ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

Adipose Tissue's Contribution to Inflammatory Bowel Disease

Akriti Hansa[1], Dr. Juhi Aggarwal[2], Aarushi Batra[3], Dr. Jyoti Batra[4]

[1] MBBS Student, Batch 2021-22, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[2] Professor & Head, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[3] Final Year MBBS, LLRM Medical College, Meerut, Uttar Pradesh, India.

[4] Professor, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

Email- [1] akritihansa2512@gmail.com, [2] jaggarwal38@gmail.com, [3] aarushibatra2305@gmail.com, [4] dean.research@santosh.ac.in

ABSTRACT:

Crohn's disease and ulcerative colitis are examples of inflammatory bowel diseases (IBDs), chronic inflammatory conditions that affect the gastrointestinal tract. Clinical and experimental evidence is growing suggesting visceral adiposity, in particular, plays a significant role in the aetiology of inflammatory bowel disease (IBD). Obesity appears to be a significant risk factor for the severity of IBD disease and clinical outcomes. Visceral adipose tissue is a metabolically active organ with multiple functions that plays a role in lipid synthesis, immune function, and endocrine function. Along the mesentery, bowel inflammation seeps into the nearby adipose tissue. Mesenteric fat regulates immunological reactions to the movement of gut microorganisms and acts as a barrier to inflammation. At the same time, the main source of the cytokines and adipokines that cause the inflammatory processes linked to IBD may be mesenteric adipose tissue. This review focuses in particular on the probable function of adipokines in the pathophysiology of IBD and the prospective application of these molecules as attractive treatment targets.

Keywords: mesenteric fat; inflammatory bowel disease; microbiome; adipokines; visceral obesity.

INTRODUCTION:

Crohn's disease (CD) and ulcerative colitis are two examples of inflammatory bowel diseases (IBDs), which are long-term inflammatory conditions that damage the digestive system (UC). About 25% of IBD patients begin to exhibit symptoms before the age of 21. IBD in children is thought to be more severe and pervasive [1]. IBD is becoming more common in both adults and children around the world. The greatest incidence rates of paediatric IBD were 23 and 15.2 per 100,000 person-years in Europe and North America, respectively, according to a 2018 review [2].

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

The imbalance between genetic predisposition, environmental variables (infections, food, smoking, drug use, stress, and socioeconomic level), and the gut microbiota is the etiopathogenesis of IBD [3]. Modulation of cytokine activity has a key role in intestinal inflammation. Adipose tissue is an endocrine and immunological organ that strongly contributes to inflammatory processes in addition to being involved in energy homeostasis.IBD pathogenesis can be affected by a multitude of adipokines (hormones and cytokines released by adipose tissue), particularly from the mesenteric fat [4]. Despite advancements in this area of study, the etiopathogenetic processes of IBD remain poorly understood.

OBESITY AND IBD:

Body mass index (BMI) 30 kg/m2 is the definition of obesity, while BMI 25 kg/m2 is the definition of overweight. IBD is frequently linked to underweight (BMI 18 kg/m2), although several studies also show that overweight and obesity are prevalent in UC/CD patients [5]. In Western nations, 20–40% of IBD patients may be overweight, while 15–40% of this population may be obese [6].30% of children with UC and 20% of children with CD, respectively, are overweight or obese [7].

In addition to an inverse relationship between childhood BMI and UC regardless of age, there is a clear correlation between CD diagnosed before the age of 30 and childhood BMI. This shows that childhood underweight might be a risk factor for UC and supports the idea that obesity is a risk factor for CD. Obesity was confirmed as a risk factor for IBD in a newly published systematic evaluation of more than 23,000 adult cases of IBD.While there was no clear correlation between BMI and the risk of UC, being overweight and obese were both independently linked to an elevated risk of CD [8].

In comparison to healthy people, patients with IBD have increased abdominal adiposity and reduced skeletal muscle mass [9]. Lean muscle mass loss over time is correlated with rising obesity rates [10]. In IBD patients, declining muscle mass may even lead to osteoporosis and more frequent bone fractures [11]. Sarcopenia has been noted as a predictor of the requirement for surgery in individuals with IBD who are overweight or obese [12,13].

Major surgical complications are also more common following sarcopenia, and better perioperative care may reduce this risk [14]. Traditional assessment techniques would not reveal malnutrition in the majority of overweight patients.

