

Coeliac disease in Pakistan: A bibliographic review of current research status

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Abstract

Coeliac disease is a common disorder worldwide but its impact in Pakistan is unknown. We reviewed the literature to investigate what is published on coeliac disease and gluten-free diet in Pakistan. Search engines including Medline, Embase, Google were used to retrieve information. Only articles published in a medical journal were included. A total of 34 articles were retrieved, 28 of which were clinical. Of these, 14 pertained to adults and 14 described paediatric patients. Most consisted of descriptions of small series of patients or individual case reports. Five articles addressed treatment issues including gluten-free diet. Most (65%) were from Pakistani journals. All publications were from Sindh or Punjab. For a common disorder, there is a paucity of high quality scientific literature on coeliac disease from Pakistan. Systematic, prospective research studies are needed to investigate the impact of coeliac disease in Pakistan including prevalence, clinical presentations and challenges of gluten-free diet.

Keywords: Coeliac disease, Gluten-free diet.

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Introduction

Coeliac disease (CD) is a disorder in which ingestion of gluten (proteins found in wheat, rye and barley) causes small intestinal villous atrophy by an immune mediated mechanism in genetically susceptible individuals.¹ This can lead to a variety of intestinal and extra-intestinal symptoms leading to poor absorption of nutrients and hence deficiencies before fat, protein, carbohydrates, vitamins and minerals such as iron and calcium. Serological tests are used to screen for CD and diagnosis is confirmed with small intestinal biopsy. The treatment of CD is a strict gluten-free diet for life.¹ If treated inadequately, CD can significantly impact the quality of life and lead to a variety of complications including nutritional deficiencies and small intestinal lymphoma.

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Celiac disease is estimated to affect about 1% of the population, making it one of the most common chronic gastrointestinal disorders.¹ To assess the impact on any disorder on a specific population, three fundamental domains are important. These include; 1) epidemiology and prevalence, 2) clinical presentation and 3) available therapies.

The objective of this review was to examine the currently available literature on CD in Pakistan. The information gained would help identify the scientific knowledge gaps in CD and provide direction to the type of research required in this area.

Methods

A review of the literature was conducted in early September 2017 to assess the body of knowledge available on CD in Pakistan. Medline, Embase and Google were used and combination of search terms: 'Pakistan', 'coeliac disease', 'coeliac disease', 'gluten-free diet', 'adults', 'children', 'research', applied in all search engines to identify information available on the topic. All links retrieved from the search were examined for relevant information. Only those articles published in a medical journal were counted and reviewed for the study, abstracts were not included. Any web sites relevant to coeliac disease in Pakistan were examined and included in the review.

Results

A total of 34 articles were retrieved. Of these, 24 were published in Pakistani medical journals. There were 28 clinical studies. Of these, 14 described a variety of clinical issues in adults with CD,²⁻¹⁵ of which 7 were case reports. In the paediatric population, there were 14 published articles¹⁶⁻²⁹ including 2 case reports. Another 5 articles dealt with treatment of CD including gluten-free diet.³⁰⁻³⁴ There was one publication describing a survey to assess knowledge of CD amongst general physicians.³⁵

Of the 28 clinical studies on CD, 16 (57%) were from the province of Sindh and the remainder from Punjab. There were no studies from Khyber-Pakhtunkhwa or Baluchistan.

Of the 34 publications, 22 (65%) were from Pakistani journals. Of these, 19 were published in one of the four

Pakistani medical journals currently indexed in PubMed.

Clinical Studies in Coeliac Disease

A summary of all the 28 clinical studies on CD is given in before Table. They have been categorized in adult and paediatric population and listed in chronological order beginning with the most recent ones reported first.

