Review paper
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EFFECTS ON HEALTH AND DIET QUALITY OF THE GLUTEN FREE DIET

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Abstract

Gluten is the glutenin-gliadin protein complex presenting in wheat, barley, rye and oat. Bread, cakes, pasta, some sauces, salad dressings, even toothpastes and cosmetic products include gluten. Gluten should be removed from the diet in the treatment of gluten-related diseases, such as celiac disease, non-celiac gluten sensitivity, and gluten ataxia. Treatment of the gluten-related diseases with the gluten-free diet has positive effects because it normalizes mucosal histology and relieves the clinical symptoms. While removing gluten from diet is associated with clinical and histological improvements, poor adherence to gluten-free diet is associated with lower quality of life and higher risk of celiac-related symptoms and complications.

The gluten free diet is thought to be beneficial for the other health problems too such as: dermatitis herpetiformis, schizophrenia and other mental disorders, atopy, fibromyalgia, endometriosis. The gluten-casein-free diet can be beneficial for autism spectrum disorder in some studies, but there is no conclusive evidence. The gluten-free diet is also applied by people without gluten-related disease and it has been popular recently. The people who avoiding gluten without gluten-related disease have applied to gluten-free diet for the following reasons: having a perceived gluten sensitivity, the healthy option idea, being interested in gluten-free products as a lifestyle. In long term, the gluten-free diet in healthy people may cause the vitamin-mineral deficiency, insufficient dietary fiber intake, constipation, reduction in quality of life. Additionally, the advantages and disadvantages of gluten-free products in terms of nutritional values compared to their gluten-containing counterparts are not clear.

As a result, the gluten-free diet is indicated only for determined medical conditions, this diet is not suitable for healthy populations. The interest in gluten-free diet necessitates the studies of about acute and chronic effects of gluten-free diet in healthy individuals.

***Key words**: Gluten-free diet, Gluten-related diseases, Effects of gluten-free diet.*

1. Introduction

Gluten is a protein complex which consist of glutenin and gliadin existing in wheat, barley, oats, rye (Guandalini and Polanco, [1]). Gluten proteins play an important role in determining the quality of baking by providing water absorption capacity, viscosity, cohesivity and elasticity properties of the dough (Dizlek, [2], Wieser, [3]). Several products such as bread, pasta, cakes, salad dressings, some sauces, and even toothpastes and cosmetic products involve gluten (Worosz and Wilson, [4]).

Celiac disease, an autoimmune enteropathy activated by gluten exposure in genetically predisposed individuals, is a lifetime intolerance to the gliadin fraction of wheat and the prolamins of barley (hordeins), rye (secalins) and possibly oats (avidins) (Garnier-Lengline *et al.,* [5], Gallagher *et al.,* [6]). The prolamins are gluten components responsible for immune-mediated response. The gliadins are a group of glutamine and proline rich proteins resistant to digestion in the gastrointestinal tract (Guandalini and Polanco, [1]).

Gluten should be removed from the diet in the treatment of gluten-related diseases, such as celiac disease, non-celiac gluten sensitivity, and gluten ataxia. Treatment of the gluten-related diseases with the gluten-free diet has positive effects because it normalizes mucosal histology and relieves the clinical symptoms (Foschia *et al.,* [7]). While removing gluten from diet is associated with clinical and histological improvements, poor adherence to gluten-free diet is associated with lower quality of life and higher risk of celiac-related symptoms and complications (Vivas *et al.,* [8]).