Abdominal computed tomography makes it feasible to precisely measure skeletal muscle mass [15]. After receiving surgical therapy for refractory IBD, patients' computed tomography scans revealed significant alterations in their body composition as compared to healthy controls. Patients were noted for having less skeletal muscle and more fat accumulation. The authors stress that sarcopenic obesity may be more common in people who are recalcitrant to IBD treatment [9].

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

Obesity, especially visceral adiposity, may affect how IBD develops and how it ends. Compared to patients with normal body weight, adult obese patients with IBD require more frequent hospital stays [16]. Similar findings were made for the paediatric IBD population; a worsening of the condition was linked to both low and high BMI at the time of diagnosis [17]. However, it is unclear if obese IBD patients are more likely to experience side effects like surgery, hospitalisation, and infection. According to research on Crohn's disease patients, overall obesity (as determined by BMI) is not always linked to a higher prevalence of IBD-related comorbidities. Similar to this, obesity has not been linked to a more severe form of ulcerative colitis in patients [6]. In contrast, obese CD patients were around 2.5 times more likely than CD patients who were not obese to have a poor surgical result, according to a research by Malik et al. [18].

In adult CD patients, a body mass index over 25 indicates a worse result and a quicker time to first surgery [19]. Obesity has consistently been identified as a risk factor for perioperative morbidity, which is primarily brought on by surgical site infections, but is also influenced by poor wound healing, the potential for increased thromboembolic complications, a longer length of hospital stay, and the requirement for short-term rehabilitation [20]. It has been demonstrated that obesity increases the likelihood of switching from laparoscopic to open surgery [21]. Obese paediatric IBD patients may also experience a more severe course of their illness, which is shown by a higher requirement for surgery [22]. On the other hand, a meta-analysis found that obese patients had considerably lower rates of hospitalisation, hormone therapy, and surgery linked to IBD than non-obese patients [23].

Numerous studies have found a link between obesity and lower overall quality of life in IBD patients [20, 21]. For instance, a recent large internet-based study of over 7000 IBD patients found that obesity was substantially associated with increased rates of anxiety, sadness, exhaustion, pain, and decreased social function [24]. Few research investigating this matter have given contradictory results, leaving open the question of whether obesity affects the IBD phenotype [20]. Obese patients may have greater rates of perineal disease, according to one retrospective review [25], while other investigations revealed no changes in disease distribution or behaviour between CD or UC patients [9,26].

Because BMI cannot distinguish between subcutaneous and visceral adipose tissue, these discrepancies may be caused by important limitations of BMI as a biomarker of adiposity [27].

Data indicate that obesity may affect the effectiveness of some common medicines used to treat IBD. It is linked to biologic drugs' quick clearance, which may lead to low trough concentrations and a less than ideal response to biological therapy [5,6]. There have been reports of worse clinical result and lower trough levels in response to infliximab [28] and adalimumab [29]. More recently, it was discovered that patients with IBD who were obese had lower trough levels of vedolizumab [30]. On therapy with azathioprine, decreased

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

clinical response and reduced 6-thioguanine levels have also been documented [21]. On the other hand, excess weight gain was not linked to higher weight-based dosage, lower serum trough levels, or a higher likelihood of treatment failure in juvenile IBD patients on maintenance infliximab therapy [31].

Infliximab-treated IBD patients from historical clinical trials with pooled data analysis did not show any differences in clinical remission or response based on BMI [32]. A systematic review and meta-analysis showing that obesity was a risk factor for anti-TNF medication failure in numerous rheumatic diseases but not in IBD [33] confirmed these findings.

Adipose-derived stromal cells, endothelial cells, fibroblasts, and leukocy

Adipose tissue is a metabolically active organ with multiple functions that plays a role in lipid storing, as well as immunological and endocrine activities. Adipocytes, preadipocytes, macrophages, stromal cells generated from adipose tissue, endothelial cells, fibroblasts, and leukocytes make up this cell type.

The distribution of adipose tissue in its two main compartments, subcutaneous and visceral [27,34]. By measuring the visceral fat area and subcutaneous fat area with abdominal magnetic resonance imaging or computed tomography, it is possible to distinguish precisely between subcutaneous and visceral adipose tissue (VAT) [15,35]. In comparison to obesity as indicated by BMI, VAT may be a better indicator of disease progression and a risk factor for CD complications [36]. According to computed tomography, the ratio of VAT to subcutaneous fat area is a reliable indicator of CD advancement and has a stronger correlation with postoperative CD recurrence than BMI [37]. Compared to healthy controls, paediatric CD patients were shown to have greater VAT volumes, and CD-related hospitalisation was associated with the rise in VAT volume [38]. The risk of penetrating illness and surgery in CD may be significantly increased by visceral obesity, as determined by VAT volume [39]. After surgery, the endoscopic recurrence of CD is at risk because to VAT. The stratification of risk in post-operative care techniques may be aided by measures of VAT [12]. Mesenteric adipose tissue, the peri-intestinal compartment of VAT, appears to be particularly significant in IBD [34].

