Inflammatory Bowel Diseases

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Liver disease is one of the most common extraintestinal manifestations of inflammatory bowel disease (IBD). IBD cause chronic inflammation and can affect various sections of the gastrointestinal tract. A particular form of inflammatory bowel disease is inflammatory bowel disease (IBD).

Crohn's disease | inflammatory bowel diseases | liver fibrosis

1. Introduction

It is estimated that about 2.5–3 million people in Europe struggle with this disease. The prevalence of inflammatory bowel disease in the United States is 70 to 150 cases per 100,000 people and is increasing [1]. In Poland, approximately 50,000 people suffer from inflammatory bowel disease, one in four of whom are minors [2][3]. Inflammatory bowel diseases include CD, UC, indeterminate colitis, and microscopic colitis [2][4][5]. Among the causes that influence the onset of IBD are genetic, immunological, and environmental factors (dietary changes, stress, overuse of antibiotics, especially in the first years of life, smoking, alcohol, progressive environmental degradation, high content of artificial preservatives in food) [1][6] (**Figure 1**).

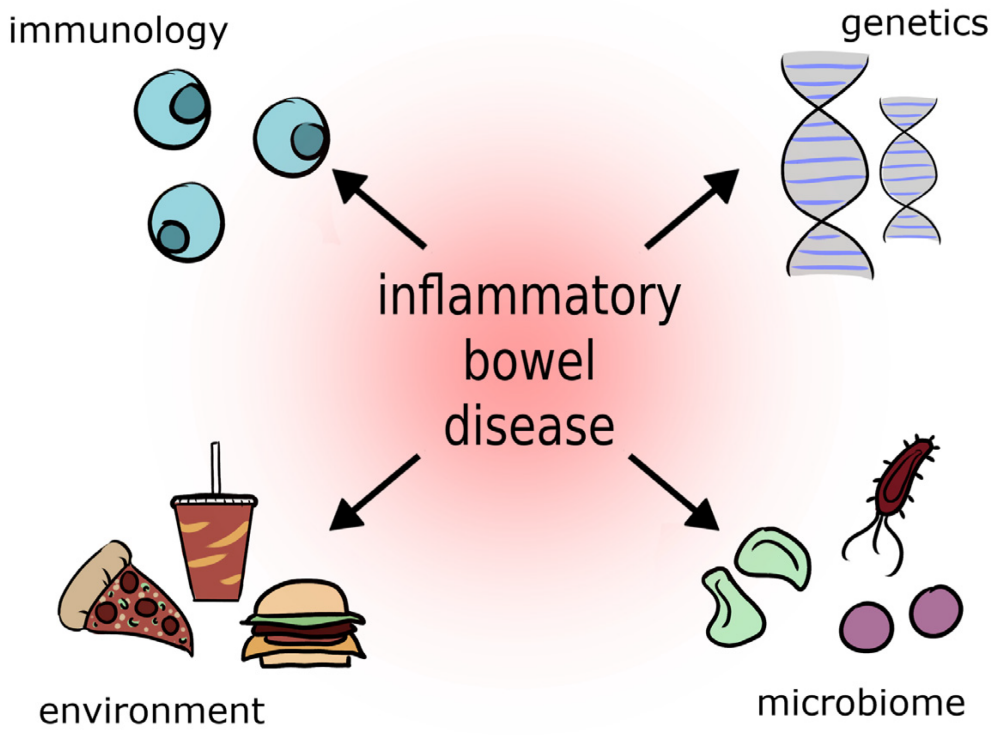

Figure 1. Etiology of Inflammatory Bowel Disease [1][6].

An example of immune factors predisposing to IBD is an imbalance of Th17/Treg cells. This balance is influenced by the gut microbiome, T Cell Receptor (TCR) signaling or cytokines, among other factors [7]. Furthermore, changes in the number of T cells can also lead to the development of LF, for example, by indirectly inducing liver damage via Th17 and Tc (cytotoxic T) cells [8]. Many authors also point out intestinal homeostasis disturbances in patients with IBD (**Table 1**). These conditions affect people of different ages. According to statistics, most patients are adults between the ages of 20 and 40, but a third of patients are adolescents and children. IBD is increasingly affecting older people. Infants are the least likely to suffer from inflammatory bowel disease [2].

Table 1. Intestinal homeostasis disturbances in patients with inflammatory bowel disease [9][10][11][12][13][14][15][16][17][18][19].

