Summary

Inflammatory Bowel Disease (IBD), including Crohn's disease (CD), Colitis ulcerosa (UC) and unclassified inflammatory bowel disease (IBD-U) are chronic diseases of the gastrointestinal tract. So far, the etiology of IBD remains unclear, which does not allow the disease to be fully cured.

During the diagnosis and monitoring of IBD, it is necessary to perform numerous tests, including endoscopic examinations. Due to the increase in the incidence of IBD among children in recent decades, it has become necessary to search for markers of intestinal damage, that would allow limiting the performance of invasive tests, especially in this age group. So far, several new markers have been introduced into clinical practice, including: C-reactive protein (CRP), ANCA (anti-neutrophil cytoplasmic antibodies) i ASCA (anti-Saccharomyces cervisiae antibodies) and fecal calprotectin (fCal).

The aim of the doctoral dissertation was to determine the applicability of selected lipids, matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) as IBD markers, and evaluation of their correlation with routinely measured markers of inflammation, clinical disease activity based on the appropriate scales such as Paediatric Ulcerative Colitis Activity Index (PUCAI) for UC and Paediatric Crohns Disease Activity Index (PCDAI) for CD, and with endoscopic disease activity assessed according to the Mayo score for UC and Simple Endoscopic Score for Crohn's Disease (SES-CD) for CD, and as well as with the assessment of IBD phenotype according to the Parris classification.

The study included children with newly diagnosed IBD hospitalized at the Department of Paediatrics, Gastroenterology, Hepatology, Nutrition and Allergology of the Medical University of Bialystok. The reference group consisted of children with normal fCal levels (<50 μg / g), after excluding inflammatory bowel disease. Informed consent was obtained from parents of all participants.

Laboratory measurements of inflammatory parameters such as CRP, erythrocyte sedimentation rate (ESR), platelet count (PLT), white blood cell count (WBC), serum albumin and fCal were measured in all children. The concentration of MMP-9 and TIMP-1 in serum and feces was determined by commercial enzyme immunoassays according to the manufacturer's instructions. The lipid concentration was assessed using ultra-high performance liquid chromatography coupled with a tandem mass spectrometer.

The first publication showed a significantly higher concentration of selected ceramides, including C16:0-Latosylceramide (C16:0-LacCer), C18:0-Ceramide (C18:0-Cer), C18:1-Ceramide (C18:1-Cer), C20:0-Ceramide (C20:0-Cer) and C24:0-Ceramide (C24:0-Cer) in the group of children with IBD in relation to the reference group. C16:0-LacCer has been found to be useful in differentiating between IBD and control group and in differentiating CD and UC patients. Moreover, a positive correlation of C18:0-Cer and C18:1-Cer with PLT and ESR was demonstrated in the group of UC patients.

In the next research, significantly higher concentrations of MMP-9 and TIMP-1 in the serum and feces of children with UC were found compared to children from the reference group. MMP-9 and TIMP-1 have been shown to be useful in differentiating UC children from the reference group, as well as in discriminating patients with different location or intensity of mucosal lesions in the colon. In the study group, a significant, positive correlation of serum MMP-9 concentration with CRP, WBC, PLT, the Mayo scale and the range of changes according to the Paris classification were demonstrated. On the other hand, the concentration of TIMP-1 in the study group correlated with CRP, ESR, PLT, the PUCAI scale and the range of changes according to the Paris classification.

The review paper, which is the last part of the doctoral dissertation, summarizes reports on metabolomic profiling in children with IBD. This work emphasizes the possibility of using metabolomics in research on new disease markers and new therapeutic targets. It was noted that the analysis of the obtained data could be used to better understand the mechanisms underlying IBD.