ADIPOKINES:

A collection of mediators known as adipokines are largely secreted by adipocytes and regulate a number of metabolic processes in the immune system, liver, brain, muscles, and pancreas [35]. Adipokines are crucial regulators of the energy metabolism. Numerous them have been shown to have functional regulatory immune systems. Recent research has examined the function of many adipokines in both intestinal inflammation and creeping fat [36].

Adiponectin: Adiponectin is a hormone exclusively secreted by adipocytes at a level inversely proportional to fat mass [41]. Adiponectin acts as an anti-diabetic and anti-

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

atherogenicfac- Int. J. Mol. Sci. 2021, 22, 4226 8 of 17 tor [36]. It is a key mediator in the pathogenesis of chronic inflammation-related metabolic diseases such as atherosclerosis or type-1 diabetes. Adiponectin activates adiponectin receptor-1 and adiponectin receptor-2. The expression of adiponectin receptors has been reported on human monocytes, B-lymphocytes, and NK cells. Adiponectin induces the direct inhibition of pro-inflammatory pathways, including those regulated by TLRs, through inhibition of nuclear factor-kappa B (NF-κB) in several cell types. Pro-inflammatory cytokines (e.g., TNF-α and IL-6) suppress adiponectin secretion in adipocytes. Adiponectin also increases the secretion of anti-inflammatory cytokines such as IL-10 and IL-1 receptor antagonist by human monocytes, macrophages, and dendritic cells. Therefore, adiponectin acts as an anti-inflammatory mediator [3].

Leptin: Initially recognised as a hormone and satiety factor, leptin (also known as OB protein) is a protein. The Greek word leptos, which meaning "thin," is whence its name originates [37]. Due to its central effects, this peptide, which is largely released by adipocytes and is encoded by the ob gene, is a crucial hormone that regulates body weight [38]. Elevated blood pressure, carcinogenesis, cardiovascular disorders, and heightened immunological response in numerous autoimmune illnesses are only a few of the physiological processes that leptin mediates [39].

Resistin: Adipocytes and immune cells, primarily macrophages and peripheral blood mononuclear cells, express and generate the adipokineresistin [4]. Due to its resistance to insulin, resistin received its name. This adipokine contributes to the aetiology of obesity and diabetes in mice. The anti-diabetic medicine rosiglitazone and rise in diet-induced and hereditary causes of obesity lower circulating resistin levels.

Chemerin: Adipocytes produce chemerin, which has dual roles in immune response and metabolic regulation. With adipogenesis, chemerin expression and secretion dramatically rise. It is a pro-inflammatory cytokine associated with insulin resistance, blood pressure regulation, and adipocyte differentiation and metabolism. It has been demonstrated that chemerin stimulates dendritic cells and macrophage chemotaxis. As a result, it acts as a chemoattractant for innate immune cells [71]. Chemerin levels are correlated with serum levels of TNF-, IL-6, and CRP and may be an indicator of the inflammatory state brought on by obesity [3].

ADIPOKINES AND IBD TREATMENT:

Because it is crucial for preserving intestinal homeostasis, adiponectin is indicated as a potential treatment approach [36]. During mouse DSS-induced colitis, a plant-derived homolog of adiponectin showed protective benefits. Adenovirus infection also dramatically lessens the severity of DSS colitis in mice when adiponectin is administered to the animals. Reducing adiponectin resistance or employing adiponectin homologs may become therapeutic alternatives in IBD because adiponectin decreased the stress signals and apoptotic

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

state in colonic epithelial cells. The numerous types and high blood levels of adiponectin make it challenging to use as a pharmaceutical medication.

