International Journal of Applied Home Science ***REVIEW PAPER***
Volume 4 (7&8), July & August (2017) : 663-670 ISSN : 2394-1413
Received : 12.07.2017; Revised : 22.07.2017; Accepted : 30.07.2017

Growing spectrum of children with celiac disease in India

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ABSTRACT

Prevalence of Celiac disease (CD) varies among different populations worldwide and the actual prevalence has been shown to be higher than before. Celiac disease was presumed to be rare in India because of low awareness and a low index of suspicion. However new epidemiological data show that CD is a common disorder in Asian countries, particularly India. CD is prevalent among predominantly wheat consuming states of North India and other states. Nevertheless, there are occasional case reports of celiac disease from South India. This apparent regional variation in occurrence of disease could be postulated as due to differences in genetic predisposition, differences in diet or both. CD is a significant paediatric health problem in north Indian children and screening programs in apparently healthy population is a worthwhile proposition.

Key Words : Celiac, Disease, Prevalence, Genetic predisposition

INTRODUCTION

Celiac disease, an autoimmune enteropathy caused by gluten in food, is now understood to be a disorder with an extremely wide range of presenting manifestations of variable severity. It is the result of sensitivity to ingested gluten in genetically susceptible people with the subsequent immune reaction leading to small bowel inflammation. This gives the characteristic mucosal lesion of increased intraepithelial lymphocytes, villous atrophy, and crypt hyperplasia in the proximal small bowel. The classic malabsorptive symptoms of diarrhoea and weight loss are only one facet of the spectrum of manifestations of this relatively common disease (Logan *et al.,* 1983and Swinson and Levi, 1980). Symptoms may be subtle and many patients have subclinical or silent disease (Bottaro *et al.,* 1999). Available data suggest that celiac disease has a prevalence of approximately 1:250-300 in western countries including the United States (Not *et al.,* 1998; Ivarsson *et al.,* 1999 and Johnston *et al.,* 1997). Celiac disease (CD) is a disease in which the mucosa of the small bowel is damaged in response to dietary gluten (Marsh and Crowe, 1995). Gluten is a protein found in wheat, rye, barley and oats2. The only currently recognised treatment for CD is the implementation

Cite this Article: Gupta, Aditi, Dunkwal, Vimla and Goyal, Madhu (2017). Growing spectrum of children with celiac disease in India. *Internat. J. Appl. Home Sci.,* **4** (7 & 8) : 663-670.

of a strict, lifelong gluten free diet (GFD).

In developing countries, serological testing in at risk groups is necessary for early identification of celiac patients. Clinical studies show that presentation with non-specific symptoms or a lack of symptoms is as common in the Asia. Wheat is a major component of the Indian diet and exposure to wheat proteins induces some degree of immune tolerance, leading to milder symptoms that may be mistaken with other GI disorders. The implementation of gluten free diet (GFD) is a major challenge for both patients and clinicians in India, especially since commercial gluten-free products are not available in this area.

Epidemiology of CD in the World :

Celiac disease is currently believed to affect about 1% of the general population world over. Nevertheless, the true prevalence of celiac sprue is difficult to ascertain because many patients have atypical symptoms or none at all. The disease has been described throughout the world including Europe, Russia, the Mediterranean countries, North and South America, South Africa, India, Australia and New Zealand but there is little good data on the disease prevalence in many of these countries. It is rare among people from a purely African – Caribbean, Chinese or Japanese background. A decade ago the prevalence rates were quoted as 1 in 1000 or lower but the recent data based on serological screening from several European countries and North America suggests that the condition may occur in 1 in 120-300 of the population.

In the past, celiac disease was considered to be a rare disorder in the United States, with a prevalence ranging from 1 in 3000 to 1 in 6000. Recent studies conducted using more appropriate experimental designs and powerful screening tools demonstrated that the celiac disease in United States is as frequent as in Europe in both risk groups and the general population (Berli *et al*., 2000). Similar results were obtained in Africa, South America and Asia, continents where celiac disease was considered a rare disorder. Combined together, these studies revealed that celiac disease is one of the most frequent lifelong genetically based disease of humankind" occurring in 1 out of every 100 to 300 individuals in the general population worldwide (Cataldo *et al.,* 2004).

