A REVIEW ON CELIAC DISEASE AND GLUTEN-FREE DIET

Rusky I. Pratama[1], Iis Rostini[1], Yuli Andriani[2]

[1] *Staff at Laboratory of Fisheries Processing Product, Faculty of Fisheries and Marine Sciences, Universitas Padjadjaran, Indonesia*
[2]*Staff at Fisheries Department, Faculty of Fisheries and Marine Sciences, Universitas Padjadjaran, Indonesia*

ABSTRACT

Celiac disease is a genetically predisposed autoimmune condition defined by an inappropriate immune response (permanent intolerance) to gluten in ingested wheat and other cereal proteins (related with gluten). After the condition is diagnosed, the mortality rate of subjects is relatively low. Celiac disease is caused by a combination of environmental (mostly gluten) and immunological and genetic factors. The amount of gluten administered at the start of the program and the steady rise in the amount of gluten exposure will guard against celiac disease development. Given the wide range of symptoms experienced by persons with celiac disease, it would be more accurate to classify it as an illness affecting many body systems (systemic) rather than a sickness affecting primarily the digestive tract (gastrointestinal). The most effective treatment for celiac disease is to eliminate gluten and similar substances totally from one's diet. In comparison to commercially available gluten-free goods, natural food ingredients are thought to have superior nutritional value in terms of energy supply, lipid composition, and vitamin content.

Keyword: *autoimmune, celiac disease, diet, gluten-free, protein*

1. INTRODUCTION

Celiac disease or celiac disease has been identified among humans for a long time. Symptoms of a disease similar to this disease, first reported in the 2nd century AD, then only in the 19th century, the symptoms and characteristics of celiac disease can be better defined. At this time several ways of dealing with it were formulated, but in fact it was only in the 1940's that it was first recognized the importance of people with this disease not to eat cereals (grains) because they can cause histological changes in the intestines. Awareness of celiac disease has increased in the last two decades and the number of newly diagnosed cases has increased dramatically. Currently, celiac disease affects about 1% of the entire population in various regions of the world [1], [2]. The estimated prevalence in the United States is that it affects 1 in 133 people in the population, while its worldwide prevalence affects 1 in 266 people. Relatives of people with this disease also have a higher prevalence of 1 in 22-39 people from the population. The disease remains underdiagnosed in many countries so the estimated number of sufferers does not reflect the true number [3].

Celiac disease is a chronic autoimmune disorder and is characterized by an abnormal immune response (permanent intolerance) to gluten in ingested wheat and other cereal proteins (associated with gluten) in genetically predisposed people. This disease can affect individuals at any age and is similar to other autoimmune diseases, this disease is found to be more common in women than in men with a ratio of 3:1 [1], [3], [4]. Research shows that the prevalence or prevalence of celiac disease has increased at least 4-5 times over the past 50 years. The reason for this increase is not clearly known although it may have something to do with aspects of exposure to certain microorganisms and antibiotics [2].

The fatality rate of subjects after the disease is diagnosed is relatively low. The number depends on how the disease is recognized and how subjects are identified in each area. The risk of decease in a population after one year

of diagnosis is 0.2 (<20 years) and 8.2 (adults >60 years) per 1000 people. People who suffer from this disease have a high risk of diseases related to the immune system [2]. The prevalence and incidence of celiac disease depends on several factors such as:

1) Individual genetic background
2) Exposure to gluten and diet in infancy

The importance of the amount of gluten given at the introduction stage and the gradual increase in the amount of gluten exposure will protect against the development of celiac disease. Important things to note are the timing of gluten introduction, the amount of gluten introduced and the pattern of breastfeeding in relation to gluten introduction.