CONCLUSIONS:

A growing body of clinical and experimental evidence suggests that the pathophysiology of IBD involves adipose tissue, particularly VAT. Pro-inflammatory, immunoregulatory, and endocrine action are all displayed by VAT. Obesity appears to be a significant risk factor for the severity of IBD disease and clinical outcomes. Uncertainty exists regarding the precise methods by which obesity mediates these consequences. This is most likely accomplished, nevertheless, by VAT taking part in immunological responses to gastrointestinal microbiota and secreting a number of important mediators with inflammation-modulating properties that alter the production of local cytokines and hormones. The regulation of lipid metabolism, insulin sensitivity, inflammation, angiogenesis, hemostasis, and immunology are only a few of the processes in which adipokines are involved. Adipokines may have a key role as mediators in IBD, according to growing clinical and experimental evidence. To completely comprehend the potential involvement of adipokines in the aetiology of IBDs and to define theirpotential usage as prospective therapeutic targets, additional study is still necessary.

REFERENCES:

1. Bousvaros, A. Use of immunomodulators and biologic therapies in children with inflammatory bowel disease. Expert Rev. Clin. Immunol. 2010, 6, 659–666. [CrossRef]
2. Sýkora, J.; Pomahaˇcová, R.; Kreslová, M.; Cvalínová, D.; Štych, P.; Schwarz, J. Current global trends in the incidence of pediatric-onset inflammatory bowel disease. World J. Gastroenterol. 2018, 24, 2741–2763. [CrossRef]
3. Gonçalves, P.; Magro, F.; Martel, F. Metabolic inflammation in inflammatory bowel disease: Crosstalk between adipose tissue and bowel. Inflamm. Bowel Dis. 2015, 21, 453–467. [CrossRef]
4. Morshedzadeh, N.; Rahimlou, M.; AsadzadehAghdaei, H.; Shahrokh, S.; Reza Zali, M.; Mirmiran, P. Association Between Adipokines Levels with Inflammatory Bowel Disease (IBD): Systematic Reviews. Dig. Dis. Sci. 2017, 62, 3280–3286. [CrossRef]
5. Jarmakiewicz-Czaja, S.; Sokal, A.; Filip, R. What was First, Obesity or Inflammatory Bowel Disease? What Does the Gut Microbiota Have to Do with It? Nutrients 2020, 12, 3073. [CrossRef]
6. Singh, S.; Dulai, P.S.; Zarrinpar, A.; Ramamoorthy, S.; Sandborn, W.J. Obesity in IBD: Epidemiology, pathogenesis, disease course and treatment outcomes. Nat. Rev. Gastroenterol. Hepatol. 2017, 14, 110–121. [CrossRef]

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

7. Jensen, C.B.; Ängquist, L.H.; Mendall, M.A.; Sørensen, T.I.A.; Baker, J.L.; Jess, T. Childhood body mass index and risk of inflammatory bowel disease in adulthood: A population-based cohort study. Am. J. Gastroenterol. 2018, 113, 694–701. [CrossRef]

8. Bhagavathula, A.S.; Clark, C.C.T.; Rahmani, J.; Chattu, V.K. Impact of Body Mass Index on the Development of Inflammatory Bowel Disease: A Systematic Review and Dose-Response Analysis of 15.6 Million Participants. Healthcare 2021, 9, 35. [CrossRef]

9. Barroso, T.; Conway, F.; Emel, S.; McMillan, D.; Young, D.; Karteszi, H.; Gaya, D.R.; Gerasimidis, K. Patients with inflammatory bowel disease have higher abdominal adiposity and less skeletal mass than healthy controls. Ann. Gastroenterol. 2018, 31, 566–571. [CrossRef] [PubMed]

10. Bryant, R.V.; Schultz, C.G.; Ooi, S.; Goess, C.; Costello, S.P.; Vincent, A.D.; Schoeman, S.N.; Lim, A.; Bartholomeusz, F.D.; Travis, S.P.L.; et al. Obesity in Inflammatory Bowel Disease: Gains in Adiposity despite High Prevalence of Myopenia and Osteopenia. Nutrients 2018, 10, 1192. [CrossRef]

11. Scaldaferri, F.; Pizzoferrato, M.; Lopetuso, L.R.; Musca, T.; Ingravalle, F.; Sicignano, L.L.; Mentella, M.; Miggiano, G.; Mele, M.C.; Gaetani, E.; et al. Nutrition and IBD: Malnutrition and/or Sarcopenia? A Practical Guide. Gastroenterol. Res. Pract. 2017, 2017, 8646495. [CrossRef]

12. Holt, D.Q.; Moore, G.T.; Strauss, B.J.; Hamilton, A.L.; De Cruz, P.; Kamm, M.A. Visceral adiposity predicts post-operative Crohn's disease recurrence. Aliment Pharmacol. Ther. 2017, 45, 1255–1264. [CrossRef] [PubMed]

