TOMASZEWSKA, Wiktoria Maria, SIUDZIŃSKI, Pawel, ŁYKO, Mateusz, SKOCZYLAS, Alicja, KURASZ, Jakub, MAJ, Wojciech, PODLASIEWICZ, Wiktoria, PALA, Katarzyna, DUDZIAK, Piotr, NOWAK, Anna and GOLIŃSKA, Maria. The Role of Vitamin D in the Pathomechanism of Inflammatory Bowel Disease (IBD) and its Therapeutic Implications - a literature review. Journal of Education, Health and Sport. 2025;77:56782. eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.77.56782
https://apcz.umk.pl/JEHS/article/view/56782

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 08.12.2024. Revised: 15.01.2025. Accepted: 17.01.2025. Published: 18.01.2025.

The Role of Vitamin D in the Pathomechanism of Inflammatory Bowel Disease (IBD) and its Therapeutic Implications - a literature review

Authors:

Wiktoria Tomaszewska [WT] - corresponding author

University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0005-6166-1659

e-mail: wiktomaszewska@o2.pl

Paweł Siudziński [PS]

University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0002-4476-9412

e-mail: pawelsiudzinski99@gmail.com

Mateusz Łyko [MŁ]

University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0009-2530-2789

e-mail: matlyk@wp.pl

Alicja Skoczylas [AS]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID:0009-0002-2185-5406
e-mail: alicjasko1999@gmail.com
Jakub Kurasz [JK]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0004-3955-1552
e-mail: jakubkurasz30@gmail.com
Wojciech Maj [WM]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0003-2869-3718
e-mail: Rottel45@gmail.com
Wiktoria Podlasiewicz [WP]
Wroclaw Medical University wybrzeże Ludwika Pasteura 1, 50-367 Wrocław
ORCID: 0009-0001-6578-5297
e-mail: wiktoria.podlasiewicz@student.umw.edu.pl
Katarzyna Pala [KP]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0004-0787-3872
e-mail: kaspal109@gmail.com
Piotr Dudziak [PD]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0000-6173-740X
e-mail: piotr-dudziak@outlook.com
Anna Nowak [AN]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0005-8833-1107
e-mail: anulla1008@gmail.com
Maria Golińska [MG]
University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0008-2772-6131
e-mail: maria.golinska99@gmail.com

ABSTRACT

Introduction: Vitamin D holds a crucial role in the pathogenesis of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). Its mechanisms of action involve immune system modulation, specifically by reducing the production of pro-inflammatory cytokines, such as IL-6 and TNF-α, while enhancing the levels of anti-inflammatory cytokines, such as IL-10. Furthermore, vitamin D contributes to the maintenance of intestinal barrier integrity by strengthening epithelial tight junctions. It also exerts a beneficial influence on the intestinal microbiota, promoting the proliferation of beneficial bacterial species, such as Faecalibacterium prausnitzii, which play a role in mitigating disease relapses and sustaining immune homeostasis. Although vitamin D supplementation demonstrates potential in reducing inflammation and improving clinical outcomes, the observed effects remain varied and require further investigation.

Aim: The purpose of this study was to analyze the mechanisms of action of vitamin D in the context of the pathogenesis of inflammatory bowel disease (IBD) and its potential therapeutic applications, with particular emphasis on clinical studies evaluating vitamin D supplementation.

Material and methods: The data was analyzed from peer-reviewed articles available in the PubMed and JoEHaS databases, covering research on the study topic from the past seven years. Particular focus was given to publications emphasizing the role of vitamin D in the pathomechanism of inflammatory bowel diseases, with priority placed on its significance in immune system regulation and its impact on the intestinal microbiome.

Conclusion: Vitamin D plays a significant role in the pathogenesis of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). A deficiency of this vitamin is associated with an increased risk of disease activity, a higher frequency of relapses, and a worse clinical outcome. Vitamin D, acting through the VDR receptor, regulates immune mechanisms, promotes intestinal barrier function, and positively influences the intestinal microbiota, which can mitigate inflammation and improve the overall course of the disease. Further research is required to ascertain the potential therapeutic benefits of vitamin D supplementation in IBD. In particular, there is a need to optimize vitamin D supplementation strategies, including the determination of the optimal dosage, forms of

administration for IBD patients. The formulation of precise therapeutic recommendations and the determination of the long-term effects of supplementation could facilitate improvements in patients' quality of life and the efficiency of treatment for these chronic inflammatory diseases.