3) Other environmental risk factors

Some factors such as:

a. Areas with high gluten intake, such as refugee camps, can increase the risk of developing celiac disease.
b. It is known that there is a slightly increased risk to the baby of patients with elective cesarean section (patient wishes, not medical needs).
c. Exposure to gastrointestinal infections in youth and adulthood has been associated with the development of celiac disease.
d. Consumption of drugs such as protein pump inhibitors and antibiotics has been found to be associated with the development of celiac disease

4) Awareness of disease (by subjects and health workers)
5) Inspection and testing method and frequency

Celiac disease is a genetic disorder, meaning that it is passed from parents to children through genetic material. In some cases, stressful events such as pregnancy, surgery, infection, or severe emotional stress can also trigger the onset of illness. When a person with celiac eats gluten, the protein from gluten interferes with the absorption of nutrients from food by damaging parts of the small intestine called the villi. The damaged villi make it nearly impossible for the body to absorb nutrients into the bloodstream and this leads to malnutrition and a number of other problems including the development of certain types of cancer, thyroid disease, osteoporosis, infertility, and the development of other autoimmune diseases [3]. Patients with this disease are usually diagnosed by examining high-risk groups, including family members with celiac disease, people with type 1 diabetes, other autoimmune disorders and Down's syndrome. Despite rapid developments in the way of diagnosis, the increasing number of these diseases is still a silent epidemic category. This is because many patients are still undiagnosed and do not receive treatment, thus it can increase the risk of developing symptoms and even being at risk for cancer and death [1], [2].

2. SYMPTOMS OF CELIAC DISEASE

An inflammatory reaction in the proximal small intestine is a hallmark of celiac disease. Increased numbers of lamina propria lymphocytes and intraepithelial lymphocytes, which are lymphocytes in the epithelium's surface layer, characterize this inflammation. The nuclei of the surface enterocytes are disorganized and shorter and broader than normal. Villi that are ordinarily tall and narrow are shortened and flattened. The depth of the cryptal layer is enhanced. Changes in the proximal small intestine can be patchy and impact different lengths of the intestine [5]. Symptoms of complications as well as the physical characteristics that celiac disease gives and shows are very diverse, ranging from disorders of the digestive tract (internal) to those that are not related to the digestive tract (external). In infant or youth, the disease usually shows the following characteristics: failure to thrive, short stature, delayed puberty, recurrent abdominal pain, diarrhea (occurring in 10% of children), steatorrhea, flatulence and anemia. Each of the children diagnosed in one study had family members who suffered from autoimmune diseases such as type 1 diabetes or thyroid disease and many of the sufferers were children who were overweight or obese (though not always). In adulthood, the common symptoms of this disease include: chronic diarrhea, abdominal bloating and pain, fatigue and impaired absorption of nutrients. Some adults also show symptoms of anemia, osteoporosis, dermatitis herpetiformis, abdominal pain, neurological or psychiatric problems, infertility, aphthous stomatic and vitamin deficiency. In addition, there are also those who complain of depression, fatigue, joint pain, sores on the inside of the mouth, migraines, nausea, numbness in the legs, osteopenia, damage to tooth enamel, farting and weight loss [1], [2], [6], [7], [8].

Many people with this disease do not show symptoms of digestive tract disorders or only show very mild symptoms but show symptoms of diseases that are not directly related to the digestive tract, such as: dermatitis herpetiformis, anemia, osteoporosis, infertility and neurological problems. Patients with celiac disease have a high risk of developing cancer, which is about 2-4 times the risk of developing non-Hodgkin's lymphoma, more than 30

times the risk of developing small bowel adenocarcinoma and 1.4 times the risk of developing the disease leading to death [2]. In more detail, some of the disorders that are known to be associated with celiac disease are:

1) Endocrine disorders: type 1 diabetes, thyroid autoimmune disorders, Addison's disease, reproductive disorders
2) Nervous disorders: cerebellar ataxia, peripheral neuropathy, cognitive disorders, psychosis (mental disorders, insanity), epilepsy, migraine. It is also known that gluten is thought to be involved in various neurological and psychiatric disorders such as schizophrenia and autism.
3) Liver disorders: primary biliary cirrhosis, autoimmune hepatitis, autoimmune cholangitis (all including liver disorders);
4) Other disorders: anemia, osteoporosis, dermatitis herpetiformis, selective IgA deficiency, Turner syndrome, idiopathic dilated cardiomyopathy, Down syndrome and other malignant diseases such as cancer.

