Jurnal Eduhealth
Volume 15, Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

A Review Of IL-17 Relation With Microbiome In Metabolic Disorder

Nuroh Najmi[1], Faisal Kuswandani[2], Anggun Rafisa[3], Falisha Febriane Balafif[4]
[1]Anatomy Pathology, Department of Oral Biology, Faculty of Dentistry Universitas Padjadjaran, [2]Pharmacy, Department of Oral Biology Faculty of Dentistry Universitas Padjadjaran, Indonesia, [3]Physiology, Department of Oral Biology Faculty of Dentistry Universitas Padjadjaran, Indonesia, [4]Microbiology, Department of Oral Biology Faculty of Dentistry Universitas Padjadjaran, Indonesia

Article Info
Keywords:
Il-17,
Microbiome,
Metabolic disorder,
cytokine.

ABSTRACT
The relationship between IL-17 and the microbiome remains an area requiring extensive research. IL-17, a pro-inflammatory cytokine, plays a crucial role in immune function, particularly in its interactions with the microbiome, especially within the intestinal digestive system. In metabolic diseases linked to inflammation, this connection underscores the importance of understanding cytokine activity and the microbiome's response within the body. In this literature review, three articles were retrieved from a single database, exploring the relationship between IL-17, metabolic diseases, and the microbiome.

This is an open access article under theCC BY-NClicense

Corresponding Author:
Nuroh Najmi
Department of Oral Biology, Faculty of Dentistry
Universitas Padjadjaran
Sekeloa Selatan no.1, Bandung- West Java, Indonesia
nuroh@unpad.ac.id

INTRODUCTION

The human digestive tract hosts a highly complex and diverse ecosystem of microorganisms, which play a crucial role in various physiological functions. These include fermenting indigestible food components, producing vitamins, protecting against pathogens, supporting immune system development, and preserving the integrity of the intestinal barrier. Within the gut, microorganisms interact to generate a wide array of metabolites derived from both dietary components and compounds produced by the host and the microbiota themselves. The effects of these microbiota-derived metabolites whether beneficial or harmful depend on the host's condition and overall health. This intricate symbiosis significantly influences human well-being (Alam & Neish, 2003). Some studies reported that gut microbiome correlated with immunity and viral infection for human.

The role of cytokine as proteins spread all over the body affects human health. The interaction between the microbiome and cytokines plays a key role in immune function, as it is linked to the production of tumor necrosis factor-α (TNF-α) and interferon-γ (IFN-γ). Alterations in the composition of the gut microbiome can disrupt its protective mechanisms, increasing the risk of infection. The gut microbiota is integral to maintaining homeostasis (Najmi, et al. 2022). Disruptions in the gut microbial ecosystem have been linked to an increased risk of metabolic and immune-related disorders in both humans and animals. Research has identified molecular interactions that connect the gut microbiota to host energy metabolism, lipid storage, and immune function. How ever, the precise mechanisms by which specific changes in gut microbiota composition contribute to the onset of obesity and

Jurnal Eduhealth
Volume 15, Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

metabolic diseases in humans remain unclear due to the complex nature of these conditions (Boulangé, et al. 2016).

Cytokines as protein can contribute improve and modulation some drugs or treatment for diseases in human body. Interleukin-17 family has been implicated as a group of proinflammatory cytokines in immune mediated diseases in the gut and connective tissue, as well as inflammatory skin conditions, we consider here if it may contribute to the pathogenesis of chronic wounds (Hadian et.al, 2019). Metabolic disorders are an escalating global health concern due to their rapidly increasing prevalence. The gut microbiota plays a pivotal role in interacting with the host by generating a wide array of metabolites, derived from either dietary sources or endogenous compounds. Alterations in the composition and functionality of the gut microbiota have been linked to metabolic disorders. Interestingly, the microbiome of the gut shares similarities with that of the oral cavity. The oral microbiome is associated with both local and systemic diseases, yet it is less frequently studied in microbiome research compared to fecal samples. There remains a significant gap in understanding the parallels and distinctions between the oral and gut microbiomes, as well as their potential interactions and mutual influences (Agus et al, 2020; Maki, et al. 2020). Currently, the role of proinflammatory cytokines, such as IL-17, and their relationship with the microbiome in metabolic disorder particularly diabetes and obesity correlated with oral health remains underexplored. Therefore, the author aims to provide a review highlighting the role and impact of IL-17 and the microbiome on metabolic disorders, while also examining their connection to oral health.