The gluten-free diet is being applied except from individuals with gluten-related disease, too and has gained popularity recently. The different consumer types such as consumers who state that they are interested in gluten-free products as a lifestyle without diagnosis of celiac disease and individuals with perceived gluten sensitivity (individuals who claim to have gluten sensitivity or celiac disease) consume gluten-free products (Worosz and Wilson, [4]). The long-term effects of gluten-free diet in individuals without celiac disease have not been investigated yet. Besides, there are some concerns for gluten-free diet. For instance, some nutrients including iron, calcium and dietary fiber may be inadequate in gluten-free diet (Choung *et al.,* [9], Saturni *et al.,* [10], and Thompson *et al.,* [11]). Additionally, it is stated that children with celiac disease who treatment with gluten-free diet consume more amounts of fat than healthy children (Ferrara *et al.,* [12]). Many gluten-free products have higher amounts of fat, saturated fat, salt, and lower amounts of vitamins and minerals than their gluten-containing equivalents (Pellegrini and Agostoni, [13]). In addition, it is observed that the commercial gluten-free products are more expensive than their gluten containing equivalents (Oyarzun *et al.,* [14]).

The aim of this review is to provide information about gluten free diet effects on general health and diet quality as well as effects on the gluten-related diseases.

2. What is the gluten-free diet?

Gluten free diet which is the treatment of celiac disease, was discovered in 1940s by the Dutch pediatrician Willem-Karel Dicke (Gobbetti *et al.,* [15], Mearin *et al.,* [16]).

In gluten free diet, wheat, rye, barley and all derivatives of these grains should be removed from the meal plan (Green *et al.*, [17], Leivers *et al.*, [18]). The consumption of oats in gluten-free diet is controversial due to the risk of contamination with wheat, barley or rye during the milling process. Therefore, it may safe to consume only non-contaminated oats in gluten-free diet (Leivers *et al.*, [18]). Rice, corn, buckwheat, millet, and quinoa can be consumed in gluten-free diet (Green *et al.*, [17]).

The non-contain gluten pseudo-cereals such as amaranth, buckwheat and quinoa are important for nutritionally quality of the gluten-free diet. These gluten-free grains include the high-quality protein, high amounts of dietary fiber, the minerals such as calcium and iron. These grains are also the source of many bioactive compounds having beneficial effects on health such as polyphenols, phytosterols, saponins and squalene (Alvarez-Jubete *et al.*, [19]). In a study that analyzed the content of mineral (calcium, sodium, magnesium, potassium, copper, manganese, zinc, iron) of the 50 gluten-free products was observed that the gluten-free products obtained from buckwheat, millet, chickpeas, oats, teff, amaranth and quinoa were have higher mineral contents than the gluten-free products obtained from the most popular raw materials such as rice, potato, corn and gluten-free wheat starch (Rybicka and Gliszczynska-Swiglo, [20]). The adding of the rich of nutritional value grains such as amaranth, quinoa, and buckwheat in gluten free diet will be beneficial for health.

The commercial gluten-free products are available in the market. Immunological analyses provide information on the gluten content of foods and, according to the law, all foods must be clearly labeled (Woodward, [21]). According to Turkish Food Codex the "gluten free" phrase can be used on condition that the gluten level in the food to be presented to the consumer does not exceed 20 mg/kg (Ministry of Food, Agriculture and Livestock, [22]). According to the European Directive from January 2012, a food can be labeled "gluten free" if it contains less than 20 ppm of gluten (Woodward, [21]). Although the tolerable gluten level varies individually, it is important to exclude all dietary gluten in the meal plan (Akobeng and Thomas [23], Woodward [21]). Patients with celiac disease should cooperate with the dietician/nutritionist in choosing the appropriate foods.

Gluten free diet requires essential and life-long changes of the daily habits. This diet may be troublesome, expensive and socially restrictive. These situations may cause difficulties for adherence to gluten free diet and may affect the quality of life of the patients. Global care objectives for patients with celiac disease should focus on improving physical symptoms and minimizing the psychosocial effects of the disease (Herrera de Guise and Casellas, [24]).

