclusion criteria:

1. Children and parents not willing to participate in the study.
2. Children with age <8 months in whom gluten is not introduced for at least 6 weeks.
3. Children and parents who are on gluten free diet.

Informants were interviewed using a structured questionnaire to asses study subjects' clinical history pointing towards celiac disease and dietary history. Physical examination including anthropometry, complete head to toe examination and systemic examination were done. Routine investigations including complete blood picture, iron profile, peripheral smear, LFT with enzymes, Sr ALP, Sr total calcium, Sr phosphates, x-ray wrist, thyroid profile and CD serology including tTG IgA levels were done.

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Serum tTG IgA levels measured using ELISA technique with reference range of 0-15units/ml being normal and >15 units/ml being considered screen positive. Serum tTG IgA was done as screening tests and the subjects whose serology comes positive are considered for upper GI endoscopy and duodenal biopsy was done for confirmation.
Based on the results the subjects are categorized into healthy and diseased with respect to CD. Subjects diagnosed with CD are further categorized into symptomatic and asymptomatic CD. Based on the symptoms they are categorized as classical CD or non-classical CD.
After diagnosis three groups are created 1. FDR TTG negative 2. FDR TTG positive 3. Index cases. All the symptoms and lab parameters are compared among these three groups.
Statistical analysis: Data analysis was done by using the statistical software SPSS version 15.0. Formulas used were ANOVA and unpaired t-test, Chi-square test and Fischer's Exact test.

3. Results

Table 1: Patient characteristics

Gender	**N**	**%**
Male	48	48
Female	52	52
Relationship distribution		
Mother	30	30
Father	20	20
Brother	22	22
Sister	28	28
Age groups in years		
<10 years	23	23
10-20 years	20	20
21-30 years	12	12
31-40 years	41	41
41-50 years	4	4
TTG Positivity		
FDR TTG +ve	10	10
FDR TTG -ve	90	90

There were 48% males and 52% females. Out of them, 50% were siblings and 50% were parents. Majority of the subjects belonged to 31-40 years of age. Out of 100, 10% were TTG +ve.

Table 2: Prevalence, sibling's vs parents

	N
Siblings positive	18
Siblings negative	32
Parents positive	22
Parents negative	28

The prevalence of TTG Ab positive association was highly significant.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE06, 2023

Table 3: Pattern of TTG values

	FDR TTG -ve	FDR TTG +ve	Index CD
Normal	90	0	1
1-2 times	0	1	2
3-5 times	0	1	4
>5 times	0	8	43

TTG was raised up to less than 5 times in 2 subjects of FDR TTG positive group whereas it was 6 subjects in index cases. The value is raised >5 times in 8 subjects of the FDR TTG+VE group and 43 subjects of the index cases. TTG was normal in 1 subject of the index cases. The association was statistically significant (p=<0.001).

4. Discussion

Because of genetic susceptibility, both first- and second-degree relatives are at a higher risk of developing CD than the general population. The risk of having CD in FDRs varies with the relationship with the index CD patient. Several studies have suggested that siblings are at higher risk of developing CD than parents and children.[19,20] Furthermore, prevalence of CD among FDRs also varies with gender. We also observed that siblings had higher prevalence of CD (sixteen-fold higher than the general population) compared to children (5-fold higher than the general population) as also observed by Rubio et al. and Gautam et al.[13,16]

There were 48% males and 52% females. Out of them, 50% were siblings and 50% were parents. Majority of the subjects belonged to 31-40 years of age. Out of 100, 10% were TTG +ve. The prevalence of TTG Ab positive association was highly significant. TTG was raised up to less than 5 times in 2 subjects of FDR TTG positive group whereas it was 6 subjects in index cases. The value is raised >5 times in 8 subjects of the FDR TTG+VE group and 43 subjects of the index cases. TTG was normal in 1 subject of the index cases. The association was statistically significant (p=<0.001). The spectrum of the symptoms of CD varies from typical symptoms such as diarrhoea, anaemia, abdominal pain and failure to thrive to atypical symptoms such as infertility, osteopenia/osteoporosis.[1,10] In the present study, only 57% of FDRs with CD had classical symptoms and 2 were totally asymptomatic. Tursi et al. have also reported 45.8% subclinical symptoms in anti-tTG-positive FDRs.[15] Seven FDRs had potential CD; hence screening of FDRs for CD using serological test is beneficial in identifying silent form of the disease.

It is now well established that all FDRs either asymptomatic or symptomatic should be screened for CD. Based on the observation that family members of patients with CD are not only at high risk of developing CD but also are at a higher risk to develop other autoimmune diseases, such as type I diabetes and autoimmune thyroiditis.[21,22] Nass et al. observed a significant increase in autoantibodies against thyroid and parietal cells in FDRs compared to controls (p = 0.006).[23] Such an observation raises an argument in favour of screening FDRs for other autoimmune diseases in addition to CD. In addition, FDRs possibly share the same environmental triggers as index patients, which are modulated by genetic factors. Recent evidence shows that HLA-DQ2 genotype influences the gut microbiota composition of healthy infants at familial risk of CD.[24] Furthermore, while CD occurs due to gluten peptide induced both acquired and innate immune response in a genetically susceptible individual[25], what decides the clinical phenotypic expression is not well known. While presence of HLA haplotype explains approximately 40% of conferred risk, there is a strong likelihood of other genetic factors playing a role in the expression of the disease.[26] One of the well-known factors which affect the clinical expression of the disease is HLA-DQ2 or -DQ8 homozygosity.[27-29]

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE06, 2023

Since many FDRs already had suffered from failure to thrive and anaemia, early detection of CD might have prevented growth failure. It is therefore advisable to screen FDRs as early as possible. However, a single serological test may not rule out future development of CD, and the appropriate interval for repeating serological screening is not well established.

5. Conclusion

The prevalence of Celiac disease was more common in siblings than parents of first degree relatives of index cases. Extra intestinal symptoms were more common in FDR TTG+ve CDs than intestinal symptoms. Diarrhoea, abdominal distension, pain abdomen, poor weight gain, failure to gain height, generalized weakness and anaemia especially iron deficiency anaemia and rickets were more common.

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ISSN: 0975-3583, 0976-2833 VOL14, ISSUE06, 2023

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