METHODS

This study conducted a literature review and article search using the PubMed database. The search utilized specific keywords, including [Il-17 and microbiome and metabolic disorder]. The article selection process followed the guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol. The process involved removing duplicate articles and further refining the selection to include studies published between 2019 and 2024, and those published in English. Book sections, studies involvoing animals, review articles, and conference proceedings were excluded. Data extraction encompassed a range of variables such as author names, article titles, publication years, study designs.

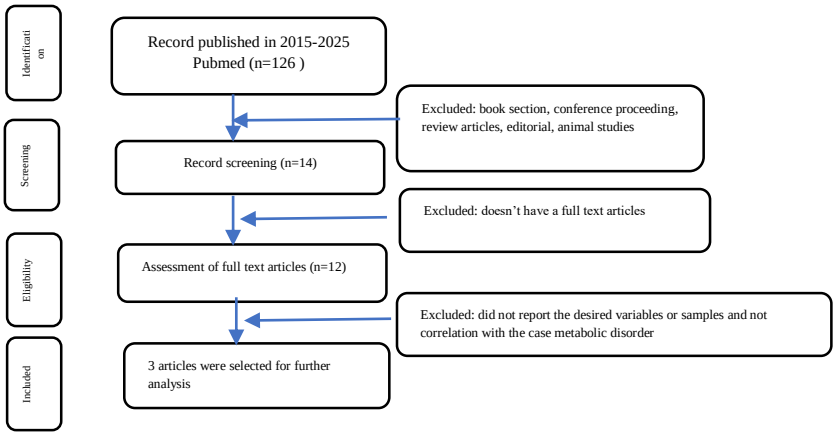

Figure 1. The article selection process flow diagram

Jurnal Eduhealth
Volume 15, Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

RESULTS AND DISCUSSION

The article selection process is outlined in Figure 1. a total of 126 articles were initially identified through the designated keywords in PubMed from 2015-2025. After meticulous removal of duplicate articles and application of the inclusion and exclusion criteria, 9 articles met the study's eligibility criteria. Table 1 provides a summary of the extracted data from the selected studies.

Table 1 Data extracted from included studies

No	Authors/ year	Title	Methods	Result
1	Li et al. / 2020	Periodontitis in elderly patients with type 2 diabetes mellitus: impact on gut microbiota and systemic inflammation	Patients with T2DM, with or without periodontitis, were enrolled in the study by their physicians. Patients provided fecal and blood samples. Measurement biochemistry and cytokine inflammation and 16S rRNA gene tag sequencing	34 identified key gut microbiota markers that distinguished participants with **different** periodontal conditions, **25 taxa were correlated with duration of diabetes**, dry mouth or the peripheral levels of pro-inflammatory cytokines (e.g., tumor necrosis factor-α, interferon-γ, prostaglandin E2, **interleukin-17**, and interleukin-6) and metabolic parameters (e.g., hemoglobin A1c), respectively.
2	Pircalabioru et al. / 2023	Impact of COVID-19 on the Microbiome and Inflammatory Status of Type 2 Diabetes Patients	30 individuals (15 T2D patients from the National Institute of Diabetes, Nutrition and Metabolic diseases. Fecal samples were collected between 3 to 7 days from the COVID-19 diagnostic	Several members of the **microbiota** were **associated** with more severe clinical and inflammatory (IL-8 **and IL-17)** parameters. the expression of the proinflammatory IL-17 gene was significantly higher for the **T2D** group
3	Wang et al. /2022	Adjuvant Probiotics of Lactobacillus salivarius subsp. salicinius AP-32, L. johnsonii MH-68, and Bifidobacterium animalis subsp. lactis CP-9 Attenuate Glycemic Levels and Inflammatory Cytokines in Patients	T1DM patients between 6 and 18 years of age were enrolled. 27 patients were administered regular insulin therapy plus capsules containing probiotic. serum levels of inflammatory cytokines and anti-inflammatory cytokine	Patients with **T1DM** who were administered probiotics showed significantly reduced fasting blood glucose levels. The HbA1c levels of the patients also improved after administration of **probiotics**. The concentrations of IL-8, **IL-17**, MIP-1b, RANTES, and

Jurnal Eduhealth
Volume 15, Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

No	Authors/ year	Title	Methods	Result
		With Type 1 Diabetes Mellitus	were assessed using enzyme-linked immunosorbent assay	TNF-a were significantly reduced and were associated with an increased TGF-b1 expression after probiotic intervention.