Dermatitis herpetiformis appears on the skin of celiac patients and affects about 10-20% of the total subjects. Characteristics that appear include wounds caused by papulovesicular and the presence of granular deposits of IgA (antibody) in the dermal papillae. Treatment is generally carried out using *dapsone* which is useful for treating symptoms that arise on the skin but a gluten-free diet is the only recommended long-term treatment [1].

Nervous function disorders are the most common symptoms outside the digestive tract and affect about 10-30% of sufferers. Cerebellar ataxia and peripheral neuropathy are the most common neurological complications that may accompany celiac disease, though, convulsions, chronic headaches, depression, and psychiatric disorders are also known to be detected in some patients. The causes of the association between celiac disease and neurological complications are still largely unknown. However, immune abnormalities in the nervous system, including the infiltration of lymphocytes in and around the patient's central nervous system, as well as the response to a gluten-free diet suggest that there are specific mechanisms that are associated with neurological symptoms. Celiac disease is also known to be associated with a number of autoimmune endocrine disorders, such as type 1 diabetes and thyroid disease and affects about 5% of sufferers. This is generally due to a genetic background. The effect of a gluten-free diet on this type of disease is believed to be very limited. Cancer is also known to occur in some people with celiac disease, including non-Hodgkin lymphoma, enteropathy-associated T-cell lymphoma, small intestinal adenocarcinoma, esophageal and oropharyngeal squamous carcinoma. A strict gluten-free diet is known to have shown effective results in reducing the risk of these malignant diseases [1].

3. WHAT IS GLUTEN?

Celiac disease arises from the interaction of environmental factors (mainly caused by gluten) with immune and genetic factors. Gluten is a general term used to describe a mixture of reserve proteins including prolamin, hordein, cecalin which are found respectively in wheat, barley and rye. The two main proteins found in gluten are glutenin and gliadin. Gliadins are responsible for most of the adverse health effects of gluten. When flour mixes with water, the gluten proteins form a sticky network that has a glue-like consistency. This glue-like property makes dough elastic and allows bakery products (and the like) to expand when baked. This mass also provides a chewy texture and is preferred in processed food products [2], [3], [4].

Wheat gliadin and glutenin (low molecular weight) both contain immunogenic peptides. In addition, the unusual amino acid composition (high prolamin and glutamine content) in gluten proteins prevents thorough digestion of these proteins in the gastrointestinal tract. Both of these proteins cannot be digested by peptidases in the stomach, pancreas and small intestine, and still leaves a long peptide consisting of 33 amino acids. This long peptide will then be absorbed by the intestine and cause a series of immune responses [2], [6]. These proteins can exert a toxic effect on the intestinal mucosa in genetically susceptible individuals by triggering a response mediated by the immune system. This response is responsible for the destruction of small intestinal villi and lymphocytes that enter the small intestinal mucosa [3], [7]. While for most people these peptides do not actually cause problems. There are also many sources of gluten whose content is hidden in other products such as oats (unless harvested separately from the wheat), sauces (marinade and soy sauce), medicinal fillers and supplements and utensils for cooking that are used together (pasta pots, grills, fryers) [2].

Types of cereals that contain gluten and should be avoided by people with celiac disease include wheat, barley, malt, rye, kamut, and triticale. Thus, people with this disease also need to avoid derivative products that use these cereal raw materials, including bread (commercial bread, white bread, donuts, muffins, croutons), dumplings, french fries, pasta, pizza, noodles (instant noodles, ramen, udon, soba, egg noodles), cakes (cake, pies, cheesecake fillings, brownies), pastry products, breakfast cereals, various types of snacks (tortilla chips, spiced snacks, potato chips), biscuits, wafers, crackers and processed meat products (including sausages, breaded dough), gravy, imitation

meat and seafood products, cream soup, soy sauce, salad dressings, malt syrup, dextrin, energy bars, confectionery (including candy bars) and certain types of alcoholic beverages (based on cereals) [3].