Articles on Treatment /Gluten-Free Diet

There were five publications on the subject of gluten-free diet as it relates to CD. A review by Rashid M and Khan AG explained the meaning of a gluten-free diet and the dangers patients with CD may face by consuming products labeled as 'gluten-free' in Pakistan due to improper labeling.³⁰ Another article by same authors discussed the scope of CD in Pakistan and the availability of gluten-free foods in the

country.³¹ It recommended that patients, health care professionals, food industry, and government regulatory agencies in Pakistan all need to learn about gluten-free diet and that any claims of a product being "gluten-free" should be critically evaluated with appropriate testing. In an editorial, Rashid M and Khan AG highlighted some of the key areas requiring investigation in CD and gluten-free diet for the medical community in Pakistan and provided suggestions for research.³²

In a paper from Institute of Food Science and Technology, University of Agriculture, Faisalabad, the researchers highlighted the nutritional value of oats as a good source of B complex vitamins, protein, minerals and fiber and proposed its use in CD.³³ The incorporation of pure, uncontaminated oat grains and oat bran in the food products could provide nutritional benefits to patients on

Table: Summary of published clinical studies on coeliac disease (CD) in Pakistan.

Author	Year	Province	Type of Study	Subjects (n)	Main Theme
ADULT					
Iqbal U ²	2017	Sindh	Case report	1	Refractory CD and azathioprine
Farina MH ³	2017	Sindh	Observational	12	Seronegative CD
Iqbal U ⁴	2017	Sindh	Case report	1	Autoimmune hepatitis and CD
Mandhwani RM ⁵	2017	Sindh	Case report	1	Refractory CD and Addisonian crises
Javeed A ⁶	2016	Punjab	Cross sectional	121	Endomysial antibody and CD
Hanif F ⁷	2015	Sindh	Case report	1	Microscopic colitis and CD
Masood N ⁸	2014	Sindh	Cross sectional	60	Clinical features of CD
Khan JM ⁹	2014	Punjab	Cross sectional	80	Psoriasis and CD
Abbas Z ¹⁰	2013	Sindh	Retrospective	77	Clinical features of CD
Arshad H ¹¹	2012	Sindh	Retrospective	404	Biopsies for malabsorption and CD
Anis S ¹²	2012	Sindh	Case report	1	Immunodeficiencies and CD
Memon MS ¹³	2010	Sindh	Retrospective	50	Clinical features of CD
Adhi M ¹⁴	2009	Sindh	Case report	1	Dermatitis herpetiformis and CD
Satti SA ¹⁵	2009	Punjab	Case report	1	Adult case of CD
PAEDIATRIC					
Waheed N ¹⁶	2016	Punjab	Cross sectional	126	Celiac crises
Muhammad AH ¹⁷	2016	Punjab	Cross sectional	60	Serological testing in CD
Lashari SK ¹⁸	2014	Sindh	Cross sectional	100	Short stature and CD
Hussain S ¹⁹	2014	Punjab	Cross sectional	52	Serological testing in CD
Waqar RM ²⁰	2013	Punjab	Cross sectional	169	Short stature and CD
Saleem N ²¹	2013	Punjab	Cross sectional	170	HLA and CD
Rabia M ²²	2012	Punjab	Cross sectional	200	Clinical features of CD
Babar M ²³	2011	Punjab	Cross sectional	40	Clinical features and crises in CD
Aurengzeb B ²⁴	2010	Punjab	Case control	50	Nutritional status in CD
Latif S ²⁵	2010	Sindh	Case report	1	Multiple autoimmunity and CD
Sultan M ²⁶	2008	Punjab	Cross sectional	214	Short stature and CD
Aziz S ²⁷	2007	Sindh	Cross sectional	49	Poor growth and CD
Zahra T ²⁸	2005	Sindh	Case report	1	Bone problems in CD
Mazahir T ²⁹	1988	Sindh	Case control	59	Malabsorption and CD

NOTE: The number of subjects (n) listed include both individuals with coeliac disease (CD) and any controls.

gluten-free diet.

A review article by Ahmed F discusses the meaning of CD and possible therapies for patients with this disorder.³⁴

Other

Gul S et al surveyed 100 general physicians in Pakistan to investigate their knowledge of the differences between irritable bowel syndrome (IBS) and CD.³⁵ The results revealed that CD is often misdiagnosed as IBS. Of the participants, only 42% considered CD a disease of small intestine while others thought it was a disorder of large intestine. The majority (88%) said that IgA-tTG antibody can be helpful in detecting CD, while 52% recommended small intestinal biopsy.

