The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89 (2), Page 6653- 6658

Serum Resistin Level as a Novel Marker of Disease Activity in Patients with Ulcerative Colitis

Mohamed Gamal Youssef, Khalid Abd El-Hamid, Omnia Samir Mohamed Sayed, Ahmed Samir Allam
Internal Medicine, Hepatology and Gastroenterology Department,
Faculty of Medicine, Ain Shams University
Corresponding Author: Mohamed Gamal Youssef,Phone No.: (+2) 01146802018, E-mail: mohamedazz3@yahoo.com

ABSTRACT
Background: IBD, occasionally referred to as "chronic inflammatory bowel disease" including Crohn's disease, ulcerative colitis (UC), and other gastrointestinal disorders are included in this group.
Aim of the Work: The aim of our study was to assess serum resistin level in disease activity and remission in patients with ulcerative colitis disease.
Patients and Methods: A cohort study for 6 months on 40 Egyptian patients presented with ulcerative colitis disease over 18 years old visiting the Outpatient Clinics or admitted in Ain Shams University Hospitals.
Results: The present study revealed a highly significant elevation of serum resistin in active ulcerative colitis patients (p-value <0.001). There was direct relationship between the activity of ulcerative colitis and serum resistin. Resistin was positively correlated with inflammatory markers (CRP and ESR) in UC patients. And there was negative relation between resistin and Hb, fecal calprotectin.
Conclusion: Serum resistin is a useful non-invasive test that was used to monitor disease activity in patients with ulcerative colitis. It positively correlated with inflammatory markers (CRP and ESR). Other studies should be done on larger size of participants to determine the the role of serum resistin as a marker of disease activity in patients with inflammatory bowel disease.
Keywords: Serum resistin level, Ulcerative colitis.

INTRODUCTION
IBD, or chronic inflammatory bowel disease, is a term that is used to describe a variety of gastrointestinal disorders, including Crohn's disease and ulcerative colitis [(1)]. IBD symptoms include episodes of abdominal pain, diarrhoea, bloody stools, weight loss, and an influx of neutrophils and macrophages that create cytokines, proteolytic enzymes, and free radicals that cause inflammation and ulceration [(1)].
IBD is a chronic condition that develops early in both males and girls. IBD has been recognised as one of the most common gastrointestinal diseases since the start of the twenty-first century, with an accelerated occurrence in newly industrialised nations. Over the second half of the 20th century, there was a remarkable increase in both the incidence and prevalence of IBD [(2)].
Crohn's disease often affects the colon, perianal region, terminal ileum, and cecum, although it can also affect any part of the intestine in an erratic manner. In contrast, ulcerative colitis affects the rectum and has a continuous pattern that might affect either the entire colon or only a portion of it [(3)].
The only sites of ulcerative colitis are those in the mucosa and submucosa with cryptitis and crypt abscesses where inflammation is observed, in contrast to what histologically seen in Crohn's disease, there are granulomas, transmural inflammation, thickened submucosa, and fissuring ulceration [(4)].
Despite the fact that the origin of IBD is still unknown, significant work has been achieved in recent years to understand its pathophysiology. Studies have shown correlations between intestinal microbiota, other environmental variables, the host's genetic predisposition, and immunological abnormalities in the aetiology of IBD [(5)].
Combinations of clinical symptoms are necessary for the diagnosis of inflammatory bowel disease (IBD), imaging results, inflammatory indicators in the lab, and endoscopic samples. Microcytic anaemia, leukocytosis, and thrombocytosis are among the hematologic abnormalities. Two indicators of inflammation, the high sensitivity C-reactive protein (hs-CRP) and erythrocyte sedimentation rate (ESR) are frequently enhanced [(6)].
Our study's objective was to measure the level of serum resistin in ulcerative colitis patients to assess for disease activity and remission.

PATIENTS AND METHODS
A cohort study for 6 months on 40 Egyptian patients presented with ulcerative colitis to assess for disease activity and for follow up during disease remission. They were over 18 years old visiting the Outpatient Clinics or admitted in Ain Shams University Hospitals.

Inclusion criteria: Patients presented with ulcerative colitis disease during activity and remission, patients more than 18 years old and newly diagnosed patients with ulcerative colitis.
Exclusion criteria: Pregnant nursing females, patients less than 18 years old, patients who refuse to participate in the study and patients with chronic diseases as DM, heart failure and renal failure.