Age of presentation and prevalence of CD appears to have changed dramatically over the last 30-40 years. Until a few years ago, gluten intolerance was thought to be a disorder almost exclusively affecting Europeans or people of European origin and they described typical features of celiac patients. Until a decade ago, CD was considered to be very rare in Middle Eastern countries. A comparison of recent studies in European and Middle Eastern countries has shown that CD is common in both areas, with an almost similar prevalence (Table 1) (Castaño *et al.,* 2004; Rawashdeh *et al.,* 1996; Shakeri *et al.,* 2004; Gursoy *et al.,* 2005; Tatar *et al.,* 2004; Shaltout *et al.,* 1989; Saadah *et al.,* 2004; Gandolfi *et al.,* 2000; Rostami *et al.,* 2004 and Weile *et al.,* 1996). This discovery can be attributed to the judicious use of serological screening tests which measure anti-gliadin antibodies (AGA) anti-endomysial antibody (EMA), and more recently anti-transglutaminase antibody (anti-tTG) hich has permitted the diagnosis of many silent and subclinical CD cases that otherwise would not have been recognized (Gandolfi *et al.,* 2001 and Rostami *et al.,* 2004).

An Italian (Tommasini *et al.,* 2004) and a Finnish (Maki *et al.,* 2003) study of mass screening with anti-tTG assay in pediatric population have estimated the prevalence of CD

Table 1: Prevalence of CD in Europe compared to Middle East population based on serological screenings

Europe prevalence	Asia prevalence
Spain 1:118	India 1:500-1:20,000
Italy 1:106	Iran 1:166
Czech 1:218	Israel 1: 157
Norway 1:262	Syria 1.5:100
Portugal 1:134	Turkey 1:87
Sweden 1:190	Anatolian adults 1:100
Netherlands 1:198	Kuwait (Chronic diarrhea) 1:18
United Kingdom 1:100	Saudi Arabia (Type 1 diabetes)
Switzerland 1:132	Japan 1:20,000

to be 1.06% and 1%, respectively. In the Finnish study (Maki *et al.,* 2003) serum samples were collected from 3564 students (aged 7 to 16 years) over a 7-year period and screened for anti-tTG and anti-endomysial antibodies. The Italian study [20] screened 3665 school children for CD over 9 months using anti-tTG and anti-endomysial antibodies.

Nowadays, the map of CD prevalence in different areas of the world is much more detailed than in the past. However, there is limited data about the prevalence of CD in Middle Eastern countries. Prevalence of CD varies among different populations worldwide and the actual prevalence of CD has been shown to be higher than before. For instance, recent studies of serum markers in blood donors have shown a prevalence of 1:681 in Brasil, 1:524 in Denmark ,1:250 in Sweden, 1:333 in Holland, 1:157 in Israel and 1:250 in the USA (Gandolfi *et al.,* 2000; Rostami *et al.,* 2004; Weile *et al.,* 1996; Shamir *et al.,* 2002 and Not *et al.,* 1998). Although the prevalence of CD in some areas in India such as South India is very low, a summary of the reviewed studies suggests a prevalence of 1% in the remaining areas of India which is similar to the frequency of this disorder in Western European countries.

Clinical presentation of Celiac disease:

Classical presenting symptoms of celiac disease are variable. Main differences are failure to thrive, anemia and muscle wasting which are features of more severe disease and are more common in Indian patients. Diarrhea, which may be acute or insidious in onset, is the commonest presenting symptom, and most patients with celiac disease, has a history of diarrhea. Diarrhea, vomiting and failure to thrive occur most frequently [23] Clinical features of Indian and western children are depicted in (Table 2).