Keywords

Inflammatory bowel diseases (IBD), Crohn's disease (CD), ulcerative colitis (UC), vitamin D, supplementation, intestinal microbiome, immunomodulatory activity.

1. Introduction

Vitamin D, although traditionally classified as a vitamin, functions in the body as a fat-soluble steroid hormone and exists primarily in two forms: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Vitamin D2 is derived primarily from plant sources, including sun-dried mushrooms and yeast, whereas vitamin D3 is obtained from animal products, such as fatty fish, or is synthesized in the skin upon exposure to ultraviolet B (UVB) radiation [1, 2]. The majority of vitamin D in the human body originates from D3, which is produced through the conversion of 7-dehydrocholesterol, a cholesterol derivative, into previtamin D3 and subsequently into vitamin D3 under the influence of UVB radiation [1,2]. A number of factors, including age, skin pigmentation, sunscreen use, geographical location, and seasonal variations, have been demonstrated to significantly impact the cutaneous synthesis of vitamin D. Studies have shown that older individuals and those with darker skin produce less vitamin D under the same UVB exposure [3, 4]. Furthermore, the use of sunscreen and reduced sunlight availability during winter months or at higher latitudes have been demonstrated to significantly decrease vitamin D synthesis. The production of vitamin D is more effectively stimulated by brief, frequent exposure to sunlight than by prolonged, infrequent exposure [2].

In the human body, vitamin D3 binds to vitamin D-binding protein (VDBP) in the bloodstream, where it undergoes two hydroxylation steps to become biologically active. The initial conversion of vitamin D3 to 25-hydroxyvitamin D [25(OH)D], the primary circulating form of the vitamin, is mediated by the cytochrome P450 enzyme CYP2R1 in the liver. The second hydroxylation step occurs in the kidneys, where the enzyme 1α-hydroxylase (CYP27B1) converts 25(OH)D into its active form, 1,25-dihydroxyvitamin D [1,25(OH)$_2$D],

also known as calcitriol. This active form of vitamin D binds to the vitamin D receptor (VDR), which is expressed in various tissues, including the skin, intestines, and immune cells. This binding regulates the expression of over 1,000 genes essential for cellular processes [1, 4].

The metabolism of vitamin D is subject to strict regulation through feedback mechanisms, with parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23) serving as pivotal mediators. PTH stimulates the production of active vitamin D in response to hypocalcemia, whereas FGF23 inhibits CYP27B1 activity, thereby regulating phosphate levels and preventing excessive vitamin D activation. In conclusion, both 25(OH)D and $1,25(OH)_2D$ are metabolized into calcitriol, which is excreted via the kidneys or bile [5].

2. Multidirectional effects of vitamin D

2.1. Role in phosphate-calcium metabolism

Vitamin D plays a pivotal role in calcium and phosphate metabolism, facilitating the absorption of these minerals in the intestines and bone mineralization. It facilitates the formation of osteoclasts, which are responsible for bone resorption, and preserves the equilibrium of minerals essential for skeletal health [6]. In this process, the active form of vitamin D, 1,25-dihydroxycholecalciferol (calcitriol), acts through the vitamin D receptor (VDR), which regulates the expression of genes related to calcium transport in intestinal epithelial cells. Calcitriol has been demonstrated to enhance the synthesis of proteins, including calbindin-D9k and calbindin-D28k, which are instrumental in the transport of calcium by enterocytes into the bloodstream. Additionally, vitamin D induces calcium ATPase activity, facilitating the efficient removal of calcium from the cell into the bloodstream.

The calcium-phosphate balance controlled by vitamin D affects many body systems. In addition to bone health, vitamin D modulates the function of the nervous, cardiovascular and immune systems. Disruption of this balance can lead to serious complications such as hypocalcemia and increased risk of fractures[7, 8].

2.2. Immunomodulatory activity of vitamin D

Vitamin D (VD) has been demonstrated to possess notable immunomodulatory properties, influencing both innate and adaptive immunity. Its active form, 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], binds to the vitamin D receptor (VDR), which is present in numerous cells of the immune system, including macrophages, dendritic cells (DCs), and lymphocytes. VDR activation regulates gene transcription, which plays a pivotal role in maintaining immune equilibrium and preventing the inflammatory processes characteristic of autoimmune disorders such as inflammatory bowel disease (IBD) [9, 10].

