A Patient 84 Years Old with Chronic Inflammatory Diarrhea Mild to Moderate Dehydration et Causa Ulcerative Pancolitis

Yulia Syarifa[1*], Arika Effiyana [2], Maria Ulfah[3]
[1]Division of Internal Medicine, RSUD Ulin, Banjarmasin, Indonesia
[2] Department of Internal Medicine, Program of Medical Education Professional Program, Faculty of Medicine and Health Science, Lambung Mangkurat University, Banjarmasin
[3]Department of Biomedicine, Program of Medicine Undergraduate Program, Faculty of Medicine and Health Science, Lambung Mangkurat University, Banjarmasin

* E-mail: maria.ulfah@ulm.ac.id

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Abstract

Background: *Ulcerative pancolitis is a chronic Inflammatory Bowel Disease (IBD) characterized by superficial mucosal ulceration, rectal bleeding, diarrhea, and abdominal pain. Unlike Crohn's disease, Ulcerative pancolitis is limited to the colon and involves inflammation confined to the mucosal layer. Ulcerative pancolitis affects the colon in a retrograde manner starting from the rectum and extending proximally. The most dominant clinical symptoms in patients with Ulcerative pancolitis are abdominal pain and diarrhea accompanied by bleeding. Additionally, other symptoms can include anemia, fatigue, weight loss, rectal bleeding, loss of appetite, dehydration, malnutrition, skin lesions, joint inflammation, and impaired growth.*
Purpose: *This study aims to reported of a Patient 84 Years Old with Chronic Inflammatory Diarrhea Mild to Moderate Dehydration et causa Ulcerative pancolitis*
Case Presentation*: A male patient, 84 years old, was admitted to Ulin Hospital Banjarmasin on March 8, 2024, with the diagnosis of chronic inflammatory diarrhea with mild to moderate dehydration, ulcerative pancolitis, leukocytosis, leukocyturia, erythrocyturia, mild anemia, elevated liver, BPH, Candidiasis oral, and Geriatric problem (inanition, immobility, infection, frailty)*
Conclusion: *This case highlights the complex clinical presentation of chronic inflammatory bowel disease in the elderly population, often complicated by multiple comorbidities. A comprehensive approach to diagnosis and management is essential to optimize patient outcomes.*

Keywords: *Ulcerative pancolitis, IBD, diarrhea, geriatric*

Diare Inflamasi Kronis dengan Dehidrasi Ringan Sedang et causa Pancolitis Ulserativa pada Geriatri 84 tahun

Abstrak

Latar Belakang: *Pankolitis ulserativa adalah penyakit peradangan usus kronis yang ditandai oleh ulserasi mukosa superfisial, perdarahan rektal, diare, dan nyeri perut. Tidak seperti penyakit Crohn, pankolitis ulserativa terbatas pada kolon dan melibatkan peradangan yang terbatas pada lapisan mukosa. Pankolitis ulserativa mempengaruhi kolon secara retrograd mulai dari rektum dan meluas ke proksimal. Gejala klinis yang dominan adalah nyeri perut dan diare disertai perdarahan. Gejala lain yaitu anemia, kelelahan, penurunan berat badan, perdarahan rektal, kehilangan nafsu makan, dehidrasi, malnutrisi, lesi kulit, peradangan sendi, dan gangguan pertumbuhan.*
Tujuan*: Studi ini bertujuan untuk melaporkan kasus seorang pasien berusia 84 tahun dengan diare inflamasi kronis disertai dehidrasi ringan hingga sedang akibat pancolitis ulserativa.*
Penyajian Kasus: *Seorang pasien laki-laki berusia 84 tahun dirawat di Rumah Sakit Ulin Banjarmasin pada 8 Maret 2024 dengan diagnosis diare inflamasi kronis disertai dehidrasi ringan hingga sedang, pancolitis ulserativa, leukositosis, leukosituria, eritrosituria, anemia ringan, peningkatan enzim hati, BPH, kandidiasis oral, dan masalah geriatri (malnutrisi, imobilisasi, infeksi, kelemahan).*
Kesimpulan: *Presentasi klinis penyakit radang usus pada pasien geriatrik cukup rumit, biasanya disertai dengan berbagai komorbiditas. Evaluasi menyeluruh dalam diagnosis dan manajemen sangat penting untuk mengoptimalisasi kondisi pasien.*