Celiac disease prevalence in India :

Celiac disease was first reported from India in 1966 in both children and adults (Walia *et al.,* 1966 and Misra *et al.,* 1966). With a lag period of almost three decades, there has been an upsurge in the reporting of celiac disease in India. We carried out an epidemiological study to evaluate the prevalence of celiac disease among school going children. Our study results revealed a prevalence of 0.3% (1 in 310) which is comparable to the disease prevalence in Western countries. Our study highlights the fact that celiac disease is not a disease which is confined to white population only but is practically universally present; though prevalence

Table 2: Clinical features of Indian and western patients with Celiac disease

Clinical features	Walker Smith (1996)	Thapa (1999)	Patwari *et al.* (2003)
Growth retardation	-	100%	100%
Anemia	13.5%	100%	100%
Diarrhea	90%	93.3%	93.8%
Abdominal distension	44.2%	73.3%	70.8%
Anorexia	48.1%	46.7%	58.5%
Pain abdomen	44.2%	20%	50.8%
Vomiting	61.5%	20%	9.2%
Irritability	57.7%	10%	13.8%
Constipation	5.8%	2%	3.1%

varies. We have observed that there is high prevalence of disease among the siblings of patients. In addition, we have reported that celiac disease is not uncommon among adults and a high index of disease awareness is required to diagnose the disease. On a epidemiological basis, CD is prevalent among predominantly wheat consuming states of North India such as Punjab, Haryana, Delhi, Rajasthan, Uttar Pardesh, Bihar and Madhya Pardesh. Nevertheless, there are occasional case reports of celiac disease from South India. This apparent regional variation in occurrence of disease could be postulated as due to differences in genetic predisposition, differences in diet or both.

CD is being increasingly reported from India and is a major cause of chronic diarrhea in children, especially in northern India (Yachha *et al.,* 1993).The prevalence of CD in Indian children is not well documented, with most of the studies focusing on high-risk groups (*e.g.,* chronic diarrhea, short stature) and not the general population. One study in school children in Punjab reported a prevalence of 1 in 310, although the authors concluded it to be an underassessment (Sood *et al.,* 2006).

The prevalence of celiac disease in India is not well documented. In various Indian studies, the prevalence of CD in children with malabsorption ranged from 10% to 26% (Yachha *et al.* (1993). CD accounts for 16% to 40% of children with chronic diarrhea (Sood *et al.,* 2006; Poddar *et al.,* 2002; and Mittal *et al.,* 2001). Inchildren with short stature, the prevalence of CD is 15% (Mittal *et al.,* 2001). The only Indian study on population screening in children for CD gives a prevalence of 1 in 310 (Sood *et al.,* 2006). The authors concluded it to be an underassessment because serum IgA level was not estimated to rule out isolated IgA deficiency, 4 patients with positive serology refused endoscopic biopsy and finally, 3 patients with positive serology had normal small bowel biopsies and were not diagnosed as CD since they did not fulfil the criteria.

Celiac disease affects people in all parts of the world. Originally thought to be a rare childhood syndrome, celiac disease is now known to be a common genetic disorder. More than 2 million people in the United States have the disease, or about 1 in 133 people. Among people who have a first-degree relative—a parent, sibling, or child—diagnosed with celiac disease, as many as 1 in 22 people may have the disease. [31]The initial reports of CD from India appeared in 1960s from wheat eating area of Punjab (Walia *et al.,* 1966) and first described from New Dehli in 1966 (Misra *et al.,* 1966). Subsequently, CD was described in