2.3. The function of vitamin D in innate immunity

With regard to innate immunity, vitamin D has been demonstrated to stimulate the production of antimicrobial peptides, including cathelicidin (CAMP) and defensin β2 (DEFB4). These peptides demonstrate a broad spectrum of antimicrobial activity, thereby enhancing mucosal immunity. Moreover, the activation of TLR2/1 receptor heterodimers has been demonstrated to increase VDR expression and intensify the production of antimicrobial peptides, thereby enhancing the immune response against infection [11].

Vitamin D also promotes the expression of pathogen recognition receptors, such as NOD2, which increases the sensitivity of the immune system to microbial ligands and supports the transcription of CAMP and DEFB4. As a result, the body eliminates pathogens more effectively. Moreover, vitamin D reduces hepcidin expression, limiting iron availability, which prevents the growth of microorganisms that depend on iron metabolism [9, 10, 11].

2.4. The function of vitamin D in acquired immunity

With regard to acquired immunity, vitamin D affects the differentiation of dendritic cells (DCs), promoting their tolerogenic phenotype. This reduces the ability of DCs to stimulate T lymphocytes and produce pro-inflammatory cytokines such as IL-12. Vitamin D alters the response profile of T lymphocytes, reducing the activity of Th1 lymphocytes, responsible for the pro-inflammatory response, and promotes the development of Th2 lymphocytes, which secrete anti-inflammatory cytokines such as IL-4 [9, 12].

Furthermore, vitamin D has been demonstrated to stimulate the production of regulatory T cells (Treg), which play a pivotal role in suppressing excessive immune responses and maintaining immune tolerance [12]. It also modulates cytokine production by increasing levels of IL-10, which is known for its anti-inflammatory properties, while simultaneously inhibiting the secretion of pro-inflammatory cytokines such as TNF-α and IFN-γ. By virtue of these mechanisms, vitamin D mitigates the likelihood of chronic inflammation, which is a fundamental underlying factor in numerous autoimmune and inflammatory diseases, including IBD [10].

2.5. The role of vitamin D in maintaining the integrity of the intestinal epithelial barrier and in regulating the composition of the intestinal microbiota

Vitamin D plays a pivotal role in maintaining the integrity of the intestinal barrier and modulating the composition and functionality of the intestinal microbiota, which is crucial in the context of inflammatory bowel disease (IBD) and other gastrointestinal disorders.

The intestinal barrier serves to separate the internal and external environments of the body, thereby protecting the host from antigens and harmful bacteria. A deficiency in this function can result in increased intestinal permeability, which in turn may lead to heightened inflammation and immune responses. Vitamin D exerts its beneficial effects on the intestinal barrier by regulating the expression of tight junction proteins, including claudins, occludins, and zonula occludens (ZO). These proteins prevent the passage of water and substances through the epithelium, thereby preserving its integrity. A deficiency in vitamin D has been linked to a reduction in the expression of these proteins, which in turn leads to a weakening of the intestinal barrier [1, 13]. Moreover, vitamin D facilitates mucus production, which safeguards epithelial cells from direct contact with intestinal contents, thereby reducing the likelihood of bacterial invasion and immune system activation [13].

Another mechanism of action of vitamin D is its capacity to regulate zonulin, a protein that is responsible for loosening tight junctions. Vitamin D has been demonstrated to reduce the expression of zonulin, which serves to further stabilize the intestinal barrier and prevent its damage [13]. Additionally, experimental studies have demonstrated that vitamin D provides

protection for the epithelium from chemical damage, including that induced by dextran sodium sulfate (DSS) and pro-inflammatory cytokines, such as TNF-α [14].

In the context of the intestinal microbiota, vitamin D plays a pivotal role in regulating its composition and function. One of the defining characteristics of IBD is dysbiosis, or microbial imbalance. This is evident in conditions such as Crohn's disease (CD) and ulcerative colitis (UC). Vitamin D facilitates the proliferation of beneficial bacterial species, including Faecalibacterium prausnitzii and Lactobacillus, which are responsible for the production of short-chain fatty acids (SCFAs), such as butyrate. Short-chain fatty acids (SCFAs) have been demonstrated to support intestinal barrier function and exhibit anti-inflammatory effects [2]. Concurrently, vitamin D diminishes the prevalence of pathogenic microorganisms, including Enterobacteriaceae and Fusobacterium, which are disproportionately represented in individuals with IBD [14].