General Information and Support Groups/Networks in Pakistan

The search engine Google was used to find web-based information on CD using the terms: 'Pakistan', 'celiac disease,' 'coeliac disease,' 'support group(s)' 'information' and 'gluten-free diet'. The site which appeared repeatedly was the Pakistani Celiac Society website and Pakistani Celiac Society' Facebook page.³⁶ This web site contains resources for patients with CD. Several other coeliac support organizations including Association of European Coeliac Societies and Coeliac UK-International Organizations provided links to the Pakistani Celiac Society on their websites.

Two other websites identified included a blog about gluten-free eating in Pakistan³⁷ and the Aga Khan University Hospital webpage about CD.³⁸

Discussion

To our knowledge, this is the first review of this nature that has assembled the available scientific information on CD in Pakistan. Our findings reveal that literature available on CD is limited and primarily consists of individual case reports or descriptions of small number of patients. According to the census conducted in 2017, the population of Pakistan is 207.8 million.³⁹ The worldwide prevalence of CD is estimated to be 1%.^{1,40} Therefore, based on this figure, one would expect to have over 2 million individuals with CD in Pakistan. The amount of available literature does not reflect on the enormous impact that CD could have on the patient population in the country.

In terms of epidemiology and prevalence, there is no information available on CD in Pakistan. Highly sensitive and specific serological tests such as IgA-tissue transglutaminase antibody are now available to screen for CD. This can be employed to determine the prevalence of

CD in the general population. The prevalence of CD has been studied in neighbouring countries such as India⁴¹⁻⁴³ and Iran,⁴⁴ both in adults and children. With overall global prevalence of CD to be around 1%⁴⁰ and population of Pakistan standing at 208 million,³⁹ there would be estimated over 2 million individuals in Pakistan with CD, many presumably undiagnosed. In our opinion, a national study to estimate the prevalence of CD in Pakistan is vital. Estimation of the prevalence would be an important first step is assessing the impact of CD in the country as it will help determine how common it is and what type of resources need to be allocated to this disorder. This will further set the foundation for developing strategies to improve awareness of this disorder leading to a timely diagnosis and advocacy for better availability of locally manufactured affordable gluten-free foods. Funding for such a study would be challenging. Currently, there are no drugs used to treat CD and hence funding support from pharmaceutical industry would not be available.

Regarding clinical presentations, there is some information available, albeit in small number of subjects. A few themes do emerge from the available studies. Adults and children with CD can present with both typical and atypical symptoms. Nutritional deficiencies are common, as delays in diagnosis can happen with atypical presentations. There may be lack of awareness and knowledge of CD amongst the health care professionals in Pakistan.³⁴

Gluten-free diet is an effective therapy for CD. However, this diet is complex given the risk of contamination of food products with gluten. Wheat is ubiquitous in the diet in Pakistan, posing further difficulties with cross contamination. There is currently no information available to assess the availability of gluten-free products, the challenges of consuming gluten-free diet or the quality of life of patients with CD in Pakistan.

Interestingly, all the published studies on CD are from the provinces of Sindh and Punjab. There are none that could be found from Khyber-Pakhtunkhwa or Baluchistan. It is difficult to conclude if CD is rare in the latter two provinces or whether this observation just reflects the fact that Punjab and Sindh are the two most populous provinces and house the majority of academic medical institutions.

Of the 34 publications retrieved, 22 (65%) were from Pakistani journals. Of these, 19 were published in one of the four Pakistani medical journals currently indexed in PubMed. There were 3 articles from Pakistani journals not indexed in PubMed. Relatively small numbers of publications on CD from Pakistan have made their way to

international medical journals.

This review has limitations. It is possible that there are publications on CD from Pakistan that were not identified as they were not indexed in any of the search engines examined.

Conclusions

In conclusion, there is a relative paucity of scientific literature on coeliac disease in Pakistan and important domains including epidemiology, clinical presentations and management remain largely unaddressed. The published articles describe only small number of patients or are merely case reports. Larger, well-designed prospective studies are needed to determine the prevalence of this disorder in Pakistan, its clinical pattern across various ages, and relationship to associated autoimmune disorders. Furthermore, there needs to be investigation of management of coeliac disease including the challenges faced by patients consuming a gluten-free diet.

Disclaimer: The abstract has not been presented or published in a conference, or published in an abstract book.

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