Kata Kunci: *Pankolitis ulserativa, radang usus, diare, geriatri*

Introduction

Inflammatory Bowel Disease (IBD) is an inflammatory condition involving the gastrointestinal tract, the exact cause of which remains unclear. (Fauzi, 2023). Broadly, IBD consists of three main types: ulcerative colitis, Crohn's disease, and when distinguishing between the two is difficult, it is categorized as indeterminate colitis. This practical categorization helps differentiate it from other inflammatory bowel conditions such as infections, ischemia, and radiation-related conditions. Ulcerative pancolitis is one of the two types of Inflammatory Bowel Disease (IBD), alongside Crohn's disease. Unlike Crohn's disease, which can affect any part of the gastrointestinal tract, Ulcerative pancolitis typically involves the large intestine and can be visualized via colonoscopy. The characteristic lesions are areas of continuous

inflammation and ulceration without normal tissue segments. (Greuter, 2019)

The pathophysiology of Ulcerative pancolitis is diverse and not fully understood. A widely accepted framework indicates a complex interplay of environmental factors and host vulnerability that predispose to the development of ulcerative colitis. The pathophysiology involves defects in the epithelial barrier, immune response, and involvement of colonic microflora. Disease onset is triggered by events that disrupt the mucosal barrier, alter the balance of healthy gut microbiota, and abnormally stimulate the intestinal immune response. Several factors contribute to the pathophysiology of Ulcerative pancolitis (UC). The intestinal microbiota shows reduced diversity and changes in metabolic profiles, characterized by a decrease in short-chain fatty acids. The mucous layer in Ulcerative pancolitis is marked by reduced synthesis of colonic mucin-2. These microbiota changes and decreased mucous layer lead to barrier dysfunction, facilitating microbial approach to the epithelial barrier. The intestinal epithelium is disrupted due to apoptosis and changes in tight junction protein expression, allowing more microbiota to cross the barrier. This activates macrophages and antigen-presenting cells (APCs), which produce chemokine expression that ultimately attracts neutrophils. Neutrophils form extracellular traps as the first line of cellular response, and immune cells infiltrate by binding to adhesion molecules expressed by blood vessel endothelium. Mature monocyte infiltration transforms into macrophages, which produce tumor necrosis factor (TNF), IL-12, IL-23, and IL-6, resulting in polarization towards T helper 1 (TH1) cells. Additionally, epithelium-derived IL-36γ inhibits regulatory T cells (Tregs) and induces T helper 9 (TH9) cell polarization, which produces IL-9. IL-36 has also been shown to induce fibrogenesis gene expression. Furthermore, IL- 13 released by natural killer T cells (NK cells) contributes to barrier dysfunction. (Khoshnevisan *et al.*, 2019)

The most prominent clinical symptoms in patients with Ulcerative pancolitis include

abdominal pain and diarrhea accompanied by bleeding. (Khan *et al.*, 2020; Yücel, 2023) Additionally, symptoms may include anemia, fatigue, weight loss, rectal bleeding, loss of appetite, dehydration, malnutrition, skin lesions, joint inflammation, and impaired growth, particularly in children. Only some patients diagnosed with Ulcerative pancolitis experience symptoms; others may occasionally suffer from fever, diarrhea with bleeding, nausea, and severe abdominal pain. Ulcerative pancolitis typically presents with nonspecific symptoms such as abdominal distension or pain throughout the colon. The main symptoms of Ulcerative pancolitis include abdominal pain accompanied by bloody diarrhea (referred to as melena) with mucus- lined streaks. This abdominal pain tends to improve after defecation. As the disease progresses, constipation may also develop. At mild stages, patients may experience loose stools, abdominal cramps, and diarrhea. The disease can progress from mild to severe, characterized by symptoms such as weight loss, fatigue, and decreased appetite. Decreased appetite can lead to nutritional deficiencies, mucus in the stool, severe rectal bleeding, fever, and anemia. In severe cases, symptoms often include high fever, significant weight loss, and may also present with symptoms like high fever, tachycardia, andpostural hypotension. (Lynch, 2024)