Furthermore, vitamin D has been demonstrated to stimulate the production of antimicrobial peptides, including cathelicidin and defensin β. These peptides have been shown to directly attack harmful bacteria, preventing their overgrowth and promoting microbial balance within the intestine [13].

3. Pathomechanism of inflammatory bowel diseases

Inflammatory bowel diseases (IBDs), which include Crohn's disease (CD) and ulcerative colitis (UC), are chronic, recurrent conditions that are characterized by inflammation of the gastrointestinal tract. The pathogenesis of these diseases is multifactorial, resulting from a complex interaction of genetic predisposition, environmental factors, immune system dysregulation, and disruption of the intestinal microbiota [15].

Genetic factors are integral to the molecular mechanism of IBD. The NOD2 gene, which plays a pivotal role in microbial pattern recognition and the activation of the immune response, is of particular significance. Mutations in this gene impair the ability to regulate intestinal bacteria, which promotes inflammation, particularly in the ileum in CD. The IL-23R genes, which regulate pro-inflammatory pathways, and ATG16L1, which plays a key role in autophagy, are also of great importance in this context, as they highlight the molecular complexity of IBD. Additionally, epigenetic mechanisms have been demonstrated to exert an

influence on the pathogenesis of IBD [13, 14]. Abnormal DNA methylation and histone modifications, such as those observed in the IL-13 and CXCL5 genes, alter immune responses and the integrity of the intestinal barrier, thereby increasing susceptibility to inflammation [14].

Environmental factors also exert a significant influence on the pathogenesis of inflammatory bowel disease. A diet that is high in fats and refined sugars, in accordance with Western dietary patterns, has been demonstrated to result in disruption of the intestinal microbiota and the promotion of inflammatory processes. Furthermore, smoking has been demonstrated to augment intestinal permeability and impair immune regulation, thereby exacerbating the course of Crohn's disease (CD). The hypothesis that urbanization and limited exposure to microorganisms in early childhood may result in an excessive immune response in later life, thereby increasing the risk of inflammatory bowel disease, is known as the hygiene hypothesis [13]. These environmental factors, in conjunction with genetic predisposition, disrupt the microbial equilibrium of the intestine, which is vital for maintaining gastrointestinal homeostasis [16].

A reduction in microbial diversity, clinically defined as dysbiosis, is a hallmark of inflammatory bowel disease (IBD). Patients with IBD exhibit decreased levels of beneficial bacteria, including Faecalibacterium prausnitzii, which inversely correlate with the severity of inflammation and the risk of relapse. A disruption of the microbiota affects immune regulation and epithelial barrier function, thereby allowing bacteria to penetrate the mucosa and induce chronic activation of the immune system [16, 17]. The intestinal barrier, comprising closely interlinked epithelial cells, mucus layers, and immune system components, plays a pivotal role in averting inflammation. Environmental factors and genetic variants can compromise the integrity of the intestinal barrier, facilitating the penetration of antigens and the subsequent stimulation of an immune response [18, 19].

IBD also demonstrates dysregulation of the immune system, manifested by the overactivation of the type 1 (Th1) and type 17 (Th17) helper T-cell pathways. These pathways generate cytokines, including TNF-α, IL-6, and IL-17, which perpetuate the inflammatory response. Furthermore, the impaired function of regulatory T cells (Treg) presents a challenge in maintaining equilibrium between pro-inflammatory and anti-inflammatory responses [17].

4. The impact of vitamin D on the progression of inflammatory bowel diseases

Inflammatory bowel diseases (IBD) are defined by chronic inflammation, with alternating periods of exacerbation and remission. Vitamin D plays a pivotal role in maintaining immune system homeostasis, particularly at the intestinal level, and exerts a pronounced influence on the pathogenesis of these diseases [6]. The integrity of the intestinal epithelium, which represents the initial line of defense against pathogens, is largely dependent on the presence of vitamin D. Studies have demonstrated that the absence of the vitamin D receptor (VDR) in intestinal epithelial cells is associated with increased colonic inflammation, worsened apoptosis, and augmented Th1 and Th17-type immune responses [20].

