Saudi Journal of Biological Sciences (2016) **23**, 462–466

King Saud University

**Saudi Journal of Biological Sciences**

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

# Screening of coeliac disease in undetected adults and patients diagnosed with irritable bowel syndrome in Riyadh, Saudi Arabia

**Abdulrahman S. Al-Ajlan** *

*College of Applied Medical Sciences, Department of Clinical Laboratory Sciences, King Saud University, Riyadh, P.O. Box 10219, Riyadh 11433, Saudi Arabia*

Received 16 February 2015; revised 21 April 2015; accepted 27 April 2015
Available online 1 May 2015

**KEYWORDS**

Coeliac disease (CD);
Irritable bowel syndrome (IBS);
Adult Saudi

**Abstract** The present study is to determine the prevalence and implication of coeliac disease (CD) among adult Saudis and compared to those with diagnosed irritable bowel syndrome. This prospective study was conducted among 980 adults. Out of that, 482 subjects (staff and students of Riyadh Health Science College) were designated as control cohorts for undetected coeliac disease. Furthermore, another contingent of 498 subjects diagnosed with irritable bowel syndrome (IBS) at Prince Salman Hospital and Al-Iman General Hospital also constituted a segment of the overall initial 1020 subjects. Both cases and control were tested for serological markers of coeliac disease (tissues transglutaminase (tTGAs) and endomysial autoantibody (EMAs) and were confirmed by histopathology test. All the positive for cases of coeliac disease were screened for iron deficiency anaemia, Vitamin D deficiency, and osteoporosis and weight assessment. The percentage of coeliac disease in control subjects and patients diagnosed with irritable bowel syndrome (IBS) were found to be 1.9% and 9.6% respectively, about 38% of the total coeliac disease patients are among females of middle age (20–39-years) and 16% of the males in the same age range. Whereas, 20% and 25% of all coeliac disease cases with ages of 40–59 were remarked as females and males respectively. The identical nature and overlap of symptoms of the two conditions could possibly result in misdiagnosis of coeliac diseases or over-diagnosis of irritable bowel syndrome. The findings of the study might also give considerable implications of the disease in the nutritional level which is noticeable.


## 1. Introduction

It is clinically acknowledged that coeliac disease can be regarded as a potent autoimmune disorder affecting various body systems. Most individuals that are prone to it are those who consume rye, barley and wheat that ultimately produce

* Tel.: +966 14695883; fax: +966 1 4693736.
E-mail address: aalajl@hotmail.com
Peer review under responsibility of King Saud University.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.sjbs.2015.04.015

gluten (Green and Cellier, 2007; Sanders et al., 2003; Kolho et al., 1998). During the digestive process, the taking in of gluten can result in morphological changes in the mucosa of the small intestine. It then, as corollary affects the smooth operation of villi, that ultimately results in malabsorption (Sanders and Hurlston, 2002). Coeliac disease is considered as a unique gastrointestinal atrophy, which is mainly associated with children, though; it has now been observed that is no longer age-sensitive (Lohi et al., 2007).

The most notable features of coeliac disease's symptoms include: defective absorption, (malabsorption), anaemia, insufficiency of iron, debilitating diarrhoea and loss of weight (Zipser et al., 2003; Green et al., 2001). It is also noticed that the diminutive body structure is one of the outstanding features of the disease. Furthermore, apart from gastrointestinal symptoms, it is pertinent to say that the disease has certain traits that are even beyond the familiar intestinal disorders. Ailments associated with the disease are those related to body parts such as brain, liver, joints, skin, bone and obstetrics (Chakravarty and Scott, 1992). It is also validated in other studies that type 1 diabetes mellitus, thyroid diseases and certain autoimmune diseases are equally associated with coeliac disease (Ludvigsson et al., 2005).