Extraction of the data shows in table 1. Some studies reported that Il-17 as inflammantory cytokine corelated with microbiome, and metabolic disorder. Li et al.(2020) reported that the dominant phyla among participants were Firmicutes, Bacteroidetes, and Proteobacteria. They observed a significant increase in the abundance of the genus *Prevotella* and a notable decrease in the genus *Faecalibacterium* within the T2DM_P group. At the species level, there were significant changes in the abundances of *Prevotella copri* and *Faecalibacterium prausnitzii* (the sole identified species in the *Faecalibacterium* genus) in this group. Clinical factors linked to T2DM, such as gastrointestinal symptoms and the use of various medications for treatment, may influence the gut microbiota by altering the ecological balance between the host and its microbiota over time. Additionally, taxa associated with periodontitis in the gut microbiota such as *Prevotella*, *Faecalibacterium*, *Haemophilus*, *Veillonella*, *Streptococcus*, *Aggregatibacter*, *Oxalobacter*, and *Eisenbergiella* were found to correlate significantly with blood levels of proinflammatory cytokines, including PGE2, IFN-γ, IL-17, IL-6, and TNF-α (Li et al. 2020). Gene sequencing studies reveal that while healthy individuals harbor a wide variety of bacterial species, the gut metagenome—the collective genetic material of gut microorganisms—plays a key role in essential functions. These include digesting and breaking down otherwise indigestible nutrients, as well as supporting the development and regulation of the host's immune system and digestive tract. Additionally, the gut microbiota produces pharmacologically active signaling molecules that influence the host's metabolism (Boulangé et al. 2016). Microbiota modulators and probiotics support the balance of gut microbiota, preserve gut membrane integrity and permeability, and promote the production of anti-inflammatory cytokines like transforming growth factor-beta (TGF-β) while suppressing proinflammatory cytokines such as TNF-alpha. Cytokines and chemokines have previously been implicated in the pathogenesis of T1DM, including IL-8, RANTES, MIP-1b, TNF-a, and IL-17. The IL-17 family also seems to contribute to tissue repair in the intestinal epithelium. Notably, an increased incidence of inflammatory bowel disease (IBD) has been observed in psoriasis and ankylosing spondylitis patients treated with secukinumab, ixekizumab, and brodalumab, though a direct causal link has not been established. As a result, therapies targeting the IL-17 family for chronic wounds may not be suitable for patients with IBD. The IL-17 family's protective role in the gut may mirror its protective function in the skin by influencing the microbiome and regulating inflammation (Hadian et al., 2018). IL-17 works in conjunction with fibroblast growth factor 2 to stimulate the expression of genes involved in repairing damaged epithelium (Song et al., 2015). Theoretically, nutrient availability could influence IL-17-driven repair mechanisms. However, our knowledge of how various bioenergetic pathways, such as glycolysis and fatty acid oxidation (FAO), affect IL-17-

Jurnal Eduhealth
Volume 15, Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

mediated tissue repair and regeneration remains incomplete (Benchara et al. 2021). A defining characteristic of obesity and its related conditions is chronic low-grade inflammation (Gregor, et al. 2011). Lipopolysaccharides (LPS), also known as endotoxins, originating from the outer membranes of Gram-negative bacteria, are believed to trigger the inflammatory processes linked to the development of obesity and insulin resistance (Chani et al. 2007). While genetic variants have been linked to an increased risk of obesity and type 2 diabetes, their overall heritability is relatively modest. Recently, the gut microbiota has emerged as a critical environmental factor influencing metabolic diseases. It is now regarded as a distinct endocrine organ that communicates with the host through molecular interactions, playing a vital role in regulating energy balance and enhancing immune function (Clarke et al. 2014). IL-17A is a cytokine produced by various immune and non-immune cells, playing dual roles in both defending against microbial infections and contributing to inflammatory diseases. The mechanisms underlying these seemingly contradictory roles of IL-17A remain unclear. The gut microbiota (GM), composed of resident probiotic bacteria in the gastrointestinal tract, has been proposed as a potential regulator of IL-17A production and function. The role of IL-17 and gut microbiome still controversial, altered or dysbiosis gut microbiota and also co-infection with other pathogens induce expression of IL-17A may be via α/β Th17 cells which results in induction of pathologic immune responses and consequently pro-inflammatory-based diseases (Mobarre&Kariminik, 2017).