Dysbiosis of the intestinal microbiota is a prevalent phenomenon among individuals diagnosed with inflammatory bowel disease (IBD). Patients with Crohn's disease (CD) demonstrate a reduction in the Firmicutes phylum, including Faecalibacterium prausnitzii, and an increase in Proteobacteria and Bacteroidetes. In contrast, the microbiota of UC patients is distinguished by a paucity of butyrate-producing bacteria and an elevated ratio of Bacteroides fragilis to Faecalibacterium prausnitzii, which mitigates the anti-inflammatory response [20]. Vitamin D supplementation has been demonstrated to influence the composition of the microbiota, enriching it with bacteria such as Megasphaera and Lactobacillus in CD patients and Enterobacteriaceae in UC patients. This may contribute to an improved disease course.

Vitamin D plays a pivotal role in modulating the immune response, influencing a shift from a pro-inflammatory (Th1, Th17) to an anti-inflammatory (Th2, Treg) profile. This process entails the inhibition of pro-inflammatory cytokine production (e.g., IL-2, IFN-γ, TNF-α, IL-17, IL-21) and the stimulation of anti-inflammatory cytokine expression (e.g., IL-4, IL-5, IL-10). Additionally, vitamin D interacts with the Wnt/β-catenin signaling pathway, which plays a pivotal role in inflammatory processes. It inhibits the activity of this pathway, thereby reducing inflammatory reactions and promoting regeneration of damaged tissues in IBD [20, 21].

5. The impact of vitamin D deficiency on the progression of inflammatory bowel diseases

A number of studies have indicated that vitamin D deficiency may be a significant contributing factor in the development of autoimmune intestinal diseases, potentially influencing the intestinal microbiota and immune system. This process is complex and multifactorial in nature. Genetic predisposition can influence vitamin D activity, impact intestinal barrier function, and regulate the level of basal immune activation [22]. Vitamin D deficiency results in impaired tightness of the intestinal mucosal barrier, increasing its permeability and thereby promoting excessive immune system activation. In conjunction with disruption of the intestinal microbiota, low levels of vitamin D facilitate the penetration of microorganisms through the damaged epithelium and their interaction with the host immune system, which can ultimately lead to the development of autoimmunity.

Vitamin D deficiency and impaired receptor signaling (VDR), resulting from insufficient dietary vitamin D supply or genetic defects, can disrupt both the structural and functional integrity of the intestinal barrier. This results in bacterial penetration into the deeper layers of the intestine, which in turn stimulates an inflammatory response. In addition to its role in maintaining intestinal barrier function, vitamin D has been demonstrated to influence the activity of immune cells [22].

It is important to note, however, that vitamin D deficiency alone is an inadequate explanation for the development of autoimmunity. Vitamin D serves as a modulating factor for other predispositions, including genetic polymorphisms in the VDR gene, metabolic abnormalities, abnormal intestinal barrier function, and the influence of environmental and dietary factors. In conclusion, the development of autoimmunity is the result of a complex interplay between genetic predisposition and non-genetic environmental factors. Vitamin D deficiency may play a significant role in the exacerbation of existing predispositions through its effects on the microbiota, intestinal epithelial integrity, and immune system regulation.

6. The potential benefits of vitamin D supplementation in the management of inflammatory bowel diseases (IBD).

The potential benefits of vitamin D supplementation in the context of inflammatory bowel disease (IBD) have been the subject of numerous clinical trials. These studies have demonstrated that vitamin D can influence the course of the disease and reduce inflammation. The results demonstrate the various applications of vitamin D in the treatment of patients with Crohn's disease (CD) and ulcerative colitis (UC) [2].

A negative correlation has been demonstrated between serum 25(OH)D levels and disease activity. One study observed that patients with Crohn's disease (CD) and ulcerative colitis (UC) who exhibited higher vitamin D levels demonstrated a reduction in clinical disease activity, as evaluated by indices such as the Crohn's Disease Activity Index (CDAI) and the Mayo Score. A correlation was observed between low vitamin D levels and a more severe disease course, as well as an elevated risk of relapse. The administration of vitamin D has been demonstrated to be efficacious in the reduction of inflammatory markers, including C-reactive protein (CRP) and calprotectin, thereby substantiating its anti-inflammatory properties [23].

Furthermore, research has demonstrated that vitamin D exerts a beneficial impact on the intestinal microbiota of patients diagnosed with Crohn's disease (CD) and ulcerative colitis (UC). In patients with CD, four weeks of supplementation resulted in an enrichment of the microbiome with beneficial bacteria, including Megasphaera and Lactobacillus. In contrast, patients with UC exhibited an increase in Enterobacteriaceae following eight weeks of supplementation [24].