Irritable bowel syndrome (IBS) is a chronic functional disorder of the gastrointestinal tract of unknown origin. According to previous studies, incidence of IBS differs depending on how a manifestation was described and it was also found that IBS is more common in females and young individuals ranging from 5% to 20% (El-Salhy et al., 2012; Sperber et al., 2005; Boivin, 2001; Spiegel, 2009). Affected individuals mostly experience chronic relapsing-remitting course like symptoms such as lower abdominal pain, diarrhea, and abdominal bloating or distension (Marsh, 1992; Ford et al., 2008; Thompson et al., 1999; Manning et al., 1978). Patients with coeliac disease also reported symptoms like bloating, abdominal pain, and chronic diarrhoea. Coeliac disease and irritable bowel syndrome are conditions that have similar symptoms. Moreover, according to previous studies, individuals who are positive with irritable bowel syndrome are prone to having a coeliac disease compared to controls without irritable bowel disease (Longstreth et al., 2006). In this study, a much broader spectrum of individuals have been investigated for coeliac disease and consequently being diagnosed. This study aims to determine the prevalence and implication of coeliac disease (CD) among adult Saudis and make comparison to those with diagnosed irritable bowel syndrome as there seems to be a sort of diagnostic haziness between CD and IBS. It is to be noted that both IBS and coeliac disease share a lot of similarities in terms of symptoms; hence, coeliac disease should be included in the differentiation exercise of diagnosing patients. On the whole, IBS symptoms often overlap with coeliac disease.

## 2. Materials and methods

### 2.1. Subjects and methods

In this study that had been conducted from January 2012 to January 2013, a total of 1020 subjects aged 20–60 were involved. Out of that, 482 subjects (staff and students of Riyadh Health Science College) were designated as control cohorts for undetected coeliac disease. Furthermore, another contingent of 498 subjects diagnosed with irritable bowel syndrome (IBS) at Prince Salman Hospital and Al-Iman General Hospital also constituted a segment of the overall initial 1020 subjects. None of the IBS patients was known have CD. We need to note here that 40 students from the control group had withdrawn from the control cohort, thus leaving us to carry out the study validly on 980 subjects. All respondents answered sets of questionnaires and underwent diagnosis conducted by a physician in accordance with Manning et al. (1978) and Rome III diagnosis criteria (Longstreth et al., 2006). The diagnosis questionnaire included GIT symptoms such as diarrhoea, vomiting, constipation, dyspepsia, abdominal pain or discomfort and indigestion related to food and lactose intolerance. Other data about family and subjects' history included; diabetes mellitus, abdominal operation, anaemia, osteoporosis, autoimmune diseases and even thyroid disorders. In addition to the anthropometric measurements, all students and staff that participated were given a leaflet explaining the purpose of the research, a written consent was signed by each participant and stating that all the names and personal data would be decoded and participation was voluntary. All participants had the right to withdraw at any stage during the study. This study was approved by ethics committee of research of college of health sciences.

### 2.2. Blood measurements and histopathology evaluation

10 ml of venous blood sample was drawn in vacutainer tubes (Rapid Serum Tubes) without anticoagulant, with 10 min clotting time at room temperature. The blood samples collected were centrifuged at 4000×*g* at 4 °C for 10 min, and then stored at −30 °C in aliquots of 300 µl for the analysis of the immunoglobulin A antibodies against human tissue transglutaminase (tTG). On the whole, serum samples were proved positive for IgA antibodies against human tTG by visual CD-LIA (Imtec-ceoliec disease-LIA, Germany). All Samples testing positive were measured for EMA known as anti-tTG antibody against transglutaminase. These were done using a commercially available enzyme-linked immunosorbent assay (ELISA; Euroimmun, Germany) kit. The anti-tissue transglutaminase IgA ELISA test is an Indirect-solid phase enzyme Assay for the quantitative measurement of IgA antibodies to transglutaminase in serum. Autoimmune ELISA kits were used for diagnostic laboratory procedures carried out according to the manufacturers' instruction for all positive samples.

Biopsy specimens from the second part of the duodenum were taken from all subjects who proved positive for EMA against transglutaminase and antigliadin antibodies (AGA). The procedure includes the following; biopsy specimens were fixed in formalin, embedded in paraffin, sectioned then treated with haematoxylin–eosin stain in accordance with Marsh criteria.

## 3. Results

A total of 980 patients were screened, of which 55 patients were found to be positive for coeliac disease, 32 were females and 23 males; age ranged between 20 years and 59 years. Among the 482 individuals included in the control group, nine patients were detected with coeliac disease (1.9%) while in the

498 cases diagnosed with irritable bowel syndrome, 48 patients were detected with coeliac disease having a 5-fold difference.