Types of cereals that do not contain gluten and are good for consumption by celiac sufferers include: corn, rice, sorghum, oats, teff (cereal from Ethiopia), millet (barley), and arrowroot. In addition, there are ingredients that are classified as pseudo-cereals such as amaranth, quinoa and buckwheat. Other food ingredients that can be consumed by celiac sufferers because they are rich in nutrients and do not contain gluten include vegetables, fruits, nuts, potatoes, sweet potatoes, cassava, soybeans, vegetable oil, dairy products, eggs, meat and fish [3].

4. WHAT CAN BE DONE TO TREAT CELIAC DISEASE?

Seeing the variety of symptoms shown by people with celiac disease, it would be more appropriate to categorize this disease as a disorder of various body systems (systemic) rather than a disorder that only occurs in the digestive tract (gastrointestinal). Currently, the most effective treatment for celiac disease is to completely eliminate gluten and related proteins from the diet, whereas food products containing wheat, rye (black wheat) and barley should be avoided [1], [9].

It should be ensured that what the patient is doing is actually a gluten-free diet because wheat and its derivatives are widely used in various processed food products, besides that commitment to this diet is not an easy thing. If indeed eating cereal is highly desirable or unavoidable then replace wheat with other types of cereals such as rice, corn, quinoa, sorghum and buckwheat which are known to be safe. Although oats are considered to be well tolerated by the majority of people with celiac disease, it should be noted that some commercial products are reported to contain cereal contaminants containing gluten [1], [7].

A gluten-free diet is an effective treatment method for people with celiac disease that leads to a complete recovery of the sufferer and reduces the risk of other complications. Although a gluten-free diet is effective when done right, many sufferers complain about it. Besides requiring the adoption of new habits, this diet is quite expensive because it requires to find a substitute for wheat (relatively cheaper in the tropics), then some people do not like it because it is socially isolated from religious celebrations and other dining events. Strictly avoiding gluten can be a challenge because there are hidden sources that are difficult to identify. As many as 20% of patients report recurrence of symptoms after diagnosis and the most common reason is exposure to gluten. Symptoms include irritable bowel syndrome, other food intolerances, colitis, and bacterial overgrowth [2]. Patient-support organizations are a great place to learn about the disease and how to eat well. National support groups can be found in almost every country and are easily accessible over the Internet. Gluten-free items vary in price by nation, but the diet is typically costly, making nutritional treatment difficult for patients with little financial resources. Gluten-free items are particularly expensive and difficult to come by in underdeveloped nations, whilst the government subsidizes them in other countries (such as the Netherlands, the United Kingdom, New Zealand, Italy, Sweden, and Finland) [6].

Symptoms usually decrease over a period of days to weeks following a gluten-free diet, but mucosal recovery generally takes longer. Subsequent therapeutic options include treatment using enzymes to break down harmful peptides in gluten and certain treatment with antibody cells, but a gluten-free diet is still the best treatment (Briani 2008). Because of the many problems faced, most subjects are more interested in non-diet treatment. Drug therapy for this disease includes detoxification of ingested gluten (glutenase), treatment of junctions in the intestinal epithelium, administration of vaccines to establish tolerance to gluten and block immune activating mechanisms [2].

5. GLUTEN-FREE DIET

There have been many gluten-free food products available in the market, but it is necessary to distinguish between products that naturally do not contain gluten and products that are made gluten-free due to the refining process. For gluten-free products that have passed the purification stage, special attention must be paid to labeling and chemical composition. The term "gluten-free" in European countries refers to foods containing less than 20 ppm of gluten, while the claim "too low in gluten" is used for breads made from cereals after going through a special processing step to remove most of the gluten and containing less than 30 mg [3]. Gluten is mostly found in breads, cereals, and pastas, but it can also be found in seasonings, sauces, marinades, soy sauce, soups, salad dressings, and ready-to-eat flavored rice. A patient must ensure that each product is gluten-free by reading food labels carefully or contacting food maker [7].