All patients were subjected to: Full history, performing a physical exam, and performing laboratory tests such as ELISA test to measure serum resistin levels.

Received: 26/6/2022
Accepted: 5/9/2022

Liver function tests: viral indicators, coagulation profile, AST, ALT, total and direct bilirubin, serum albumin, renal function tests, and a list of other tests HCVab, HBsAg HBA1c, Fasting glucose, ESR, CRP and quantitative fecal calprotectin, Colonoscopy and radiology. Pelvi-abdomen ultrasound, MRI enterography and Echocardiography.

Ethical Approval:

The study was approved by the Ethics Board of Ain Shams University, an informed written consent was taken from each participant in the study and confidentiality of the data were assured. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistics

SPSS V17 was used. **Chi-Square test** was employed to investigate the association between two qualitative variables. **ANOVA test** was used in quantitative data to compare various items in the same group. **ROC-curve** was used to calculate the cutoff value, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). P-values of 0.001, 0.05, and less than 0.05 are all regarded as significant, extremely important.

RESULTS

Table (1): Demographic data and characteristics of the studied patients

Demographic data			
Age (years)	**Range**	18-55	
	Mean ± SD	32.725±10.112	
		N	**%**
Gender	**Male**	22	55.00
	Female	18	45.00
Smoking	**No**	30	75.00
	Current	7	17.50
	Ex-smoker	3	7.50
Diabetes	**No**	40	100.00
	Yes	0	0.00
Hypertension	**No**	37	92.50
	Yes	3	7.50

Table (1) showed that 40 patients with active ulcerative colitis 22 males (55%) and 18 females (45%) with age ranged from 18 to 55 years.

Table (2): Medications among the studied patients

Medications	**Active**		**Remission**		**Chi-Square**	
	N	**%**	**N**	**%**	**X^2**	**P-value**
Non	4	10.00	0	0.00	4.459	0.485
Corticosteroids	8	20.00	10	25.00		
Mesalamine	13	32.50	14	35.00		
Balsalazide	2	5.00	3	7.50		
Olsalazine	1	2.50	1	2.50		
Corticosteroids& Mesalasine	12	30.00	12	30.00		
Total	40	100.00	40	100.00		

Table (2) showed that there was no statistical significant difference regarding medications among the studied patients.

Table (3): Extension of ulcerative colitis among the studied populations

Ulccerative colitis extension	**Active**		**Remission**		**Chi-Square**	
	N	**%**	**N**	**%**	**X^2**	**P-value**
Left sided	16	40.00	26	65.00	20.017	<0.001*
Extensive	16	40.00	0	0.00		
Proctitis	8	20.00	14	35.00		
Total	40	100.00	40	100.00		

Table (3) showed that there was high statistical significant difference regarding extension of ulcerative colitis among the studied populations**.**

Table (4): Activity of ulcerative colitis among the studied population

Truelove and Witts	Active		Remission		Chi-Square	
	N	%	N	%	X^2	P-value
Mild	11	27.50	32	80.00	25.102	<0.001*
Moderate	18	45.00	8	20.00		
Severe	9	22.50	0	0.00		
Fulminant	2	5.00	0	0.00		
Total	40	100.00	40	100.00		

Table(4) shows that there was statistically significant change in Truelove and Witts criteria during disease activity and remission