From Table 1, it is clear that a higher proportion of coeliac disease was found among females in the middle age group of 20–39 years. 38% of all detected with coeliac disease in the same age group were females compared to 16% of males. In the age group of 40–59 years, the prevalence of coeliac disease was found higher among males, – 25% compared to 20% among females.

Serological markers of coeliac disease (tTGAs and EMA) were tested in all 55 cases and controls in the laboratory at the King Fahd Medical City Laboratory, followed by confirmation of diagnosis by a pathologist. 93% of cases were positive for both tTGAs and EMA, 4.7% of cases were found to be positive for tTGAs and negative for the EMAs and 2.4% of cases found to be positive for the EMAs and negative for tTGAs. Consequently, all the 55 cases tested for histological diagnosis proved the presence of coeliac disease in all the 55 patients.

The most credible and standard diagnosis of coeliac disease can be traced to the histopathology description of the disease. Accordingly, the main pathology of coeliac disease involves negative serological anti-bodies of the disease, villous atrophy and crypt hyperplasia with cell infiltration in the small bowel.

Of the 55 cases diagnosed in the course of this study, the repercussions of undetected or latent coeliac disease were calculated thus: Underweight patients constituted 72.7%; those detected with iron deficiency anaemia were 34.5% of the 55 cases, those with vitamin D insufficiency had reached 67.3%. Also, osteoporosis and dermatitis carriers in the group were 61.8% and 7.3%, respectively (Table 2, Fig. 1).

**Table 2** Diseases detected in 55 patients with coeliac disease.

| Disease detected | Number of patients | |
|---|---|---|
| | Positive | Negative |
| Underweight | 40 | 15 |
| Iron deficiency anaemia | 19 | 36 |
| Vitamin D. deficiency | 37 | 18 |
| Osteoporosis | 34 | 21 |
| Dermatitis | 4 | 51 |

## 4. Discussion

The study in essence, gives an approximation of the preponderance of serological markers coupled with biopsy-authenticated coeliac disease with respect to a person carrying irritable bowel syndrome, (IBS). In the same vein, the study clearly delineates the prevalence of coeliac disease in adults that have not been detected despite the fact that there are limited data on coeliac disease in Saudi Arabia. The dominance of positive serological results with biopsy-proven coeliac disease was 1.9% in the control undetected group, while the same procedure for the irritable bowel syndrome (IBS) patients with coeliac disease was 9.6%. We need to note here that the current results are in virtual agreement with our previous study (Al-Ajlan, 2013).

In many countries of western hemisphere, it is estimated that about 1% of the populace are indeed carrying coeliac disease and studies have shown that in the west, the upsurge grows correspondingly with the ageing of the population (Mustalahti et al., 2010). In Scotland, according to recent studies, the incidence of paediatric coeliac disease increased 6.4-fold over 20 years (White et al., 2013). Furthermore, in Finland, according to one report, the incidence of coeliac disease was 1.5% among children (Mäki et al., 2003), 2% in adults and 2.7% in the elderly (Vilppula et al., 2009). In the United States, the prevalence among the populace is about 1% (Alberto et al., 2012). As a result of the serological studies carried out in Australasia, Europe and South America, between 0.5 and 1% of the people in these countries carry the disease undetected (West et al., 2003; Fasano et al., 2003). The implications of identifying latent coeliac disease among the populace are not clear as there is a paucity of reported data arising from few selected cases as regards death and other psychological features earlier noticed in the latent coeliac disease.

Furthermore, only few research studies have succeeded in analyzing the welter of socio-demographic underpinnings with respect to the disease largely due to low size of the available sample. Among adults of the general populace, screenings have captured only a few number of hitherto undiagnosed cases. As a result, such studies are unable to clearly examine any linkage in comparison to the people in general (Mustalahti et al., 1999). In fact, the density of bone mineral and anthropometric measurement have been the main focal points of the earlier studies that seek to know the differences between clinically diagnosed coeliac disease and the undetected ones. Such studies delineate that people with latent coeliac disease tend to have insignificant levels of low bone density and measurements in line with harmless subnormal nutritional level (Scott et al., 2000). A study carried out on a cohort in Cambridge, UK, indicates that negative health effect such as mild anaemia arises from latent coeliac disease and osteoporosis. Interestingly, the study implicitly shows a diminished danger of cardiovascular ailment going by the observation of lower blood pressure, mass body index and lower serum cholesterol among persons carrying the latent coeliac disease. Of course, given the potent consequences of these results, there is a need to undertake an epidemiological assessment to ascertain it.