2.1 What are the areas of the usage gluten free diet?

Gluten is enriched from prolines and glutamines, and as a consequence, it is incompletely digested by the pancreatic, gastric and brush border peptidases, leaving large peptides up to a length of 33 amino acids. These peptides get in the lamina propria of the small intestine through paracellular or transcellular pathways. In this area, in affected people, an adaptive immune answer happens due to deamidation of gliadin molecules by the tissue transglutaminase which is the predominant autoantigen of celiac disease. Deamidation enhances the immunogenicity of gliadin, facilitating binding to human leukocyte antigen -DQ2 or -DQ8 molecules on antigen presenting cells. Gliadin peptides are after presented to gliadin reactive CD4+ T cells. In this period, antibodies against the tissue transglutaminase, gliadin are made via uncertain mechanisms. These antibodies might promote to extra-intestinal impressions of celiac disease, like gluten ataxia and dermatitis herpetiformis (Kupfer and Jabri, [25], Lebwohl *et al.*, [26], and Schumann *et al.*, [27]).

Gluten-free diet should be practised in the treatment of gluten-related diseases, such as celiac disease, gluten ataxia, non-celiac gluten sensitivity and dermatitis herpetiformis.

The celiac disease is a systemic, lasting lifelong, immune-mediated disease that causes inflammation in the small intestines activate by the consumption of gluten (Foschia *et al.*, [7], Krigel and Lebwohl [28]). Environmental and genetic factors play role in the pathogenesis of celiac disease (Leivers *et al.*, [18]). The genetic factors in celiac disease are human leukocyte antigen -DQ2 and -DQ8 haplotypes; positive human leukocyte antigen -DQ2 and/or -DQ8 may lead to destruction of villous structure in small intestine (Foschia *et al.*, [7], Leivers *et al.,* [18], and Schumann *et al.,* [27]). The environmental factors in celiac disease are lack of breastfeeding, inappropriate timing of complementary feeding, cesarean delivery, gastrointestinal infections, using of antibiotics (Lebwohl *et al.,* [26], Leivers *et al.,* [18]).

Non-celiac gluten sensitivity is a clinical phenotype of individuals experiencing intestinal and non-intestinal symptoms by consuming gluten-containing foods after a diagnosis of celiac disease or wheat allergy is excluded. The differences of non-celiac gluten sensitivity from celiac disease; genetic and serological markers are not known and duodenal villus atrophy is not seen (Krigel and Lebwohl, [28]).

Gluten ataxia is defined as idiopathic sporadic ataxia with positive serological markers for gluten sensitivity. It is an autoimmune disease characterized by cerebellum damage that results in ataxia (Sapone *et al.,* [29]).

Dermatitis herpetiformis is a skin disease of gluten sensitivity, presenting with blistering rash and pathognomonic cutaneous IgA deposits (Sapone *et al.,* [29]). This disease is characterized with urticarial plaques, blisters on elbows, buttocks and knees, and it may also affect other areas of the body (Foschia *et al.,* [7]).

The medical nutrition therapy is gluten-free diet for the gluten-related diseases such as celiac disease, non-celiac gluten sensitivity, dermatitis herpetiformis and gluten ataxia (Pietzak, [30]). The treatment of celiac disease and dermatitis herpetiformis with gluten-free diet provides improvement in malabsorption, nutritional deficiencies, symptoms and supplies to decrease in comorbidities. The gluten-free diet is also beneficial to reduce symptoms of non-celiac gluten sensitivity and wheat allergy (Reilly, [31]).

Except for gluten-related diseases, gluten-free diet may be helpful in cases of schizophrenia and other mental disorders, atopy, fibromyalgia, endometriosis (Niland and Cash, [32]). Although some studies have shown benefits of the gluten-casein-free diet in the autism spectrum disorder, there is no conclusive evidence for its application (Mari-Bauset *et al.,* [33]).

2.2 What are the possible effects of gluten-free diet on health?

Adherence to gluten-free diet, the best standard in the treatment of celiac disease, plays an important role in alleviation of clinical symptoms, prevention of long-term celiac disease-related complications, improvement of nutritional status and quality of life (Bascuñán *et al.,* [34]).

The gluten-free diet is also applied by people without gluten-related disease and it has been popular recently. In United States of America, the National Health and Nutrition Examination Survey (NHANES) 2009 - 2014 data, it was showed that although there was no diagnosis of celiac disease, frequency of individuals avoiding from gluten increased more than three-fold (Choung *et al.,* [9]).