Asian (India and West Pakistan) migrant population in UK (Nelson *et al.*, 1973). Similar to this study (Sood *et al.*, 2006) revealed the adult celiac disease in a northern Indian hospital. Adult celiac disease was diagnosed if disease manifestations started after 15 years of age The mean duration of illness in the 96 patients (mean [SD] age 32.9 [11.4] years; 50 men) diagnosed over the 6-year study period was 7.3 (2.4) years. Diarrhea was present in 67.7% of cases; 18.7% presented with refractory iron-deficiency anemia, and 9.4% with abdominal symptoms like flatulence and distension. All patients had significant improvement in symptoms and hematological and biochemical parameters after dietary gluten restriction. Adult celiac disease is not rare and usually presents as diarrhea, abdominal distension flatulence and refractory anemia. In a field study conducted among school children in Punjab, A total of 4347 school children (1967 girls, 2380 boys, age range 3-17 years) were screened for celiac disease (Sood *et al.,* 2006). Celiac disease (CD) is being increasingly reported from the wheat-eating population of north India. However, the exact prevalence of CD in children is not known as population screening studies are scarce. The prevalence of CD thus was 1%, which was in concordance with screening studies using serological markers conducted in the West. Celiac disease, not uncommon condition in Northern India, usually manifests as stunted growth, anaemia and diarrhoea (Patwari *et al.,* 2003). Exact prevalence of celiac disease is not known in our country because of lack of awareness, lack of investigation facilities and lack of expertise in field of paediatric gastroenterology, high prevalence of protein energy malnutrition and infection, varied picture of celiac disease and lack of facilities for serological tests (Thapa, 1999). According to similar studies exact incidence of disease in India is not known. CD is estimated to constitute 26 % of all cases of malabsorbtion syndrome or 4-5 % of all chronic diarrhoeas In PGI, Chandigarh, 20-40 new patients are seen every year and CD constitutes 7% of indoor admissions and about 5% of the patients attending Pediatric Gastroenterology clinic (Khoshoo *et al.,* 1988). Celiac disease has also been reported from Lucknow.

Celiac or allergy to wheat is a fastest growing problem also among the children in Rajasthan(India). Records from J K Lone Hospital in Jaipur show a steady rise in the number of cases of celiac disease diagnosed in the past three years. In 2005, around 48-such cases were reported, which rose to 104 in 2006 and 160 in 2007. Although the figures of 2008 are still not available, experts working in this field say the numbers will be around 200 fresh cases (20% more than the previous year). These are the figure from just one hospital and if experts are to be believed the number of cases will be much higher (*www.Fortis Healthcare.mht*).

Conclusion :

Celiac disease was presumed to be rare in India because of low awareness and a low index of suspicion. However new epidemiological data show that CD is a common disorder in Asian countries, particularly India. There is a need for a more uniformly designed evaluation of CD for the entire country and a mapping of HLA DQ in the same areas along with a gluten consumption assessment, since a variable frequency of CD in different parts of India may exist as is the case for other countries.Since commercial gluten-free products are not readily available and significantly more expensive than their gluten-containing products in

this area, therefore the main concern is the implementation of a GFD for Indian patients. This information will be useful to dietitians and gastroenterologists who counsel celiac patients, and to celiac advocacy groups for seeking financial support from the government. It is concluded that CD is a significant pediatric health problem in north Indian children and screening programs in apparently healthy population is a worthwhile proposition.

Nevertheless, serious thought should be given to identifing the possible reasons for the increasing prevalence of disease in India. Is it just an increased awareness of the disease? Is it that the wheat of today differs appreciably in composition or characteristics from the wheats of times past? Is it that the enormous potential benefits from the genetically improved crops are causing people to ignore such unforeseen effects? Is it that the alteration of just one or two genes with known traits through biotechnology to increase yield or quality in the already popular crop variety leads to this menace? Or is it that conventional plant breeding methods leading to the introduction of unknown genes (wild variety) whose traits have not been studied are causing an increase in incidence? Most of these concerns are technical issues that need to be addressed through appropriate research. First and foremost, the specific peptide sequence of the gliadin responsible for triggering intestinal inflammation needs to be identified. Gene-altered wheat and its products have found their way into the Indian markets. The alarming increase in the incidence of celiac disease invokes fears about the type and quality of wheat being used. The hypothetical risks posed by its use need to be scientifically evaluated.

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