The current study is basically aimed at ascertaining the dominance of coeliac disease among the patients that meet the conditions of the Rome111 yardstick for irritable bowel syndrome (IBS) and who were referred to gastroenterology unit of the Al-Iman General Hospital, Riyadh, within the gamut of last three years. There is a prevalence of irritable bowel syndrome of 15–25% among the global population. On the other hand, the prevalence of coeliac disease is put at 0.5–1% (12, 29). It is to be noted that both IBS and coeliac

**Table 1** Distribution of age and sex ranges in the 55 patients found to be positive for coeliac disease among 980 individuals.

| No. of male patients with coeliac disease | No. of female patients with coeliac disease | Age range |
|---|---|---|
| 5 | 12 | 20–29 |
| 4 | 9 | 30–39 |
| 7 | 7 | 40–49 |
| 7 | 4 | 50–59 |

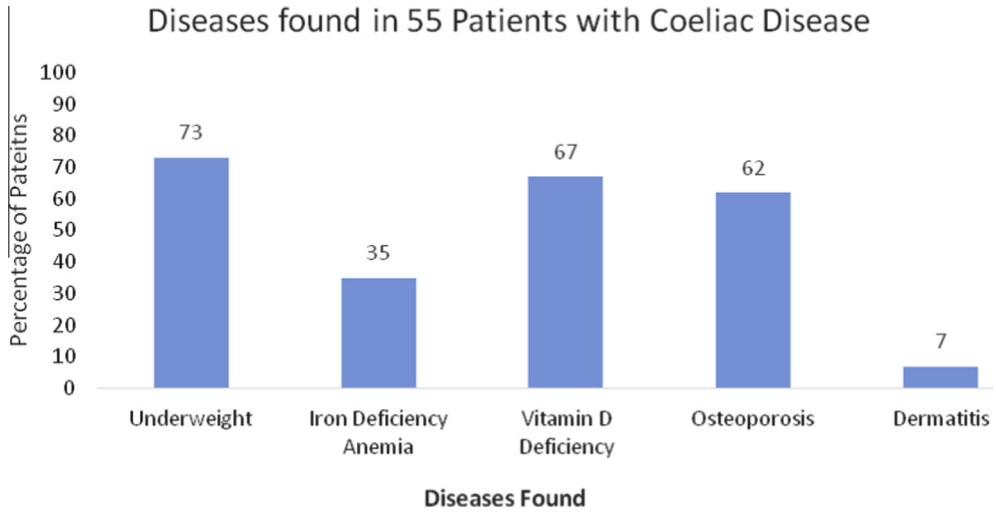


**Figure 1** Showing repercussions of undetected or latent coeliac disease.

disease share a lot of similarities in terms of symptoms. As they have virtually similar symptoms, there is a risk that patients with coeliac disease could be wrongly diagnosed of irritable bowel syndrome. This apparent risk could be so hazardous in two irritable bowel syndrome variants such as irritable bowel syndrome – diarrhoea and irritable bowel syndrome-mixed. Another potential danger in this situation is that in both diseases, patients are jolted by taking wheat products. For coeliac disease, the trigger is due to gluten allergy, while in the case of irritable bowel syndrome, the effect can emanate from long sugar polymer fructose found in the wheat (Heizer et al., 2009).

This study has shown that there are far-reaching consequences for undiagnosed coeliac diseases such as underweight, osteoporosis, insufficiency of iron and vitamin D. Indeed, the overriding factors in support of this study can be itemized thus: A-The study participants (both the control and those with cases of irritable bowel syndrome) were randomly selected. B-The control and those with cases of IBS tend to be positive of coeliac disease by testing for both EMAs and tTGAs antibodies and proven by histological diagnosis. C-The Canadian Association of Laboratory Medicine has certified the laboratory used for the analysis of serological antibodies of coeliac disease. This study has used subjects from a wide age range and gender. However, there are certain limitations to the study which cannot be ignored. These are: A-The array of controls and registered cases were not extensive. There was insufficiency of tests regarding allergic and food history in the patient's notes and detailed documentation of family.