Case Presentation

The patient was referred from RS Islam and presented to the Emergency Department of RSUD Ulin with complaints of liquid bowel movements (diarrhea) persisting for the past month, worsening over the last 7 days. The diarrhea has been continuous, occurring more than 7 times a day, with a watery consistency and a brownish color. About a week ago, there was blood mixed with the stool, but this has since resolved. The stool does not contain visible mucus, blackish coloration, or solid particles. During bowel movements, the patient often experiences sudden cramping and pain, which feels gripping and can persist after defecation. Based on these symptoms, the

patient's condition appears consistent with a flare-up or exacerbation of ulcerative colitis, characterized by increased frequency of watery diarrhea, abdominal cramping, and a recent history of rectal bleeding. It is crucial for the medical team to assess and manage this acute phase to prevent complications and improve the patient's condition. The patient also experiences a decreased appetite, especially noticeable over the past 2 weeks, which has resulted in weight loss as indicated by looser fitting clothes, although the patient has not weighed themselves. The patient prefers to eat only soft foods or drink milk. Meals consist of only consuming 3-4 spoonfuls, or half a glass of milk caused the patient's body to feel weak. The patient also experienced nausea and vomiting during their previous hospitalization. The vomit contained mucus and occurred 2-3 times a day. There was no presence of blood or undigested food in the vomit. Additionally, the patient has been feeling pain in the upper abdomen, which does not radiate to other parts of the abdomen. In the past month, the patient has experienced a decrease in urinary frequency, now urinating only 2-3 times a day, with a small volume per void, sometimes requiring straining to empty the bladder fully. There is no sensation of incomplete emptying, pain during urination, burning sensation, blood in urine, or sandy texture in urine. For the past 2 days, the patient has used a catheter for urination. Other complaints such as lower back pain, fever accompanied by chills, are denied. The patient also denies experiencing other systemic symptoms such as headache, shortness of breath, or cough.

The patient was recently hospitalized at RS Islam for 5 days and subsequently referred for additional evaluation and management. They deny a history of diabetes mellitus and hypertension, as well as any previous trauma or malignancy, particularly involving the intestines. This medical history details the recent hospitalization and indicates the absence of chronic conditions such as diabetes or hypertension, along with no known history of intestinal trauma or malignancy. There is no family history of

similar complaints among the patient's relatives, including diabetes mellitus, hypertension, or malignancy.

Physical Examination

In physical examination, the patient appears moderately unwell with a focused and alert mental status (E4V5M6). They weigh 45 kg and stand at 160 cm tall, indicating an underweight status with a BMI of 17.57 kg/m². Vital signs show stable blood pressure at 120/60 mmHg, a slightly elevated pulse rate of 100 beats per minute, a respiratory rate of 22 breaths per minute, and a normal temperature of 37.2°C. Oxygen saturation levels are 98% on room air, and the patient reports minimal pain with a Visual Analog Scale (VAS) reading of 1-2.

Figure 1. Geriatric patient with IBD complications

Upon examination, the patient's head is normocephalic with predominantly black hair interspersed with white. Their eyes show no conjunctival pallor or icteric sclera. Sunken eyes are noted. In the mouth, dry mucous membranes of the lips are present, along with a coated tongue covered with pseudomembrane on the oral mucosa. There is no gum bleeding, stomatitis, typhoid tongue, or inflammation or enlargement of the tonsils. Examination of the neck reveals no enlargement of cervical lymph nodes or the thyroid gland. The jugular venous pressure is measured at 5+2 cmH2O. Upon abdominal examination, the patient's abdomen appears supple, devoid of visible veins, stretch marks, bruises, or umbilical hernia. Bowel sounds are audible at a rate of 12 per minute. Palpation reveals tenderness upon pressure in the epigastric region. The liver and spleen are non-palpable, and skin turgor returns slowly. Percussion reveals no shifting dullness or palpable fluid waves. On rectal toucher, the anal sphincter tone is strong, and the mucosa feels smooth. Hemorrhoids are palpable at

approximately 2 cm in size at the 11 o'clock position. There is no palpable mass or immobile mass detected, and there is no pain upon movement. No melena is observed, and the stool is liquid in consistency with no visible blood. The upper pole of the prostate gland is not palpable.