13. Adams, D.W.; Gurwara, S.; Silver, H.J.; Horst, S.N.; Beaulieu, D.B.; Schwartz, D.A.; Seidner, D.L. Sarcopenia Is Common in Overweight Patients with Inflammatory Bowel Disease and May Predict Need for Surgery. Inflamm. Bowel Dis. 2017, 7, 1182–1186. [CrossRef] [PubMed]

14. Ryan, E.; McNicholas, D.; Creavin, B.; Kelly, M.E.; Walsh, T.; Beddy, D. Sarcopenia and Inflammatory Bowel Disease: A Systematic Review. Inflamm. Bowel Dis. 2019, 25, 67–73. [CrossRef]

15. Zhang, T.; Ding, C.; Xie, T.; Yang, J.; Dai, X.; Lv, T.; Li, Y.; Gu, L.; Wei, Y.; Gong, J.; et al. Skeletal muscle depletion correlates with disease activity in ulcerative colitis and is reversed after colectomy. Clin. Nutr. 2017, 36, 1586–1592. [CrossRef] [PubMed]

16. Pavelock, N.; Masood, U.; Minchenberg, S.; Heisih, D. Effects of obesity on the course of inflammatory bowel disease. Bayl. Univ. Med. Center Proc. 2019, 32, 14–17. [CrossRef]

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

17. Yerushalmy-Feler, A.; Ben-Tov, A.; Weintraub, Y.; Amir, A.; Galai, T.; Moran-Lev, H.; Cohen, S. High and low body mass index may predict severe disease course in children with inflammatory bowel disease. Scand. J. Gastroenterol. 2018, 53, 708–713. [CrossRef]

18. Malik, T.A.; Manne, A.; Oster, R.A.; Eckhoff, A.; Inusah, S.; Gutierrez, A.M. Obesity is Associated With Poor Surgical Outcome in Crohn's Disease. Gastroenterol. Res. 2013, 6, 85–90. [CrossRef]

19. Hass, D.J.; Brensinger, C.M.; Lewis, J.D.; Lichtenstein, G.R. The impact of increased body mass index on the clinical course of Crohn's disease. Clin. Gastroenterol. Hepatol. 2006, 4, 482–488. [CrossRef]

20. Johnson, A.M.; Loftus, E.V. Impact of obesity on the management of inflammatory bowel disease. Gastroenterol. Hepatol. 2020, 16, 350–359.

21. Harper, J.W.; Zisman, T.L. Interaction of obesity and inflammatory bowel disease. World J. Gastroenterol. 2016, 22, 7868–7881. [CrossRef] [PubMed]

22. Long, M.D.; Crandall, W.V.; Leibowitz, I.H.; Duffy, L.; del Rosario, F.; Kim, S.C.; Integlia, M.J.; Berman, J.; Grunow, J.; Colletti, R.B.; et al. ImproveCareNowCollaborative for Pediatric IBD. Prevalence and epidemiology of overweight and obesity in children with inflammatory bowel disease. Inflamm. Bowel Dis. 2011, 17, 2162–2168. [CrossRef]

23. Hu, Q.; Ren, J.; Li, G.; Wu, X.; Li, J. The Impact of Obesity on the Clinical Course of Inflammatory Bowel Disease: A Meta-Analysis. Med. Sci. Monit. 2017, 23, 2599–2606. [CrossRef]

24. Jain, A.; Nguyen, N.H.; Proudfoot, J.A.; Martin, C.F.; Sandborn, W.J.; Kappelman, M.D.; Long, M.D.; Singh, S. Impact of Obesity on Disease Activity and Patient-Reported Outcomes Measurement Information System (PROMIS) in Inflammatory Bowel Diseases. Am. J. Gastroenterol. 2019, 114, 630–639. [CrossRef]

25. Blain, A.; Cattan, S.; Beaugerie, L.; Carbonnel, F.; Gendre, J.P.; Cosnes, J. Crohn's disease clinical course and severity in obese patients. Clin. Nutr. 2002, 21, 51–57. [CrossRef] [PubMed]

26. Flores, A.; Burstein, E.; Cipher, D.J.; Feagins, L.A. Obesity in Inflammatory Bowel Disease: A Marker of Less Severe Disease. Dig. Dis. Sci. 2015, 60, 2436–2445. [CrossRef] [PubMed]