## 5. Recommendations

To preclude the problem of over-diagnosis of IBS or misdiagnosis of coeliac disease, all patients with IBS should be handled by an experienced gastroenterology consultant as per the criteria stipulated in Rome111 Classification. Since it has been observed that the symptoms of coeliac disease and IBS tend to overlap, it would be highly beneficial to carry out serological tests for coeliac disease for a person who has IBS symptoms. This could be useful as specific and sensitive test for diagnosis of coeliac disease. It is clinically valid to adopt the position of British Society of Gastroenterology that patients with IBS should, as a matter of urgency, perform full blood count test plus erythrocyte sedimentation rate and C-reactive protein, coupled with thyroid function (Spiller et al., 2007). Given the paucity of research in the area of coeliac disease and IBS in Saudi Arabia, it will be relevant to undertake further research and epidemiological studies with substantial number of cases. By doing that, the above results could be solidified, thus validated.

## Acknowledgements

The author wishes to thank all the academic staff and students of Riyadh College of Health Sciences who participated in this study. Furthermore, I wish to extend my gratitude and best wishes to the patients who actively participated in our study. I would also desire to register my immense gratitude to the laboratory technicians and the pathologist Dr. Isam Elshiekh Altahir, and of course, my special thanks go to specialist Mr. Moncef M. Gharsallah for his untiring efforts.

## References

Al-Ajlan, A., 2013. Prevalence and implications of coeliac disease in undetected adults compared to those diagnosed with irritable bowel syndrome (IBS) in Riyadh, Saudi Arabia. HealthMed 7 (12), 3097–3098.

Alberto, R.T., Jonas, F.L., Tricia, L.B., Joseph, A.M., James, E.E., 2012. The prevalence of celiac disease in the United States. Am. J. Gastroenterol. 107, 1538–1544.

Boivin, M., 2001. Socioeconomic impact of irritable bowel syndrome in Canada. Can. J. Gastroenterol. 15, 8–11.

Chakravarty, K., Scott, D.G., 1992. Oligoarthritis—a presenting feature of occult coeliac disease. Br. J. Rheumatol. 31, 349–350.

El-Salhy, M., Gundersen, D., Hatlebakk, J.G., Hausken, T., 2012. Irritable Bowel Syndrome. Nova scientific Publisher, New York.

Fasano, A., Berti, I., Gerarduzzi, T., Not, T., Colletti, R.B., Drago, S., Elitsur, Y., Green, P.H., Guandalini, S., Hill, I.D., Pietzak, M., Ventura, A., Thorpe, M., Kryszak, D., Fornaroli, F., Wasserman, S.S., Murray, J.A., Horvath, K., 2003. Prevalence of celiac disease in at-risk and not at-risk groups in the United States: a large multicenter study. Arch. Intern. Med. 163 (3), 286–292.

Ford, A.C., Forman, D., Bailey, A.G., Axon, A.T.R., Moayyedi, P., 2008. Irritable bowel syndrome: a 10-year natural history of symptoms, and factors that influence consultation behavior. Am. J. Gastroenterol. 103 (5), 1229–1239.

Green, P.H., Cellier, C., 2007. Celiac disease. N. Engl. J. Med. 357, 1731–1743.

Green, P.H.R., Stavropoulos, S.N., Panagi, S.G., Goldstein, S.L., Mcmahon, D.J., Absan, H., Neugut, A.I., 2001. Characteristics of adult celiac disease in the USA: results of a national survey. Am. J. Gastroenterol. 96, 126–131.

Heizer, W.D., Southern, S., McGovern, S., 2009. The role of diet in symptoms of irritable bowel syndrome in adults: a narrative review. J. Am. Diet. Assoc. 109, 1204–1214.

Kolho, K.L., Farkkila, M.A., Savilahti, E., 1998. Undiagnosed coeliac disease is common in Finnish adults. Scand. J. Gastroenterol. 33, 1280–1283.

Lohi, S., Mustalahti, K., Kaukinen, K., Laurila, K., Collin, P., Rissanen, H., 2007. Increasing prevalence of coeliac disease over time. Aliment. Pharmacol. Ther. 26, 1217–1225.