The potential efficacy of vitamin D supplementation in reducing relapse rates is a topic of ongoing investigation. However, the results of these studies are inconclusive due to the heterogeneity of the studies in terms of doses, forms of administration, and duration of intervention. Furthermore, research suggests that vitamin D may enhance the efficacy of biologic therapies, such as anti-TNF-α antibody treatment. Patients with normal vitamin D levels demonstrated a greater likelihood of achieving remission and a reduced incidence of primary loss of response to treatment, suggesting a potential synergistic effect of vitamin D in conjunction with biologic therapies [25].

It is recommended that vitamin D levels be monitored in patients with inflammatory bowel disease (IBD) and that supplementation be provided in cases of deficiency. A dosage of 2,000 IU or more has been demonstrated to be efficacious in elevating vitamin D levels above 30 ng/ml, thereby facilitating improvements in inflammatory parameters such as CRP and fecal calprotectin, and reducing intestinal permeability.

In conclusion, the results of clinical trials indicate that vitamin D may play an important role in modifying the course of IBD by reducing inflammation, improving intestinal barrier integrity and modulating the microbiota. Nevertheless, the inconsistency of findings and the necessity for standardisation of clinical trial protocols highlight the requirement for further investigation in this field [26, 27].

Conclusions

A review of the literature indicates that vitamin D supplementation is a promising avenue for understanding the pathogenesis and potential treatment of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). A paucity of vitamin D has been demonstrated to be significantly associated with elevated disease activity, increased frequency of relapses and diminished clinical outcomes, including an elevated risk of hospitalisation and the necessity for surgical interventions. Vitamin D, via the vitamin D receptor (VDR), modulates pivotal immune functions, reducing the synthesis of pro-inflammatory cytokines such as IL-6 and TNF-α, while enhancing the production of anti-inflammatory cytokines such as IL-10. Furthermore, it reinforces the structure of tight junctions in the intestinal epithelium, thereby reducing the permeability of the intestinal barrier and preventing damage and the subsequent development of inflammation.

It has been demonstrated that vitamin D supplementation can result in a reduction in inflammatory markers, including C-reactive protein (CRP) and faecal calprotectin. Additionally, it has been shown to modulate the composition of the intestinal microbiota by promoting the growth of beneficial bacteria, such as Faecalibacterium prausnitzii. In patients with Crohn's disease (CD) and ulcerative colitis (UC), higher serum 25-hydroxyvitamin D (25(OH)D) levels have been observed to correlate with reduced clinical disease activity, as assessed by indices such as the Crohn's Disease Activity Index (CDAI) and the Mayo Score, as well as a lower incidence of relapses.

Although vitamin D supplementation has been demonstrated to enhance the efficacy of biologic therapies, such as anti-TNF antibody treatment, by increasing the likelihood of remission, its impact on clinical symptoms remains inconclusive, underscoring the necessity for further investigation. It is recommended that vitamin D levels be monitored in patients with IBD and that supplementation be used in doses tailored to individual needs, with the objective of achieving optimal 25(OH)D levels above 30 ng/ml.

In conclusion, although vitamin D appears to be a promising adjunct to IBD therapy, there is still a paucity of high-quality clinical trials that can unequivocally confirm these effects.

Disclosure:

Author's contribution:

Conceptualization: WT, KP

Methodology: KP, PS

Software: WP, WM

Check: AS, AN

Formal analysis: JK, MG

Investigation: MŁ, PD

Resources: WT, AN

Data curation: KP, AS

Writing rough preparation: WT, MŁ

Writing review and editing:WM, WT

Visualization: PS, JK

Supervision: WT,, MG

Project administration: WT

Supplementary Materials: They have not been provided.

Funding Statement: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

All authors have read and agreed to the published version of the manuscript.