27. Eder, P.; Adler, M.; Dobrowolska, A.; Kamhieh-Milz, J.; Witowski, J. The Role of Adipose Tissue in the Pathogenesis and Therapeutic Outcomes of Inflammatory Bowel Disease. Cells 2019, 8, 628. [CrossRef]

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

28. Harper, J.W.; Sinanan, M.N.; Zisman, T.L. Increased body mass index is associated with earlier time to loss of response to infliximab in patients with inflammatory bowel disease. Inflamm. Bowel Dis. 2013, 19, 2118–2224. [CrossRef] [PubMed]

29. Bultman, E.; de Haar, C.; van Liere-Baron, A.; Verhoog, H.; West, R.L.; Kuipers, E.J.; Zelinkova, Z.; van der Woude, C.J. Predictors of dose escalation of adalimumab in a prospective cohort of Crohn's disease patients. Aliment Pharmacol. Ther. 2012, 35, 335–341. [CrossRef]

30. Dreesen, E.; Verstockt, B.; Bian, S.; de Bruyn, M.; Compernolle, G.; Tops, S.; Noman, M.; Van Assche, G.; Ferrante, M.; Gils, A.; et al. Evidence to Support Monitoring of Vedolizumab Trough Concentrations in Patients With Inflammatory Bowel Diseases. Clin. Gastroenterol. Hepatol. 2018, 16, 1937–1946. [CrossRef]

31. Rodin, I.; Chan, J.; Meleady, L.; Hii, C.; Lawrence, S.; Jacobson, K. High body mass index is not associated with increased treatment failure in infliximab treated pediatric patients with inflammatory bowel disease. JGH Open 2019, 23, 446–453. [CrossRef] [PubMed]

32. Singh, S.; Proudfoot, J.; Xu, R.; Sandborn, W.J. Obesity and Response to Infliximab in Patients with Inflammatory Bowel Diseases: Pooled Analysis of Individual Participant Data from Clinical Trials. Am. J. Gastroenterol. 2018, 113, 883–889. [CrossRef] [PubMed]

33. Singh, S.; Facciorusso, A.; Singh, A.G.; VandeCasteele, N.; Zarrinpar, A.; Prokop, L.J.; Grunvald, E.L.; Curtis, J.R.; Sandborn, W.J. Obesity and response to anti-tumor necrosis factor-α agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. PLoS ONE 2018, 13, e0195123. [CrossRef]

34. Bilski, J.; Mazur-Bialy, A.; Wojcik, D.; Surmiak, M.; Magierowski, M.; Sliwowski, Z.; Pajdo, R.; Kwiecien, S.; Danielak, A.; PtakBelowska, A.; et al. Role of Obesity, Mesenteric Adipose Tissue, and Adipokines in Inflammatory Bowel Diseases. Biomolecules 2019, 9, 780. [CrossRef]

35. Goldmannova, D.; Spurna, J.; Krystynik, O.; Schovanek, J.; Cibickova, L.; Karasek, D.; Zadražil, J. Adipocytokines and new onset diabetes mellitus after transplantation. J. Appl. Biomed. 2018, 16, 247–254. [CrossRef]

36. Weidinger, C.; Ziegler, J.F.; Letizia, M.; Schmidt, F.; Siegmund, B. Adipokines and Their Role in Intestinal Inflammation. Front. Immunol. 2018, 9, 1974. [CrossRef]

37. Sitaraman, S.; Liu, X.; Charrier, L.; Gu, L.H.; Ziegler, T.R.; Gewirtz, A.; Merlin, D. Colonic leptin: Source of a novel proinflammatory cytokine involved in IBD. FASEB J. 2004, 18, 696–698. [CrossRef] [PubMed]

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

38. Singh, U.P.; Singh, N.P.; Guan, H.; Busbee, B.; Price, R.L.; Taub, D.D.; Mishra, M.K.; Fayad, R.; Nagarkatti, M.; Nagarkatti, P.S. The emerging role of leptin antagonist as potential therapeutic option for inflammatory bowel disease. Int. Rev. Immunol. 2014, 33, 23–33. [CrossRef]

39. Barbier, M.; Vidal, H.; Desreumaux, P.; Dubuquoy, L.; Bourreille, A.; Colombel, J.F.; Cherbut, C.; Galmiche, J.P. Overexpression of leptin mRNA in mesenteric adipose tissue in inflammatory bowel diseases. Gastroenterol. Clin. Biol. 2003, 27, 987–991. [CrossRef].