Supporting Examination

Upon routine blood laboratory examination, the patient shows findings of anemia, hypoalbuminemia, elevated urea and creatinine levels, hypernatremia, and increased SGOT levels. Analysis of stool samples reveals positive findings for benzidine, Gram-negative bacteria, mucus, erythrocytes, leukocytes, and Entamoeba histolytica. Urinalysis indicates cloudy appearance, 2+ protein-albumin, faint 2+blood, positive nitrites, 1+ leukocytes, 3+ crystals, and 3+ bacteria.

The EKG interpretation reveals sinus rhythm with a normal frontal axis. The heart rate is 102 beats per minute, and the rhythm is regular. The PR interval measures 0.12 seconds, and there are no visible P waves suggestive of mitral or pulmonary P waves. The duration of the P wave is 0.08 seconds, and the QRS complex duration is 0.08 seconds, with no evidence of right bundle branch block (RBBB) or left bundle branch block (LBBB). R-R intervals are regular, and there are no significant ST segment elevations, depressions, or T wave inversions observed. There is no evidence of atrial enlargement based on the EKG findings.

The chest X-ray, taken in anteroposterior projection with the patient in maximum inspiration, reveals normal findings with no tracheal deviation or cardiac enlargement observed. Both the right costophrenic sinus and left cardiophrenic sinus appear sharp. There are no signs of consolidation, thickening in the left hilum, or abnormal bronchovascular markings, and no air-fluid levels are noted. Soft tissue appears normal without swelling, and bones are intact. Overall, the impression from the chest X-ray is that the heart and lungs are within normal limits, indicating no significant abnormalities in these areas. The abdominal ultrasound reveals bilateral grade 2

hydronephrosis and prostatic enlargement. No distinct colorectal mass is visualized, and there is no evidence of intrahepatic metastasis. Furthermore, there is no enlargement detected in the paraaortic or parailiac lymph nodes. Radiologically, the liver, gallbladder, spleen, and pancreas appear normal. These findings suggest urinary and prostatic abnormalities without significant colorectal or metastatic lesions, with normal appearances of the abdominal organs on imaging.

In the bacterial culture examination, no aerobic bacterial growth was detected. Colon in loop examination suggests a suspected filling defect in the rectum due to a mass, and multiple urinary bladder stones are also suspected. Additionally, the colonoscopy findings indicate pancolitis ulcerative and internal hemorrhoids.

Geriatric Assesment

Based on geriatric assessment that the RAPUH questionnaire, the patient is assessed as frail with a score of 4. The FRAILTY assessment indicates severe frailty with a score of 7. Activities of Daily Living (ADL) assessment shows complete dependency with a score of 3, while Instrumental Activities of Daily Living (IADL) indicate total dependency with a score of 0. The Mini COG and Mini- Mental State Examination could not be evaluated. The Mini Nutritional Assessment reveals malnutrition with a score of 9. The Risk Fall Assessment indicates a high risk with a score of 10. The Geriatric Depression Scale was unable to be evaluated. The Charlson Comorbidity Index indicates significant comorbidities with a score of 4 (53%). The Norton scale assesses a high risk of pressure ulcers with a score of 11. The Performance Scale (ECOG) indicates complete inability to perform self-care activities.

Diagnosis and Management

Based on the anamnesis, physical examination, and diagnostic tests, the diagnosis for this patient is Chronic Inflammatory Diarrhea with mild to moderate dehydration, possibly due to Ulcerative pancolitis. This is accompanied by leukocytosis, leukocyturia, erythrocyturia, mild anemia, elevated liver enzymes, benign

prostatic hyperplasia (BPH), candidiasis oral, and geriatric issues such as inanition, immobility, infection susceptibility, and frailty.