CONCLUSION

Extensive experimental research is still needed to fully understand the correlation between IL-17, the microbiome, and metabolic diseases. Numerous studies have highlighted this relationship, supported by microbiome sequencing data from patients with metabolic disorders. These findings suggest that cytokines play a critical role in various physiological and pathological conditions in the human body. IL-17, in particular, is a pro-inflammatory cytokine that contributes to pathological immune responses, often leading to the development of inflammation-driven diseases. Its role in modulating immune responses and its interaction with the gut microbiome in the context of metabolic diseases warrant deeper investigation to uncover potential therapeutic targets.

REFERENCES

Alam A, Neish A. (2003). Role of gut microbiota in intestinal wound healing and barrier function. Tissue Barriers, 6:1539595.

Najmi, N., Megantara, I., Andriani, L., Goenawan, H., Lesmana, R. 2022. Importance of gut microbiome regulation for the prevention and recovery process after SARS-CoV-2 respiratory viral infection (Review). Biomed Rep 16(4):25. doi: 10.3892/br.2022.1508

Bencara, H., McGeachy, MJ., Gaffen, SL. 2021. The metabolism-modulating activity of IL-17 signaling in health and disease. J Exp Med. 218 (5): 320202191

Li, P., Lu,H., Wu, H ,. Huang S., Chen L , Qifeng Gui Q ., Zhou W ., Yang Y , Wu Y , Zhang H, Zhang Q ., Yang H. 2020. Periodontitis in elderly patients with type 2 diabetes mellitus: impact on gut microbiota and systemic inflammation. Aging, 12(24): 25956- 25980

Hu S, Vila AV, Gacesa R., Collij V., et al. 2021. Whole exome sequencing analyses reveal gene– microbiota interactions in the context of IBD. Gut; 70:285–296. doi:10.1136/gutjnl-2019-319706.

Kumar, PS., Monteiro, MF., Casari, RCV. Subgingival Host-Microbial Interactions in Hyperglycemic Individuals. Journal of Dental Research, 99 (6).

Pircalabioru, GG., Grigore, GA., Barbu, IC., Chifiriuc, MC., Savu O. 2023. Impact of COVID-19 on the Microbiome and Inflammatory Status of Type 2 Diabetes Patients. Biomedicines; 11(179). https://doi.org/10.3390/biomedicines11010179

Garidou L, Pomié C, Klopp P, et al. The gut microbiota regulates intestinal CD4 T cells expressing RORgt and controls metabolic disease. Cell Metab 2015; 22:100–112

Humans Xin Zhou., Jethro S. Johnson., Daniel Spakowicz., Wenyu Zhou., Yanjiao Zhou., Erica Sodergren., Michael Snyder., George M. Weinstock. 2023. Longitudinal Analysis of Serum Cytokine Levels and Gut Microbial Abundance Links IL-17/IL-22 With Clostridia and Insulin Sensitivity in Humans. Diabetes 2020;69:1833–1842. https://doi.org/10.2337/db19-0592.

Wang, CH., Yen, HR., Lu WL., Ho, HH., Kuo, YW., Huang, YY., Tsai SY., Lin, HC. 2022. Adjuvant Probiotics of Lactobacillus salivarius subsp. salicinius AP-32, L. johnsonii MH-68, and Bifidobacterium animalis subsp. lactis CP-9 Attenuate Glycemic Levels and Inflammatory Cytokines in Patients with Type 1 Diabetes Mellitus. Front. Endocrinol. 13:754401. doi: 10.3389/fendo.2022.754401.

Hadian, Y., Bagood, MD., Dahle, SE., Sood, A., Isseroff, RR. 2019. Interleukin-17: Potential Target for Chronic Wounds. Mediators of Inflammation, 1-10

Boulangé, CL ., Luisa Neves, AL., Chilloux, J., Jeremy K. Nicholson, JK. Dumas, ME. 2016. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. Genome Medicine. 8:42 DOI 10.1186/s13073-016-0303-2.

Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. Annu Rev Immunol. 2011;29:415–45. doi:10.1146/annurev-immunol-031210-101322.

Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, Bastelica D, et al. Metabolic endotoxemia initiates obesity and insulin resistance. Diabetes. 2007;56:1761–72. doi:10.2337/db06-1491.

Clarke G, Stilling RM, Kennedy PJ, Stanton C, Cryan JF, Dinan TG. Minireview: Gut microbiota: the neglected endocrine organ. Mol Endocrinol. 2014;28:1221–38. doi:10.1210/me.2014-1108.

Mobarrez, BD., Kariminik, A. 2017. Gut Microbiota and IL-17A: Physiological and Pathological Responses. Probiotics & Antimicro. Prot. DOI 10.1007/s12602-017-9329-z.