References

1. Vernia F, Valvano M, Longo S, Cesaro N, Viscido A, Latella G. Vitamin D in Inflammatory Bowel Diseases. Mechanisms of Action and Therapeutic Implications. Nutrients. 2022 Jan 9;14(2):269. doi: 10.3390/nu14020269. PMID: 35057450; PMCID: PMC8779654.
2. Infantino C, Francavilla R, Vella A, Cenni S, Principi N, Strisciuglio C, Esposito S. Role of Vitamin D in Celiac Disease and Inflammatory Bowel Diseases. Nutrients. 2022 Dec 3;14(23):5154. doi: 10.3390/nu14235154. PMID: 36501183; PMCID: PMC9735899.
3. Mailhot G, White JH. Vitamin D and Immunity in Infants and Children. Nutrients. 2020 Apr 27;12(5):1233. doi: 10.3390/nu12051233. PMID: 32349265; PMCID: PMC7282029.
4. Saponaro F, Saba A, Zucchi R. An Update on Vitamin D Metabolism. Int J Mol Sci. 2020 Sep 8;21(18):6573. doi: 10.3390/ijms21186573. PMID: 32911795; PMCID: PMC7554947.
5. Rusińska A, Płudowski P, Walczak M, Borszewska-Kornacka MK, Bossowski A, Chlebna-Sokół D. Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland-Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies-2018 Update. Front Endocrinol (Lausanne). 2018 May 31;9:246. doi: 10.3389/fendo.2018.00246. PMID: 29904370; PMCID: PMC5990871.
6. Valeria Dipasquale, Giovanna Lo Presti, Gregorio Paolo Milani, Antonio Corsello, Carlo Agostoni, Claudio Romano. Vitamin D in Prevention of Autoimmune Diseases. *Front. Biosci. (Landmark Ed)* 2022, 27(10), 288.
7. Fleet JC. Vitamin D-Mediated Regulation of Intestinal Calcium Absorption. Nutrients. 2022 Aug 16;14(16):3351. doi: 10.3390/nu14163351. PMID: 36014856; PMCID: PMC9416674.
8. Jiang H, Horst RL, Koszewski NJ, Goff JP, Christakos S, Fleet JC. Targeting 1,25(OH)2D-mediated calcium absorption machinery in proximal colon with calcitriol glycosides and glucuronides. J Steroid Biochem Mol Biol. 2020 Apr;198:105574. doi: 10.1016/j.jsbmb.2019.105574. Epub 2019 Dec 24. PMID: 31881310.

9. Battistini C, Ballan R, Herkenhoff ME, Saad SMI, Sun J. Vitamin D Modulates Intestinal Microbiota in Inflammatory Bowel Diseases. Int J Mol Sci. 2020 Dec 31;22(1):362. doi: 10.3390/ijms22010362. PMID: 33396382; PMCID: PMC7795229.
10. Ao T, Kikuta J, Ishii M. The Effects of Vitamin D on Immune System and Inflammatory Diseases. Biomolecules. 2021 Nov 3;11(11):1624. doi: 10.3390/biom11111624. PMID: 34827621; PMCID: PMC8615708.
11. Infantino C, Francavilla R, Vella A, Cenni S, Principi N, Strisciuglio C, Esposito S. Role of Vitamin D in Celiac Disease and Inflammatory Bowel Diseases. Nutrients. 2022 Dec 3;14(23):5154. doi: 10.3390/nu14235154. PMID: 36501183; PMCID: PMC9735899.
12. Bikle DD. Vitamin D Regulation of Immune Function. Curr Osteoporos Rep. 2022 Jun;20(3):186-193. doi: 10.1007/s11914-022-00732-z. Epub 2022 May 4. PMID: 35507293; PMCID: PMC9065668.
13. Battistini C, Ballan R, Herkenhoff ME, Saad SMI, Sun J. Vitamin D Modulates Intestinal Microbiota in Inflammatory Bowel Diseases. Int J Mol Sci. 2020 Dec 31;22(1):362. doi: 10.3390/ijms22010362. PMID: 33396382; PMCID: PMC7795229.
14. Zhang YG, Lu R, Wu S, Chatterjee I, Zhou D, Xia Y, Sun J. Vitamin D Receptor Protects Against Dysbiosis and Tumorigenesis via the JAK/STAT Pathway in Intestine. Cell Mol Gastroenterol Hepatol. 2020;10(4):729-746. doi: 10.1016/j.jcmgh.2020.05.010. Epub 2020 Jun 1. PMID: 32497792; PMCID: PMC7498955.
15. Törüner M, Ünal NG. Epigenetics of Inflammatory Bowel Diseases. Turk J Gastroenterol. 2023 May;34(5):437-448. doi: 10.5152/tjg.2023.22515. PMID: 37158530; PMCID: PMC10334590.
16. Diez-Martin E, Hernandez-Suarez L, Muñoz-Villafranca C, Martin-Souto L, Astigarraga E, Ramirez-Garcia A, Barreda-Gómez G. Inflammatory Bowel Disease: A Comprehensive Analysis of Molecular Bases, Predictive Biomarkers, Diagnostic Methods, and Therapeutic Options. Int J Mol Sci. 2024 Jun 27;25(13):7062. doi: 10.3390/ijms25137062. PMID: 39000169; PMCID: PMC11241012.
17. Battistini C, Ballan R, Herkenhoff ME, Saad SMI, Sun J. Vitamin D Modulates Intestinal Microbiota in Inflammatory Bowel Diseases. Int J Mol Sci. 2020 Dec 31;22(1):362. doi: 10.3390/ijms22010362. PMID: 33396382; PMCID: PMC7795229.
18. Ryan FJ, Ahern AM, Fitzgerald RS, Laserna-Mendieta EJ, Power EM, Clooney AG, O'Donoghue KW, Claesson MJ. Colonic microbiota is associated with inflammation