Longstreth, G.F., Thompson, W.G., Chey, W.D., Houghton, L.A., Mearin, F., Spiller, R.C., 2006. Functional bowel disorders. Gastroenterology 130 (5), 1480–1491.

Ludvigsson, J.F., Montgomery, S.M., Ekbom, A., 2005. Celiac disease and risk of adverse fetal outcome: a population-based cohort study. Gastroenterology 129, 454–463.

Mäki, M., Mustalahti, K., Kokkonen, J., Kulmala, P., Haapalahti, M., Karttunen, T., Ilonen, J., Laurila, K., Dahlbom, I., Hansson, T., Höpfl, P., Knip, M., 2003. Prevalence of celiac disease among children in Finland. N. Engl. J. Med. 348, 2517–2524.

Manning, A.P., Thompson, W.G., Heaton, K.W., Morris, A.F., 1978. Towards positive diagnosis of the irritable bowel. BMJ 277, 653–654.

Marsh, M.N., 1992. Gluten, major histocompatibility complex, and the small intestine. A molecular and immunobiologic approach to the spectrum of gluten sensitivity ('celiac sprue'). Gastroenterology 102, 330–354.

Mustalahti, K., Collin, P., Sievanen, H., et al, 1999. Osteopenia in patients with clinically silent coeliac disease warrants screening. Lancet 354, 744–745.

Mustalahti, k., Catassi, C., Reunanen, A., 2010. The reverence of celiac disease in Europe: results of a centralized, international mass screening project. Ann. Med. 42, 587–595.

Sanders, D.S., Hurlston, D.P., 2002. Changing face of adult coeliac disease: experience of a single university hospital in south Yorkshire. Postgrad. Med. J. 78, 31–33.

Sanders, D.S., Patel, D., Stephenson, T.J., Ward, A.M., McCloskey, E.V., Hadjivassiliou, M., Lobo, A.J., 2003. A primary care cross-sectional study of undiagnosed coeliac disease. Eur. J. Gastroenterol. Hepatol. 15, 407–413.

Scott, E.M., Gaywood, I., Scott, B.B., 2000. Guidelines for osteoporosis in coeliac disease and inflammatory bowel disease. British Society of Gastroenterology. Gut 46 (Suppl. 1), 1–8.

Sperber, A.D., Shvartzman, P., Friger, M., Fich, A., 2005. Unexpectedly low prevalence rates of IBS among adult Israeli Jews. Neurogastroenterol. Motil. 17 (2), 207–211.

Spiegel, B.M., 2009. The burden of IBS: looking at metrics. Curr. Gastroenterol. Rep. 11, 265–269.

Spiller, R., Aziz, Q., Creed, F., Emmanuel, A., Houghton, L., Hungin, P., Jones, R., Kumar, D., Rubin, G., Trudgill, N., Whorwell, P., 2007. Guidelines on the irritable bowel syndrome: mechanisms and practical management. Gut 56, 1770–1798.

Thompson, W.G., Longstreth, G.F., Drossman, D.A., Heaton, K.W., Irvine, E.J., Müller-Lissner, S.A., 1999. Functional bowel disorders and functional abdominal. Gut 45, II43–II47.

Vilppula, A., Kaukinen, K., Luostarinen, L., Krekelä, I., Patrikainen, H., Valve, R., Mäki, M., Collin, Pet., 2009. Increasing prevalence and high incidence of celiac disease in elderly people: a population-based study. BMC Gastroenterol. 9, 49.

West, J., Logan, R.F., Hill, P.G., Lloyd, A., Lewis, S., Hubbard, R., Reader, R., Holmes, G.K.T., Khaw, K.-T., 2003. Seroprevalence, correlates, and characteristics of undetected coeliac disease in England. Gut 52, 960–965.

White, L.E., Merrick, V.M., Bannerman, E., Russell, R.K., Basude, D., Henderson, P., Wilson, D.C., Gillett, P.M., 2013. The rising incidence of celiac disease in Scotland. Pediatrics 2013, 0932.

Zipser, R.D., Patel, S., Yahya, K.Z., Baisch, D., Monarch, E., 2003. Presentations of adult celiac disease in a nationwide patient support group. Dig. Dis. Sci. 48, 761–764.