Potential risks of gluten-free diet are: constipation, undesired weight gain, missed diagnosis of celiac disease, nutrient deficits, quality of life impairment, and potential for toxicity (Reilly, [31]).

The possible negative health effects of gluten-free diet include hyperglycemia and increased risk of coronary artery disease (Niland and Cash, [32]).

In a double-blind, randomized, cross-over design study conducted with healthy adults was found that gluten-free pasta obtained from rice and corn flour was increased postprandial glycemia compared to conventional wheat pasta (Johnston *et al.,* [35]). In a significant percentage of overweight/obese individuals with celiac disease, body weight may increase with gluten-free diet. The reason for this situation is that nutrient absorption may be increased by the improving of the intestinal surface with a gluten-free diet. It should be determined whether weight gain may be observed with gluten-free diet in individuals without gluten sensitivity or celiac disease. The fact that a food has a gluten-free label does not mean that it does not contain energy. So, when consuming gluten-free products, energy contents should be considered. In addition, gluten free diet may be associated with weight gain because it is poor in whole grains and dietary fiber (Gaesser and Angadi, [36]).

Gluten-free diet has caused weight gain in underweight patients with celiac disease (has improved body mass index) and has also supplied weight loss in overweight/obese patients with celiac disease (Cheng *et al.,* [37]). Published report showing that gluten-free diet is provided weight loss in individuals without gluten sensitivity or celiac disease has not been found (Gaesser and Angadi, [36]). In this context, it has been suggested that the effects of gluten free diet on body weight in healthy individuals should be evaluated in the long term. In the prospective, long-term, cohort study of individuals without celiac disease, no relationship was found between dietary gluten intake and risk of coronary heart disease. However, it should be taken into consideration that due to reducing the consumption of beneficial whole grains, the avoidance of gluten may affect cardiovascular risk (Lebwohl *et al.,* [38]). For these reasons, gluten-free diet is not recommended except for gluten-related diseases.

Besides, not consuming sufficient diversity of gluten-free products are considered to be risk for toxins. This is due to the fact that rice, which may be effective in the consummation of inorganic arsenic, commonly exists in gluten-free processed products (Reilly, [31]).

2.3 What are the possible effects of gluten-free diet on diet quality?

The nutritional status of celiac patients in the diagnosis depends on the length of the active period of the disease, the degree of intestinal inflammation, the degree of malabsorption and the dietary intake of the patients. The commonly seen nutritional deficiencies of the patients at the time of diagnosis celiac involve the deficiencies of iron, calcium, zinc, vitamin B12 and folate. After diagnosis of celiac disease, to adherence gluten-free diet has reduced the symptoms, serum antibodies have been become normal level and has been improved the intestinal mucosa. Therefore, nutritional status of patients with celiac disease applying gluten-free diet is influenced by nutrient quality of gluten-free products and nutritional preferences of the patients (Melini and Melini, [39]).

The negative effects of gluten-free diet in terms of diet quality are inadequate intake of micronutrients and dietary fiber, increased consumption of the foods which have high fat content (Niland and Cash, [32]). Outcomes of gluten-free diet consumption are to decrease in intake of complex carbohydrates, dietary fiber, vitamins and minerals and to increase in fat intake (Rosell and Matos, [40]). In a study that investigated of the packaged food labels was observed that the gluten-free products had higher fat and carbohydrate contents and had lower protein content than gluten-containing products (Kulai and Rashid, [41]). In another study was found that the amounts of thiamine, riboflavin, niacin, folate and iron of gluten-free products were lower than gluten-containing products (Thompson [42, 43]).