Intestinal Epithelial Barrier Disturbances	Intestinal Microbiota Disturbances
-increased expression of claudin-1–reduction of mucus secretion, which increases the risk of enteritis (CD and UC) -increased expression of claudin-2–Increased pores in TJ (CD and UC) -decreased expression of claudin–3,5,8 (CD)–reduction of intestinal barrier properties -decreased expression of claudin–3,4,7 (UC)–reduction of intestinal barrier properties -increased expression of occludin (active UC) -ZO1 dysfunction–decrease in stabilised claudin strands -TNF-α–decrease in normal TJ function and increase in intestinal epithelial apoptosis -IL-1β i IFN-γ–reduction of TJ integrity by affecting occludins and ZO1 -IFN-λ–occurrence of Paneth cell defect -dysfunction of ILC3 -secretion of chemokines by EIC–causes and maintains inflammation in IBD (e.g. CXCR1 (+) CXCR2 (+) IL-23)	Increase in the amount of the following bacteria: -*Proteobacteria* (degradation of intestinal mucus) np. *Haemophilus, Pasteurellaceae* -*Streptococcus* -*Fusobacterium* (degradation of intestinal mucus) -*Enterobacteriaceae* np. *E. Coli* (AIEC) Decrease in the amount of the following bacteria: -*Firmicutes* np. *Faecalibacterium prausnitzii, Roseburia* (SCFA producing bacteria) -*Euryarchaeota* -*Bacteroidetes* np. *Prevotella* spp. -*Bifidobacterium* Increase in the amount of following fungus: -*C. albicans* -*C. parapsilosis* -*Aspergillus clavatus* (CD) -*Cryptococcus neoformans* (CD) -*Ascomycota*

CD-Crohn's Disease, UC-Ulcerative Colitis, TJ-tight junction, ZO-zonula occludens, TNFα-tumor necrosis factor α, IL-1β- Interleukin-1 beta, IFN-γ- Interferon gamma, IFN-λ-interferon lambda, ILC3-innate lymphoid cells-3, EIC-intestinal epithelial cells, CXCR-CXC chemokine receptor, SCFA-short chain fatty acids.

2. Symptoms and Diagnostics of Inflammatory Bowel Disease

People with inflammatory digestive disease often experience abdominal pain, nausea, and appetite disorders. Vomiting, diarrhoea, and a subfebrile state are common. These symptoms cause impaired absorption, leading to nutrient deficiencies and hypovitaminosis [20]. Among patients diagnosed with chronic IBD, the incidence rate of depression is 15–30%, with up to 80% of patients experiencing anxiety during disease exacerbation compared to fully healthy individuals. This is caused by the deterioration of quality of life by interfering with normal physical and mental functioning. Patients rarely need psychological support, which is an important part of a holistic approach to their care [21]. IBD sufferers often exclude various foods from their diet, identified with their ailments. Because of this, they may experience hypoproteinemia and low levels of vitamins. In serum, A, D, K, C and B have low concentrations of minerals, iron, zinc, magnesium, resulting in reduced immunity, problems with wound healing,

and more frequent infections occur. Inflammatory bowel diseases increase the risk of osteoporosis and osteopenia as a consequence of vitamin D and calcium deficiency, which affect between 3% and 30% of patients [20]. Inflammatory bowel disease leads to serious and life-threatening complications ranging from intestinal perforation, joint, skin, eye, and liver disease to colon cancer [20].

UC is one of the diseases of the IBD. It involves inflammation of the mucosa of the colon, leading to widespread and shallow ulcerations. Symptoms: diarrhoea, mucus, and blood fragments may appear, abdominal cramps and pain, sudden feeling of pushing on the stool, lack of appetite, significant weight loss. Occasionally, UC often produces extraintestinal symptoms, such as uveitis and scleritis, joint pain, erythema nodosum, alopecia, liver disease, thrombosis, and anemia [1][2][22].

Another disease of inflammatory bowel disease is CD. It is chronic and progresses slowly. Inflammation occupies the intestinal mucosa partially and sometimes even entirely, leading to fistulas, abscesses, and ulcers. The most common symptoms are abdominal pain and cramps of varying severity, vomiting, diarrhoea, nausea, flatulence, and extraintestinal symptoms.

Both of these conditions prevent normal functioning. Patient reports indicate that they sometimes use the bathroom up to 20 times a day [1][2][22].

The diagnosis of IBD is based on invasive and noninvasive methods. For the proper diagnosis of IBD, an endoscopic examination, gastroscopy, and colonoscopy must be performed, which requires adequate preparation, often causing stress and anxiety in patients. It is contraindicated in cases of exacerbation of the disease [23]. Sometimes a histopathological examination of the specimen is necessary. This is followed by a radiographic examination or magnetic resonance imaging of the intestines.

Determining the biomarkers calprotectin and lactoferrin in the stool is helpful for diagnosing IBD [6]. These proteins are released into the gastrointestinal tract as a response to intestinal inflammation. Calprotectin is secreted by immune cells located in the deeper layers of the intestine [20][24][25][26]. The test of a stool sample for the presence of lactoferrin protein also provides valuable information on intestinal status. Lactoferrin is produced by mucosal epithelial cells and is crucial for normal mucosal defence of the gastrointestinal tract [27][28]. Elevated fecal lactoferrin levels signify an increased mucosal immune response to food or bacterial antigens and may indicate a chronic state of inflammatory gastrointestinal disease. If this is the case, a further diagnosis is recommended [24][27][28][29].

IBD have in common that disease exacerbations alternate with moments of remission, when symptoms resolve completely or partially. Treatment should be tailored to the stage of the disease, the patient's condition, and the specific symptoms present. Complete cure is not possible, so therapy consists of pharmacological maintenance of the remission state and alleviation of symptoms [24][25][26][30].

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