The management provided at Tulip rooms RSUD Ulin Banjarmasin includes both non- pharmacological and pharmacological interventions. Non-pharmacologically, the patient is on a diet of Gold Sure milk 2x100 ml, egg custard 2x1, and fruit juice 2x1 to aid nutritional and hydration recovery. Pharmacologically, IV fluids consisting of Gabaxa + D5% 400 ml and Aminofusin Hepar are administered to address dehydration. Additionally, Kalbamin therapy at a rate of 1500 ml per day for 3 days is initiated for managing mild anemia. Antibiotic treatment includes Inj. Moxifloxacin 1x400 mg and Inj. Ceftrazidime 1x1 gr to combat infections. Lansoprazole drip at 6 mg per hour is given to reduce gastric acid production. Oral medications such as Curcuma 3x1, Zinc 20 mg 1x1, Vitamin A 6000 IU 1x1, Probiotic 2x1 sachets, Nystatin Drop 4x4 ml, Attapulgite 2 tablets for diarrhea, and Decubal ointment 2x1 are also administered for comprehensive care.

Discussion

The main symptoms of Ulcerative pancolitis include diarrhea, rectal bleeding, tenesmus, presence of mucus, and abdominal pain. While Ulcerative pancolitis can manifest acutely, symptoms typically develop over weeks to years. Sometimes diarrhea and bleeding are

infrequent and mild, causing patients to delay seeking treatment. Extraintestinal manifestations may include fever, anemia, arthralgia, weight loss, and involvement of the eyes (such as episcleritis, uveitis) and erythema nodosum. (Vavricka *et al.*, 2015; Yang *et al.*, 2018)

Medical therapy for Ulcerative pancolitis includes corticosteroids, amino salicylates, and immunosuppressants. (Djojoningrat, 2015) Antibiotics may be used to eliminate pro- inflammatory agents. Glucocorticoids are the preferred medications for Crohn's disease and moderate to severe ulcerative colitis. Prednisone,

methylprednisolone, or steroid enemas are commonly prescribed. In severe cases, parenteral corticosteroids are administered. (Xu, 2016; Greuter, 2019)

Surgical therapy is considered when conservative or medical treatments fail, or when there are severe side effects, perforation, peritonitis, sepsis, massive bleeding, or signs of severe dysplasia or cancer. (De Nunzio, 2016; Kranz *et al.*, 2024)

Malnutrition often occurs in patients with Ulcerative pancolitis due to decreased food intake, loss of nutrients through diarrhea, and increased nutritional needs during inflammatory phases. A balanced diet is crucial for these patients, focusing on easily digestible foods and dividing intake into several small meals throughout the day. In this case, the patient is receiving a diet that includes Gold Sure milk 2x100 ml, egg pudding 2x1, and fruit juice 2x1, aimed at providing essential nutrients and supporting nutritional management amidst the challenges posed by ulcerative colitis. (Djojoningrat, 2015)

The patient also experiences mild to moderate dehydration and is receiving several types of fluids to support their condition. Gabaxa + D5% 400ml contains gabapentin, commonly used to treat neuropathic pain, epilepsy, and other neurological disorders. D5% solution is a 5% glucose solution administered intravenously to provide fluids and glucose to the patient. Asering 1000ml/24 hours is an electrolyte solution containing sodium, potassium, and chloride, used to replace fluids and electrolytes lost due to dehydration or other fluid losses. The administration of these medications and solutions aims to manage pain, support nutritional recovery, replace fluids and electrolytes, and manage inflammation in patients with conditions such as Ulcerative pancolitis that may involve neurological disturbances, nutritional deficiencies, or inflammation. (Djojoningrat, 2015)

Leukocytosis, leukocyturia, and erythrocyturia are indicative of inflammation within the urinary system. When these three symptoms occur together, they often signify an

infection in the lower urinary tract, such as in the bladder or urethra. Leukocytosis refers to an elevated count of white blood cells in the blood, which is the body's response to infection or inflammation. Leukocyturia, the presence of leukocytes in the urine, also indicates inflammation or infection in the urinary system. Erythrocyturia, the presence of red blood cells in the urine, may indicate bleeding within the urinary tract. (Finnerup *et al.*, 2016)

Normocytic normochromic anemia, characterized by red blood cells that are normal in size and hemoglobin content but reduced in quantity, can serve as a chronic marker in ulcerative colitis. Ulcerative colitis, a form of inflammatory bowel disease (IBD), often causes chronic bleeding in the large intestine and rectum, leading to iron deficiency and anemia. This is attributed to various mechanisms, including chronic inflammation, ulceration of the intestinal walls, and ongoing blood loss. (Lichtenstein, 2006)