Unbalanced dietary intake of individuals with celiac disease in terms of both macro- and micronutrients is concerned. Unbalanced nutrient intake by increased protein and fat ingestion and by decreased carbohydrate consumption is seen in individuals with celiac disease (Mariani *et al.,* [44]). In a case-control study evaluating nutritional habits by non-consecutive 3 day-food intake record of celiac and healthy individuals was found that the celiac individuals had higher consumption of added sugar and total fat compared to the control group. Furthermore, it was observed that the celiac individuals consumed protein-rich foods such as meat, fish, eggs higher and consumed starch-rich foods lower (Babio *et al.,* [45]). In Turkey, in a study was found that the individuals with celiac disease consumed lower energy, protein and higher fat compared to healthy control individuals (Balamtekin *et al.,* [46]). Additionally, the patients with celiac disease have consumed lower amounts of minerals such as calcium, iron, magnesium, zinc and they have also consumed lower amounts of vitamins such as vitamin E, folic acid, thiamine compared to the healthy individuals (Babio *et al.,* [45], Balamtekin *et al.,* [46]).

There is concern about commercial or natural gluten-free foods are unbalanced in terms of nutrients and have hypercaloric content (Pellegrini and Agostoni, [13]). In United Kingdom, in a study were classified gluten-free and gluten-containing foods according to their fat, saturated fatty acids, sugar and salt content using the food labels. As a result, although not consistent, it was stated that more gluten-free foods were classified as containing high and medium fat, saturated fatty acids, salt and sugar compared to the gluten-containing foods (Fry *et al.,* [47]). In Canada, when examining gluten-free products and gluten-containing products which targeting children consumers, it was found that generally the gluten-free products had lower levels of sodium, protein, total fat and saturated fat contents. However, it was also found that the percentage of energy from sugar was similar between the gluten-free products and the gluten-containing products (Elliott, [48]). In Italy, in a study was observed that the gluten-free products were lower protein content compared to gluten-containing products in all food groups, and there was no difference in the content of total fat between the products according to status of including gluten. It was also found that the amount of saturated fat in the gluten-free biscuit and pasta groups was higher. In the same study was stated that the total energy content was lower in the gluten-free bread group and higher in the gluten-free pasta group. Moreover, it was found that salt content was higher in gluten-free pasta and rusks and lower in gluten-free biscuits (Cornicelli *et al.,* [49]). These results have shown that nutrient content of gluten-free products and gluten-containing products may vary according to food groups and countries.

For a patient with celiac, whether or not a food contains gluten may be more important than nutritional quality of food. However, the importance of nutritional quality should also be kept in mind. Dietitians should consider the dietary quality when examining the adherence to gluten-free diet of patients with celiac disease. Evaluation of consumption of vegetables and fruits, protein intake, addition of gluten-free grains to the diet, attention to intake of sugar and fat will be beneficial for improving the dietary quality of people with celiac disease.

In addition to these, gluten-free diet has also negative socio-economic impacts such as increased economic costs and social difficulties (Niland and Cash, [32]). For instance, Arias-Gastelum *et al.,* [50], found that gluten-free products were more expensive than gluten-containing products.

3. Conclusions

- Even though gluten-free diet is safe and effective, it is indicated only for specific medical conditions, it is not appropriate in the general population.

- There is a need for comprehensive long-term studies on the effects of gluten-free diet on healthy individuals.

4. References

[1] Guandalini S., and Polanco I. (2015). *Nonceliac gluten sensitivity or wheat intolerance syndrome?* J. Pediatr. 166, (4), pp. 805-811.

[2] Dizlek H. (2011). *The Formation of Gluten and Its Limiting-Preventing Factors*. Electronic Journal of Food Technologies, 6, (2), pp. 14-22.

[3] Wieser H. (2007). *Chemistry of gluten proteins*. Food Microbiol., 24, (2), pp. 115-119.

[4] Worosz M. R., and Wilson N. L. (2012). *A Cautionary Tale of Purity, Labeling and Product Literacy in the Gluten-Free Market*. Journal of Consumer Affairs, 46, pp. 288-318.