The loss of gluten protein from our products and diet can alter the composition of macro and micro nutrients and thus change their nutritional value. Wheat is not only consumed as a major source of protein but also iron, folate and B vitamins (thiamine, riboflavin and niacin), where gluten-free products are often low in these

nutrients. Many gluten-free products available in the market often contain higher levels of carbohydrates and fat than gluten-containing foods. For example, gluten-free bread uses starch as the basic ingredient with a high glycemic index, low protein content and high fat. Gluten-free biscuits are generally richer in saturated fatty acids than gluten-containing foods. All of these characteristics have a negative effect on health and need to be considered carefully if we are to follow a healthy gluten-free diet [3].

It is also known that commercial gluten-free products contain lower levels of folate, iron and B vitamins than gluten-free foods. In addition, individuals who follow a gluten-free diet generally have a lower dietary fiber intake than individuals who follow a diet containing foods containing gluten. This is because gluten-free products are generally made from starch or flour that has been removed from the outside of the grain so that it has a lower fiber content. Research conducted on adults and children shows that approximately 20-38% of people with celiac disease have nutritional complications, such as calorie and protein imbalances, deficiencies in dietary fiber, minerals and vitamins. The more severe the damage suffered by the wall of the small intestine, the greater the nutritional deficiency suffered (lower iron, copper, folate, vitamin B_{12} and zinc content) [3], [10].

6. ALTERNATIVE SOURCES OF BALANCED NUTRITION FOR PEOPLE WITH CELIAC DISEASE

The distribution of daily calorie intake recommended for children with celiac disease who follow a gluten-free diet in order to maintain a healthy and balanced diet is not different from that recommended for ordinary people. The total daily calories obtained from dietary intake should ideally be 55% from complex and simple carbohydrates, 15% from dietary protein and 25-30% (or less of this value) from fat. The intake of unsaturated fats (monounsaturated and polyunsaturated) should be prioritized. Monounsaturated fatty acids should provide more than 15% of total calories and polyunsaturated fatty acids should provide 10% of total calories. These very beneficial nutrients are found in abundance in high-fat fish such as the tuna, mackerel, sardines and salmon family. In addition, fish is also a source of high-quality protein and contains other important nutrients (besides unsaturated fatty acids and protein) such as minerals and vitamins. Thus, people with celiac disease need to be informed and it is recommended that this daily calorie intake should be maintained to remain ideal by consuming nutritious foods [3].

It is highly recommended to choose foods that naturally do not contain gluten because they are known to have more balanced and complete macro and micro nutrients. In fact, this natural food ingredient is considered to have higher nutritional value in terms of energy supply, fat composition and vitamin content compared to commercially available gluten-free products. From a variety of foods that are naturally gluten-free and available in the market, it would be better to eat nutrient-rich foods such as fish. Where fish can replace wheat as a source of protein and also contains a complete composition of unsaturated fatty acids [3]. Milk, butter, and cheese; fresh, frozen, or canned fruits and vegetables; fresh meats, fish, poultry, eggs, beans, seeds, nuts; corn, and rice are all gluten-free. Gluten-free eating and baking has become easier in recent years, thanks to a rise in the number and quality of gluten-free food products available on the internet and in some grocery shops, but at a higher cost than gluten-containing goods. Gluten-free breads, buns, rolls, pizza crusts, doughnuts, pastas, pretzels, cereals, and desserts are available readymade. Breads, pancakes, muffins, desserts, and other baked goods can be made with baking mixes and flours [7].

7. CONCLUSIONS

Celiac disease is a chronic autoimmune disorder that affects a small percentage of the world's population or about 1%. People who suffer from this disease have a high risk of diseases related to the immune system which depends on several factors such as genetic background, exposure to foods containing gluten, various environmental factors, as well as awareness and knowledge of sufferers and the surrounding environment. One of the best way to prevent this disease from happening include doing a gluten free diet by consuming various gluten free products available in the market or looking for alternative sources of other fresh food ingredients that are richer in nutrients.

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