and host epigenomic alterations in inflammatory bowel disease. Nat Commun. 2020 Mar 23;11(1):1512. doi: 10.1038/s41467-020-15342-5. PMID: 32251296; PMCID: PMC7089947.

19. Stange EF, Schroeder BO. Microbiota and mucosal defense in IBD: an update. Expert Rev Gastroenterol Hepatol. 2019 Oct;13(10):963-976. doi: 10.1080/17474124.2019.1671822. Epub 2019 Oct 11. PMID: 31603356.
20. Santana PT, Rosas SLB, Ribeiro BE, Marinho Y, de Souza HSP. Dysbiosis in Inflammatory Bowel Disease: Pathogenic Role and Potential Therapeutic Targets. Int J Mol Sci. 2022 Mar 23;23(7):3464. doi: 10.3390/ijms23073464. PMID: 35408838; PMCID: PMC8998182.
21. Yamamoto EA, Jørgensen TN. Relationships Between Vitamin D, Gut Microbiome, and Systemic Autoimmunity. Front Immunol. 2020 Jan 21;10:3141. doi: 10.3389/fimmu.2019.03141. PMID: 32038645; PMCID: PMC6985452.
22. Yamamoto E, Jørgensen TN. Immunological effects of vitamin D and their relations to autoimmunity. J Autoimmun. 2019 Jun;100:7-16. doi: 10.1016/j.jaut.2019.03.002. Epub 2019 Mar 8. PMID: 30853311.
23. Szymczak-Tomczak A, Ratajczak AE, Kaczmarek-Ryś M, Hryhorowicz S, Rychter AM, Zawada A, Słomski R, Dobrowolska A, Krela-Kaźmierczak I. Pleiotropic Effects of Vitamin D in Patients with Inflammatory Bowel Diseases. J Clin Med. 2022 Sep 27;11(19):5715. doi: 10.3390/jcm11195715. PMID: 36233580; PMCID: PMC9573215.
24. Wark G, Samocha-Bonet D, Ghaly S, Danta M. The Role of Diet in the Pathogenesis and Management of Inflammatory Bowel Disease: A Review. Nutrients. 2020 Dec 31;13(1):135. doi: 10.3390/nu13010135. PMID: 33396537; PMCID: PMC7823614.
25. Dragasevic S, Stankovic B, Kotur N, Milutinovic AS, Milovanovic T, Stojkovic Lalosevic M, Stojanovic M, Pavlovic S, Popovic D. Genetic Aspects of Micronutrients Important for Inflammatory Bowel Disease. Life (Basel). 2022 Oct 18;12(10):1623. doi: 10.3390/life12101623. PMID: 36295058; PMCID: PMC9604584.
26. Martínez-García RM, Jiménez-Ortega AI, Salas-González MD, Peral-Suárez Á, Ruiz Martínez P. *Role of diet in the prevention and development of Crohn's Disease*. Nutr Hosp. 2024 Sep 23;41(Spec No3):57-61. Spanish. doi: 10.20960/nh.05460. PMID: 39279751.
27. Biłogras, J., Karamus, K., Rejmak, R., Borowska-Łygan, M., Tomaszewski, J., Strużek, K. and Urban, W. 2024. Effect of vitamin D supplementation. Journal of

Education, Health and Sport. 76, (Dec. 2024), 56537. DOI:https://doi.org/10.12775/JEHS.2024.76.56537.