Benign Prostatic Hyperplasia (BPH) in this patient is most likely age-related. BPH is a condition where the prostate gland enlarges non-cancerously in older men. Advanced age is a primary risk factor for the development of BPH, with its prevalence increasing with age. Aging processes lead to hormonal changes in the male body, including increased levels of dihydrotestosterone (DHT), which can stimulate prostate growth. In addition to age, other factors contributing to BPH development may include family history, genetic factors, and exposure to certain hormones. (Kranz *et al.*, 2024)

Candidiasis oral is a fungal infection caused by Candida albicans or other Candida species affecting the mucous membranes of the mouth and throat. Several risk factors for oral candidiasis include antibiotic use, weakened immune system, inhalation steroid use, diabetes mellitus, and other medical conditions that affect the immune system. A common therapy for oral candidiasis is nystatin, an effective antifungal agent used to treat Candida fungal infections in the mouth and throat. The patient has been prescribed nystatin drops 4x4ml as part of their treatment regimen. (Lyu, 2016)

Frailty and immobility are common conditions among elderly individuals, often arising from chronic illness, physical weakness, or loss of motivation. Immobility restricts physical movement due to reasons such as injury, chronic illness, or physical weakness, leading to decreased bodily function, reduced quality of life, and increased risks of complications such as vascular and pulmonary diseases. Infections are prevalent among the elderly due to a weakened immune system with age, making them vulnerable to conditions like urinary tract infections, pneumonia, or skin infections, which can significantly impact their health and quality of life if not promptly addressed. Frailty is a complex condition characterized by physical weakness, cognitive decline, and vulnerability to physical or psychological stress. It often results from various factors including aging, chronic diseases, and social isolation or lack of emotional support. Frail individuals are at higher risk for adverse events such as falls, dependency, and mortality. (Clegg, 2013)

Managing geriatric problems often involves a multidisciplinary approach that includes medical care, physical rehabilitation, social support, and lifestyle modifications. It is crucial to conduct a comprehensive evaluation of each individual experiencing geriatric issues and design a tailored treatment plan according to their needs. The goal is to enhance quality of life and minimize the risk of complications through coordinated efforts across various healthcare disciplines. (Rohatinsky *et al.*, 2024)

Conclusions

It has been reported that an 84-year-old male patient with Chronic inflammatory diarrhea, dehydration, and other health issues, anemia, liver problems, BPH, and malnutrition.

The patient received intravenous fluids, antibiotics (Moxifloxacin and Ceftrazidime), medications to reduce stomach acid (Lansoprazole), and supplements (zinc, vitamin A, probiotics). He was also given medication to treat diarrhea (Attapulgite) and a skin ointment (Decubal). This case

demonstrates the complexity of chronic inflammatory bowel disease in elderly patients, frequently complicated by multiple underlying conditions. A comprehensive strategy for diagnosis and management is essential to achieve optimal patient results.

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Reffernce

Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013) Frailty in elderly people, *Lancet*, p*(London, England)*, *381*(9868), 752–762 doi: https://doi.org/10.1016/S0140-6736(12)62167-9.

De Nunzio, C., Presicce, F., & Turabo, A. (2016). Inflammatory mediators in the development and progression of benign prostatic hyperplasia. *Nature Reviews Urology*, 13(10), 613–626. doi: https://doi.org/10.1038/nrurol.2016.168.

Djojoningrat, D. (2015) *Inflammatory Bowel Disease Buku Ajar Ilmu Penyakit Dalam* Dalam: Setiati S, Alwi I, Sudoyo AW, Simadibrata M, Setiyohadi B, Syam AF, editor (penyunting). Buku Ajar Ilmu Penyakit Dalam. Edisi ke-6. Jakarta: Interna Publishing; hlm 1814-22.

Fauzi, M. F. A., Irawan, M. R., Safitri, N. A., et al. (2023) 'Studi Literatur: Patofisiologi, Diagnosis Dan Penatalaksanaan Kolitis Ulseratif', *Jurnal Ilmu Kedokteran dan Kesehatan*, 10(12), pp. 3496–3503.