[5] Garnier-Lengline H., Cerf-Bensussan N., and Ruemmele F. M. (2015). *Celiac disease in children*. Clin. Res. Hepatol. Gastroenterol., 39, (5), pp. 544-551.

[6] Gallaghera E., Gormley T. R., and Arendt E. K. (2004). *Recent advances in the formulation of gluten-free cereal-based products.* Trends in Food Science and Technology 15, (3-4), pp. 143-152.

[7] Foschia M., Horstmann S., Arendt E. K., and Zannini E. (2016*). Nutritional therapy - Facing the gap between coeliac disease and gluten-free food*. Int. J. Food Microbiol., 239, pp. 113-124.

[8] Vivas, S., Arias, L., and Vaquero, L. (2015). *Follow-Up of CD Patient: Is Mucosal Recovery a Goal of Therapy?* In: Arranz E., Fernández-Bañares F., Rosell C. M., Rodrigo L. and Peña A. S. (Eds.), Advances in the Understanding of Gluten Related Pathology and the Evolution of Gluten-Free Foods, OmniaScience, pp. 409-423.

[9] Choung R. S., Unalp-Arida A., Ruhl C. E., Brantner T. L., Everhart J. E., and Murray J. A. (2017). *Less Hidden Celiac Disease but Increased Gluten Avoidance Without a Diagnosis in the United States: Findings from the National Health and Nutrition Examination Surveys From 2009 to 2014.* Mayo Clinic Proceedings, 92, (1), pp. 30-38.

[10] Saturni L., Ferretti G., and Bacchetti T. (2010). *The Gluten-Free Diet: Safety and Nutritional Quality*. Nutrients, 2, (1), pp. 16-34.

[11] Thompson T., Dennis M., Higgins L. A., Lee A. R., and Sharrett M. K. (2005). *Gluten-free diet survey: are Americans with coeliac disease consuming recommended amounts of fibre, iron, calcium and grain foods?* J Hum. Nutr. Diet, 18, (3), pp. 163-169.

[12] Ferrara P., Cicala M., Tiberi E., Spadaccio C., Marcella L., Gatto A., Calzolari P., and Castellucci G. (2009). *High fat consumption in children with celiac disease*. Acta Gastro-Ent. Belg., 72, (3), pp. 296-300.

[13] Pellegrini N., Agostoni C. (2015). *Nutritional aspects of gluten-free products*. J. Sci. Food Agr., 95, (12), pp. 2380-2385.

[14] Oyarzun A., Nakash T., Ayala J., Lucero Y., and Araya M. (2015). *Following Gluten Free Diet: Less Available, Higher Cost and Poor Nutritional Profile of Gluten-Free School Snacks*. International Journal of Celiac Disease, 3, (3), pp. 102-107.

[15] Gobbetti M., Pontonio E., Filannino P., Rizzello C. G., De Angelis M., and Di Cagno R. (2018). *How to improve the gluten-free diet: The state of the art from a food science perspective*. Food Res. Int., 110, pp. 22-32.

[16] Mearin, M. L, Montoro-Huguet, M., Polanco, I., Ribes-Koninckx, C., and Santolaria, S. (2015*). Clinical Manifestations of Celiac Disease and Diagnostic Criteria: Differences Among Children, Adolescents and Adults*. In: Arranz E., Fernández-Bañares F., Rosell C. M., Rodrigo L. and Peña A. S. (Eds.), Advances in the Understanding of Gluten Related Pathology and the Evolution of Gluten-Free Foods, OmniaScience, pp. 291-339.

[17] Green P. H., Lebwohl B., and Greywoode R. (2015). *Celiac disease*. J. Allergy Clin. Immunol., 135, (5), pp. 1099-1106.

[18] Leivers C., Martin G., Gasparetto M., Shelley H., and Valente M. (2014). *Coeliac disease*. Paediatrics and Child Health, 24, (11), pp. 481-484.

[19] Alvarez-Jubete L., Arendt E. K., and Gallagher E. (2010). *Nutritive value of pseudocereals and their increasing use as functional gluten-free ingredients*. Trends Food Sci. Tech., 21, (2), pp. 106-113.