Table (5): Comparison between the studied groups as regards lab investigations

		Time		Differences		Paired Test	
		Active	Remission	Mean	SD	t	P-value
Hb (g/ dl)	Range	6.7 - 14	9.5 - 16	-1.845	2.693	-4.333	<0.001*
	Mean ±SD	10.513 ± 1.826	12.358 ± 1.681				
TLC (10'3/uL)	Range	4.8 - 14	4.8 - 14	0.120	3.676	0.206	0.838
	Mean ±SD	8.248 ± 2.433	8.128 ± 2.322				
PLT (10'3/uL)	Range	107 - 514	107 - 514	1.825	160.013	0.072	0.943
	Mean ±SD	261.325 ± 104.288	259.500 ± 104.158				
ESR (mm/hr)	Range	10 - 105	5 - 60	27.875	31.863	5.533	<0.001*
	Mean ±SD	49.950 ± 28.669	22.075 ± 15.436				
CRP (mg/L)	Range	8 - 105	5 - 66	19.988	30.208	4.185	<0.001*
	Mean ±SD	47.698 ± 28.213	27.710 ± 16.452				
Albumin (gm/dl)	Range	2.4 - 5.4	2.4 - 5.4	-0.032	0.974	-0.211	0.834
	Mean ±SD	4.075 ± 0.814	4.108 ± 0.776				
AST (IU/L)	Range	16 - 73	17 - 73	-1.775	27.345	-0.411	0.684
	Mean ±SD	35.125 ± 16.491	36.900 ± 17.406				
ALT (IU/L)	Range	19 - 72	19 - 70	-2.075	18.226	-0.720	0.476
	Mean ±SD	37.050 ± 10.749	39.125 ± 11.715				
INR	Range	0.73 - 1.3	0.77 - 1.3	-0.039	0.174	-1.437	0.159
	Mean ±SD	1.010 ± 0.133	1.050 ± 0.135				
S.Creat (mg/ dl)	Range	0.6 - 1.3	0.6 - 1.3	-0.003	0.016	-0.990	0.328
	Mean ±SD	0.980 ± 0.203	0.983 ± 0.204				
Fecal Calprotectin (µg/mg)	Range	124 - 984	20 - 170	410.425	251.434	10.324	<0.001*
	Mean ±SD	491.550 ± 261.588	81.125 ± 37.218				

Table (5) shows that there was statistically significant difference between the studied groups as regard haemoglobin, CRP, ESR and fecal calprotectin during disease activity and remission

Table (6): Comparison between level of resistin during disease activity and remission

S. Resistin	Time		Differences		Paired Test	
	Active	Remission	Mean	SD	t	P-value
Range	12 - 40	6 - 30	10.933	7.893	8.760	<0.001*
Mean ±SD	26.250 ± 7.150	15.318 ± 6.820				

Table (6) shows that there was statistically significant positive relation in serum resistin during disease activity and remission

Table (7): Relation between activity, extension of ulcerative colitis and serum resistin

		S. Resistin Active				ANOVA	
		N	Mean	±	SD	F	P-value
Ulccerative colitis extension Active	Left sided	16	25.938	±	7.009	6.574	0.004*
	Extensive	16	29.750	±	5.615		
	Proctitis	8	19.875	±	6.105		
Truelove and Witts Active	Mild	11	19.818	±	5.307	5.780	0.002*
	Moderate	18	28.056	±	6.188		
	Severe	9	29.889	±	5.600		
	Fulminant	2	29.000	±	12.728		

Table(7) shows that there was statistically positive relationship between the activity , extension of ulcerative colitis and resistin

Table (8): Relation between level of Hb, ESR, CRP, fecal calprotectin and serum resistin

Correlations		
	S. Resistin Active	
	r	P-value
Hb Active	-0.174	0.283
ESR Active	0.529	<0.001*
CRP Active	0.429	0.006*
Fecal Calprotectin Active	-0.218	0.177

Table (8) shows that there was statistically significant positive relationship between ESR , CRP and resistin , but negative relationship between Hb , fecal calprotectin and resistin.

DISCUSSION

Recurrent episodes of gastrointestinal tract inflammation brought on by an improper immune response to gut bacteria are the defining feature of inflammatory bowel disease (IBD). Two idiopathic intestinal diseases that differ in the location and depth of their involvement in the colon wall are referred to as "inflammatory bowel disease" (IBD). In ulcerative colitis, the intestinal mucosa is diffusely irritated (UC). Any type of ulcerative colitis, including the sigmoid, distal ulcerative colitis, or the entire colon up to the cecum, might be affected by proctitis, the type of UC that typically affects the rectum (pancolitis). Crohn's disease (CD) can cause transmural ulcers anywhere throughout the GI tract, but it most usually affect the terminal ileum and colon. Both disorders are divided into categories based on their severity (mild, moderate, or severe). Additionally, there are three phenotypes of CD: penetrating, stricturing, and inflammatory [(7)].

A variety of clinical symptoms, inflammatory laboratory markers, imaging findings, and endoscopic biopsies must be employed to determine the presence of inflammatory bowel disease (IBD). Leukocytosis, microcytic anaemia, and thrombocytopenia are a few examples of hematologic diseases. High-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR), two indications of inflammation, are typically elevated [(6)].