Finnerup, N.B., Attal, N., Haroutounian, S., McNicol, E, Baron, R., Dworkin, R. H., Gilron, I., Haanpää, M., Hansson, P., Jensen, T. S., Kamerman, P. R., Lund, K., Moore, A., Raja, S. N., Rice, A. S., Rowbotham, M., Sena, E., Siddall, P., Smith, B. H., & Wallace, M. (2015). Pharmacotherapy for Neuropathic Pain In Adults: A Systematic Review and Meta-analysis. *The Lancet. Neurology*, *14*(2), 162–173. doi: 10.1016/S1474-4422(14)70251-0.

Greuter, T & Vavricka, S. R. (2019) Extraintestinal manifestations in inflammatory bowel disease - epidemiology, genetics, and pathogenesis., Expert Review of Gastroenterology & Hepatology, 13(4), 307-317. https://doi.org/10.1080/17474124.2019.1574569

Khan, I. A. Yousaf, S., Anwar, T., Ali, M., Sarfraz, M., & Mohsin, A. (2020). Characteristics and Associations Of Ulcerative Pancolitis in Pakistani Population. The Professional Medical Journal, 27(05), 1079-1084. doi: 10.29309/TPMJ/2020.27.05.4446.

Khoshnevisan, R. Vakili, F., Klein, C., Kotlarz, D., Nasirian, M., Sherkat, R., … & Rezaei, A. (2019). An Analysis And Survey Of Interleukin-10 Receptor Mutation In Inflammatory Bowel Disease (IBD) In The First Iranian IBD cohort. Journal of Laboratory Medicine, 43(4), 185-189. https://doi.org/10.1515/labmed-2019-0005.

Kranz, J. Bartoletti, R., Bruyère, F., Cai, T., Geerlings, S., Köves, B., Schubert, S., Pilatz, A., Veeratterapillay, R., Wagenlehner, F. M. E., Bausch, K., Devlies, W., Horváth, J., Leitner, L., Mantica, G., Mezei, T., Smith, E. J., & Bonkat, G. (2024). European Association of Urology Guidelines on Urological Infections: Summary of the 2024 Guidelines. *European urology*, *86*(1), 27–41. doi: 10.1016/j.eururo.2024.03.035.

Lichtenstein G.R., Abreu M.T., Cohen R, Tremaine, W,. (2006). American Gastroenterological Association Institute Technical Review on Corticosteroids, Immunomodulators, and Infliximab in Inflammatory Bowel Disease, *Gastroenterology, 130(3), 940–987. https://doi.org/10.1053/j.gastro.2006.01.048*

Lyu, X., Zhao, C. and Yan, Z. (2016) 'Efficacy of nystatin for the treatment of oral candidiasis : a systematic review and meta-analysis. *Drug design, development and therapy*, *10*, 1161–1171. https://doi.org/10.2147/DDDT.S100795

Lynch, W.D.& Hsu, R. (2024) *Ulcerative Colitis*. StatPearls Publishing. https://pmc.ncbi.nlm.nih.gov/articles/PMC8002778/

Rohatinsky, N. *et al.* (2024) Older Adults With Inflammatory Bowel Disease In Canada. Gastroenterology Nursing, 47(1), 41–51. doi: 10.1097/SGA.0000000000000776.

Vavricka, S. R. Schoepfer, A., Scharl, M., Lakatos, P. L., Navarini, A., & Rogler, G. (2015). Extraintestinal Manifestations of Inflammatory Bowel Disease. *Inflammatory bowel diseases*, *21*(8), 1982–1992. doi: 10.1097/MIB.0000000000000392.

Xu, X.M and Zhang, H. (2016) miRNAs as new molecular insights into inflammatory bowel disease: Crucial regulators in autoimmunity and inflammation. *World journal of gastroenterology*, *22*(7), 2206–2218. doi: 10.3748/wjg.v22.i7.2206.

Yang, B. Choi, N. K., Kim, M. S., Chun, J., Joo, S. H., Kim, H., … & Lee, J. (2018). Prevalence of Extraintestinal Manifestations in Korean Inflammatory Bowel Disease Patients. Plos One, 13(7), e0200363. https://doi.org/10.1371/journal.pone.0200363

Yücel, İ. (2023) *Health and Technology Journal (HTechJ)*, *1*(5), 455–460. https://doi.org/10.53713/htechj.v1i5.95