[20] Rybicka I., and Gliszczynska-Swiglo A. (2017). *Minerals in grain gluten-free products. The content of calcium, potassium, magnesium, sodium, copper, iron, manganese, and zinc*. J. Food Compos. Anal., 59, pp. 61-67.

[21] Woodward J. (2015). *Coeliac disease*. Medicine, 43, (4), pp. 234-238.

[22] Ministry of Food, Agriculture and Livestock. (2017). *Turkish Food Codex Food Labeling and Consumers Information Regulation (Number:29960) Appendix-16* (in Turkish). <URL: http://www.resmigazete.gov.tr/eskiler/2017/01/20170126M1-6.htm. Accessed 29 April 2019.

[23] Akobeng A. K., and Thomas A. G. (2008). *Systematic review: Tolerable amount of gluten for people with coeliac disease.* Aliment. Pharmacol. Ther., 27, (11), pp. 1044-1052.

[24] Herrera De Guise C., and Casellas F. (2015). *Quality of Life and Psychological Distress in the Patient with CD*. In: Arranz E., Fernández-Bañares F., Rosell C. M., Rodrigo L. and Peña A. S. (Eds.), Advances in the Understanding of Gluten Related Pathology and the Evolution of Gluten-Free Foods, OmniaScience, pp. 425-440.

[25] Kupfer S. S., and Jabri B. (2012). *Celiac Disease Pathophysiology*. Gastrointestinal Endoscopy Clinics of North America, 22, (4), pp. 639-660.

[26] Lebwohl B., Sanders D. S., and Green P. H. R. (2018). *Coeliac disease*. Lancet, 391, (10115), pp. 70-81.

[27] Schumann M., Siegmund B., Schulzke J. D., and Fromm M. (2017). *Celiac Disease: Role of the Epithelial Barrier.* Cell Mol. Gastroenterol. Hepatol., 3, (2), pp. 150-162.

[28] Krigel A., and Lebwohl B. (2016). *Nonceliac Gluten Sensitivity*. Adv. Nutr., 7, (6), pp. 1105-1110.

[29] Sapone A., Bai J. C., Ciacci C., Dolinsek J., Green P. H., Hadjivassiliou M., Kaukinen K., Rostami K., Sanders D. S., Schumann M., Ullrich R., Villalta D., Volta U., Catassi C., and Fasano A. (2012). *Spectrum of gluten-related disorders: Consensus on new nomenclature and classification*. BMC Med., 10, pp. 13-25.

[30] Pietzak M. (2012). *Celiac disease, wheat allergy, and gluten sensitivity: when gluten free is not a fad*. JPEN, 36, (1 Suppl), pp. 68-75.

[31] Reilly N. R. (2016). *The Gluten-Free Diet: Recognizing Fact, Fiction, and Fad.* J. Pediatr., 175, pp. 206-210.

[32] Niland B., Cash B. D. (2018). *Health Benefits and Adverse Effects of a Gluten-Free Diet in Non-Celiac Disease Patients*. Gastroenterol. Hepatol., 14, (2), pp. 82-91.

[33] Mari-Bauset S., Zazpe I., Mari-Sanchis A., Llopis-Gonzalez A., Morales-Suarez-Varela M. (2014). *Evidence of the gluten-free and casein-free diet in autism spectrum disorders: a systematic review*. J. Child Neurol., 29, (12), pp. 1718-1727.

[34] Bascunan K. A., Vespa M. C., and Araya M. (2017). *Celiac disease: Understanding the gluten-free diet.* Eur. J. Nutr., 56, (2), pp. 449-459.

[35] Johnston C. S., Snyder D., and Smith C. (2017). *Commercially available gluten-free pastas elevate postprandial glycemia in comparison to conventional wheat pasta in healthy adults: a double-blind randomized crossover trial.* Food Funct., 8, (9), pp. 3139-3144.