Fecal inflammatory markers like calprotectin and lactoferrin, which can also be high in other inflammatory disorders, can help distinguish IBD from irritable bowel syndrome. In IBD, calprotectin significantly correlates with mucosal inflammation and may be used as a proxy for inflammation; normalisation denotes mucosal healing [(8)].

Either UC or CD remission is the intended outcome of treatment. IBD is categorised into three categories for treatment: disease that is mild, moderate, or severe. Previously reserved medications are increasingly utilised early on diseases that are less severe. Treatment for UC is heavily influenced by the severity of the condition and the occurrence of extraintestinal symptoms. Mesalamine and other aminosalicylate medications are the mainstays for people with mild to moderate illness that is only present in the rectum. To initiate or maintain remission, mesalamine is administered rectally, but it may also be coupled with oral therapy. Mescaline may not be effective for some people with moderate illness who are also resistant to immunomodulators like TNF-alpha monoclonal antibodies (infliximab) or oral glucocorticoids. For the uncontrolled condition, up to 25% of all UC patients needed a total colectomy [(9)].

Adipokines, which have a significant impact on metabolism, immunology, and inflammation, can be secreted by adipose tissues. Resistin is one of the adipokines that may be found in human serum and is mostly produced by macrophages. It is a cysteine-rich peptide with different biological effects and initially proposed to regulate obesity, glucose metabolism and insulin sensitivity. Some researchers reported that human resistin may also play a major role in regulating inflammation [(9)]. Resistin has pro-inflammatory properties. According to several studies, patients with IBD had higher levels of resistin in their blood, which

were considerably decreased by anti-inflammatory treatment [10].

In the current study, the group of ulcerative colitis patients were studied to investigate serum resistin level during disease activity and remission.

The present study revealed a highly significant elevation of serum resistin in active ulcerative colitis patients (p-value<0.001), which means that there is direct relationship between elevation of serum resistin level and activity of ulcerative colitis. Serum resistin was positively correlated with inflammatory markers (CRP and ESR) in UC patients. And there were negative relation between serum hemoglobin, fecal calprotectin and resistin. These results were in agreement with the results of previous studies in some respects and in contrast to them in some other respect. Our study showed that mean age of our patients ranged from 18 to 55 years with mean ± SD of 32.725 ± 10.112 which is younger in comparison with another study **Silje Thorsvik et al.,2017** which showed the mean age of their study 43.5 ± 14.6

About smoking our study showed that 7 (17.5 %) were smokers, which is in agreement study of **Peters *et al.*** [11], which showed that about 16% of their study population are smokers.

Our study was conducted on 40 patients with active ulcerative colitis 22 males (55%) and 18 females (45%) with age ranged from 18 to 55 years but in **Nasim *et al.*** [12] There were 50 patients with active ulcerative colitis 28 men and 22 women, their ages ranging between 24-42 years with a mean value of 33.27 ± 9.70 years. This agrees with our study.

In our study, patients with active UC were divided into 11 (27.5%) mild in disease activity, 18 (45%) moderate in disease activity, 9 (22.5%) severe in disease activity, 2 (10%) patients with fulminant activity and patients with remission 32 (80%) mild, 8 (20%) moderate. About extension of ulcerative colitis, 16 (40%) in disease activity had left sided colitis, about 26 (65%) in disease remission had left sided colitis, about 16 (40%) in disease activity had extensive colitis and 0 (0%) in disease remission had extensive colitis. About 8 (20%) in disease activity and 14 (35%) in disease remission had proctitis. In **Mohammed *et al.*** [13] study patients with active UC were divided into 17 (47.22%) patients with mild activity, 11 (30.56%) patients with moderate activity, 8 (22.22%) patients with severe activity, 11 (31.4%) patients with ulcerative proctitis, 18 (51.4%) patients with left-sided UC and 7 (20%) patients with extensive UC