[36] Gaesser G. A., and Angadi S. S. (2012). *Gluten-free diet: Imprudent dietary advice for the general population?* J. Acad. Nutr. Diet, 112, (9), pp. 1330-1333.

[37] Cheng J., Brar P. S., Lee A. R., and Green P. H. (2010). *Body mass index in celiac disease: Beneficial effect of a gluten-free diet*. J. Clin. Gastroenterol., 44, (4), pp. 267-271.

[38] Lebwohl B., Cao Y., Zong G., Hu F. B., Green P. H. R., Neugut A. I., Rimm E. B., Sampson L., Dougherty L. W., Giovannucci E., Willett W. C., Sun Q., and Chan A. T. (2017). *Long term gluten consumption in adults without celiac disease and risk of coronary heart disease: Prospective cohort study*. BMJ, 357, pp. 1892.

[39] Melini V., and Melini F. (2019). *Gluten-Free Diet: Gaps and Needs for a Healthier Diet*. DOI: 10.3390/nu11010170.

[40] Rosell C. M., and Matos M. E. (2015). *Market and Nutrition Issues of Gluten-Free Foodstuff*. In: Arranz E., Fernández-Bañares F., Rosell C. M., Rodrigo L. and Peña A. S. (Eds.), Advances in the Understanding of Gluten Related Pathology and the Evolution of Gluten-Free Foods, OmniaScience, pp. 675-713.

[41] Kulai T., Rashid M. (2014). *Assessment of Nutritional Adequacy of Packaged Gluten-free Food Products*. Can. J. Diet Pract. Res., 75, (4), pp. 186-190.

[42] Thompson T. (1999). *Thiamin, riboflavin, and niacin contents of the gluten-free diet: Is there cause for concern?* J. Am. Diet Assoc., 99, (7), pp. 858-862.

[43] Thompson T. (2000). *Folate, iron, and dietary fiber contents of the gluten-free diet.* J. Am. Diet Assoc., 100, (11), pp. 1389-1396.

[44] Mariani P., Viti M. G., Montuori M., La Vecchia A., Cipolletta E., Calvani L., and Bonamico M. (1998). *The gluten-free diet: A nutritional risk factor for adolescents with celiac disease?* J. Pediatr. Gastr. Nutr., 27, (5), pp. 519-523.

[45] Babio N., Alcazar M., Castillejo G., Recasens M., Martinez-Cerezo F., Gutierrez-Pensado V., Masip G., Vaqué C., Vila-Marti A., Torres-Moreno M., Sánchez E., and Salas-Salvadó J. (2017). *Patients with Celiac Disease Reported Higher Consumption of Added Sugar and Total Fat Than Healthy Individuals.* J. Pediatr. Gastr. Nutr., 64, (1), pp. 63-69.

[46] Balamtekin N., Aksoy C., Baysoy G., Uslu N., Demir H., Köksal G., Saltık-Temizel I. N., Özen H., Gürakan F., and Yüce A. (2015). *Is compliance with gluten-free diet sufficient? Diet composition of celiac patients.* Turkish J. Pediatr., 57, (4), pp. 374-379.

[47] Fry L., Madden A. M., and Fallaize R. (2018). *An investigation into the nutritional composition and cost of gluten-free versus regular food products in the UK.* J. Hum. Nutr. Diet, 31, (1), pp. 108-120.

[48] Elliott C. (2018). *The Nutritional Quality of Gluten-Free Products for Children*. Pediatrics, 142, (2), pp. 20180525.

[49] Cornicelli M., Saba M., Machello N., Silano M., and Neuhold S. (2018). *Nutritional composition of gluten-free food versus regular food sold in the Italian market.* Dig. Liver Dis., 50, (12), pp. 1305-1308.

[50] Arias-Gastelum M., Cabrera-Chavez F., Vergara-Jimenez M. D., and Ontiveros N. (2018). *The gluten-free diet: Access and economic aspects and impact on lifestyle.* Nutr. Diet Suppl., 10, pp. 27-34.