Jihan A *et al.* [14] demonstrated that, compared to levels before therapy, after three months of treatment, resistin levels in the blood were considerably lower in active CD and UC patients (P values of 0.01 and 0.04 for CD patients and 0.039 and 0.004 for UC patients, respectively). CRP levels significantly decreased in both CD and UC patients after treatment, which is matching with our results. According to **Valenkin *et al.*** [15], resistin and visfatin levels increased more in groups of patients with active illness than in groups of patients in remission, highlighting the effect of treatment. Prior to treatment, the median serum resistin and visfatin levels in CD patients were 12.2 ± 2 ng/ml and UC patients were 11.2 ± 2 ng/ml, respectively, which did not agree with findings of **Karmiris K *et al.*** [16]. **Marek *et al.*** [17] discovered that compared to healthy controls (10.7 1.1 ng/mL), CD (19.3 12.5 ng/mL; P 0.05) and UC (23.2 11.0 ng/mL; P 0.05) patients had significantly higher baseline serum resistin concentrations. The serum resistin levels dropped (14.5 4.0 ng/mL; P 0.05) because only those in the UC group received treatment. Blood resistin concentrations in CD patients were found to be significantly higher than those in healthy controls, according to research of **Jixiang D *et al.*** [18] (SMD = 1.76, 95% CI = 0.64 to 2.88, p = 0.002). Additionally, compared to healthy controls, UC patients showed higher serum resistin levels (SMD = 2.10, 95% CI = 1.03 to 3.17, p 0.001). The serum resistin levels in UC patients were higher than those in healthy controls, which suggest that CD and UC may be contributed to the increased serum resistin levels (SMD = 2.10, 95% CI = 1.03 to 3.17, p 0.001). Resistin levels were greater in patients with active and remission disease compared to controls in a study of **Konrad *et al.,*** [19], which was conducted on IBD patients. Gender, disease duration, localisation, and type were all important factors that influence on the difference in adiponectin levels between IBD patients and controls. In juvenile CD (n = 18), **Frivolt *et al.*** [20] likewise noted increased resistin levels at diagnosis that was decreased following infliximab treatment over 14 weeks. Also, **Jacob *et al.*** [21] found significant greater reductions in resistin levels (P = 0.002) at 12 months among patients on biologics compared to those not on biologics.

Karásková *et al.* [22] reported that there are 58 kids with IBD, mean age of 15 and 15years (boys: 32; girls: 26) and twenty healthy controls (age = 15 (12-16), number of boys = 11, number of girls = 9) of the same sex and age were included in their study. Patients with IBD had considerably higher CRP levels than healthy controls, but in our investigation, there were 40 adult patients; 22 men (55%) and 18 women (45%) with a mean ± SD of 32.725 ± 10.112. In this study, resistin and CRP had a positive correlation (rho = 0.52). Leukocyte counts and CRP levels were found to be independent predictors of resistin levels, which is consistent with our findings.

Patients with IBD had considerably greater resistin levels than controls, according to **Konrad *et al.*** [19] study (P 0.0001). In both CD and UC patients, resistin levels significantly linked with elevated white blood cell count, C-reactive protein (CRP), and disease activity (P or = 0.0001).

CONCLUSION

A helpful noninvasive test called serum resistin used to track the progression of ulcerative colitis in patients, positively correlated with inflammatory

markers CRP and ESR. Other studies should be done on larger size of participants to determine the function of serum resistin as a disease activity indicator in patients with IBD.

DECLARATIONS

- **Consent for Publication:** I confirm that all authors accepted the manuscript for submission
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of Interest:** The authors declared no conflicts of interest regarding the publication of this paper.

REFERENCES

1. **Szigethy E, McLafferty L, Goyal A, (2010):** Inflammatory bowel disease, Child and Adolescent Psychiatric Clinics of North America, 19 (2): 301–318.
2. **Ng S, Kaplan G, Tang W *et al*. (2019):** Population Density and Risk of Inflammatory Bowel Disease. Am. J. Gastroenterol., 114: 107–15.
3. **Khor B, Gardet A, Xavier R (2011):** Genetics and pathogenesis of inflammatory bowel disease. Nature, 474 (7351): 307–317. doi: 10.1038/nature10209.
4. **Gajendran M, Loganathan P, Catinella A *et al*. (2018):** A comprehensive review and update on Crohn's disease. Disease-a-Month, 64 (2): 20–57.doi: 10.1016/j.disamonth .2017.07.001
5. **Kaser A, Zeissig S, Blumberg R (2010):** Inflammatory bowel disease. Annual Review of Immunology, 28 (1): 573–621. doi: 10.1146/annurev-immunol-030409-101225
6. **Lee J, Kim E, Moon W (2019):** Chronological Review of Endoscopic Indices in Inflammatory Bowel Disease. Clin Endosc., 52 (2): 129-136
7. **Dmochowska N, Wardill H, Hughes P (2018):** Advances in Imaging Specific Mediators of Inflammatory Bowel Disease. Int J Mol Sci. , 19(9):2471. doi: 10.3390/ijms19092471.
8. **Oliveira S, Oliveira S, Monteiro I (2017):** Diagnosis and management of inflammatory bowel disease in children. BMJ, 357: j2083. doi: 10.1136/bmj.j2083. PMID: 28566467; PMCID: PMC6888256.and disease activity. J Gastroenterol., 47: 519–530.
9. **Nguyen V, Mays J, Lang M *et al*. (2018):** Knowledge Gaps in the Management of Postoperative Crohn's Disease: A US National Survey. Dig Dis Sci., 63 (1): 53-60
10. **Waluga M, Hartleb M, Boryczka G (2014):** Serum adipokines in inflammatory bowel disease. World J. Gastroenterol., 20: 6912–6917.
11. **Thorsvik S, Damås J, Granlund A *et al.(2017):***Fecal neutrophil gelatinase-associated lipocalin as a biomarker for inflammatory bowel disease. J Gastroenterol Hepatol. ,32(1):128-135. doi: 10.1111/jgh.13598.
12. **Peters L, Perrigoue J, Mortha A *et al*. (2017):** A functional genomics predictive network model identifies regulators of inflammatory bowel disease, Nature Genetics, 49 (10): 1437–1449.
13. **.Nasim A Nasim A, Behrooz M *et al*. (2018):** Circulating resistin in ulcerative colitis, relation with anthropometric, body composition and inflammatory parameters .Progress in Nutrition, 20: 132-136
14. **Mohammed G, Heba A, Eiman A *et al*. (2020):** Correlation between Neutrophil Gelatinase- Associated Lipocalin and Endoscopic, Histopathologic and Clinical Activities of Ulcerative Colitis.Journal of Advances in Medicine and Medical Research, 32 (5): 136-144
15. **Jihan A, Jihan A, Hosam M *et al.* (2014):** Circulating Resistin and Visfatin Levels in Patients with Inflammatory Bowel Disease as Predictors of Treatment Response. Afro-Egypt J Infect Endem Dis., 4 (2): 96-101
16. **Valenkin Valentini L, Wirth E *et al.* (2009):** Circulating adipokines and the protective effects of hyper-insulinemia in inflammatory bowel disease. Nutrition, 25: 172-81.
17. **Karmiris K, Karmiris K, Koutroubakis I *et al.* (2006):** Circulating levels of liptin, adeponectin, resistin and ghrelin in inflammatory bowel disease Inflamm Bowel Dis., 12: 100-105.
18. **Marek W, Marek W, Marek H *et al.* (2014):** Serum adipokines in inflammatory bowel disease World J Gastroenterol., 20 (22): 6912–6917.
19. **Jixiang D, Jixiang D, Yuting C *et al.* (2020):** Elevated serum levels of resistin in inflammatory bowel disease: a meta-analysis, https://www.researchgate.net/publication/342761967_Elevated_serum...
20. **Konrad A, Konrad A, Lehrke M *et al*. (2007):** Resistin is an inflammatory marker of inflammatory bowel disease in humans. Eur J Gastroenterol Hepatol., 19: 1070–1074.
21. **Frivolt K, Frivolt K, Schwerd T *et al*. (2018):** Hyperadiponectinemia during infliximab induction therapy in pediatric Crohn disease. J Pediatr Gastroenterol Nutr., 66: 915–919.
22. **Jacob A, Jean P, Rishi G B *et al*. (2021):** Adipokine Resistin Levels at Time of Pediatric Crohn Disease Diagnosis Predict Escalation to Biologic Therapy Inflammatory Bowel Diseases, 27 (7): 1088–1095
23. **Karásková E, Karásková E, Kubickova V *et al.* (2022):** Circulating levels of WISP-1 (Wnt1-inducible signaling pathway protein 1) and other selected adipokines in children with inflammatory bowel disease. Physiol Res., 71 (2): 275-284. doi: 10.33549/physiolres.934854.