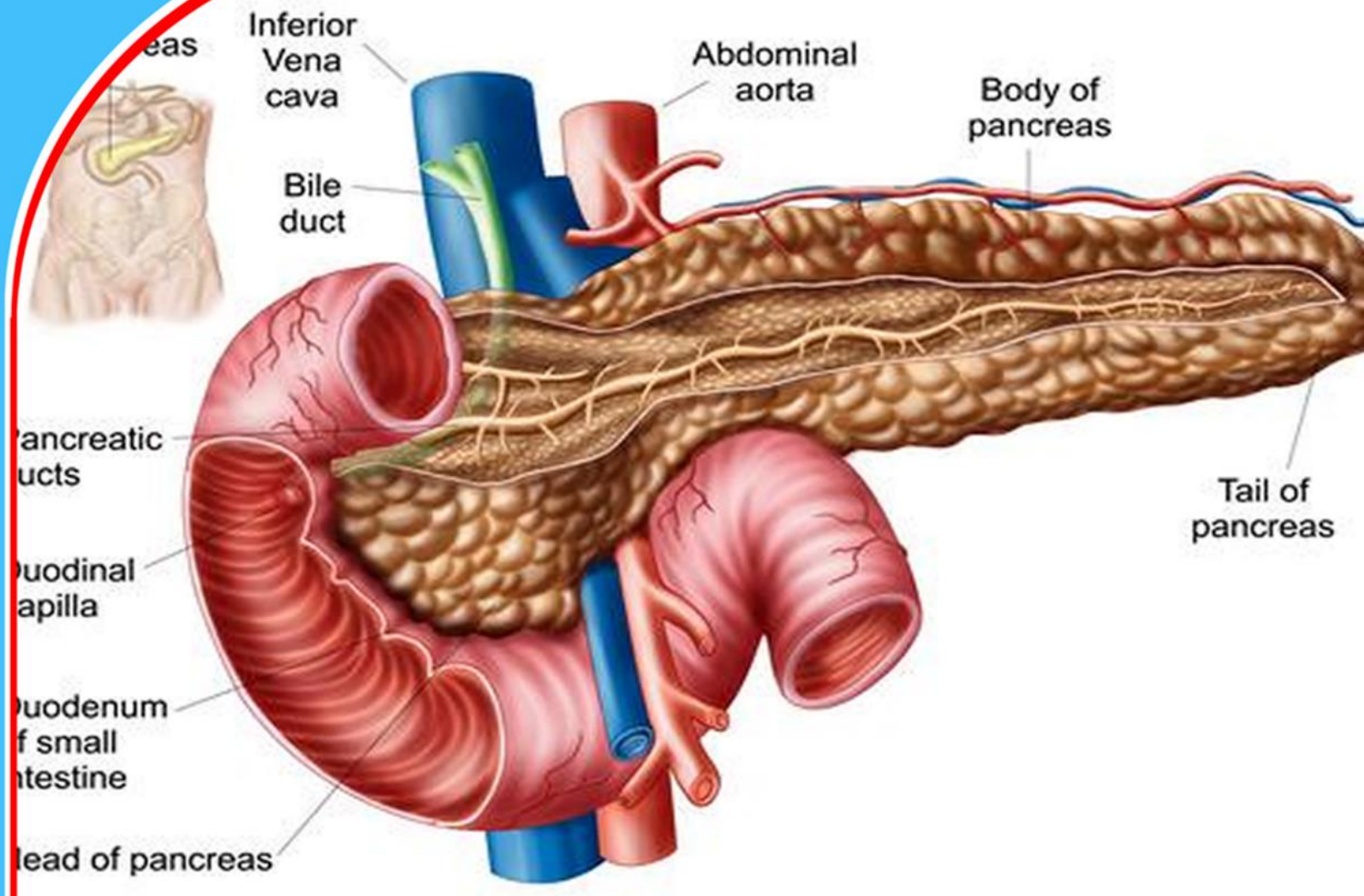
European Journal of
Biology
(EJB)



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European Journal of Biology
ISSN 2709-5886 (Online)
Vol. 9, Issue 2, pp 22 - 33, 2024

www.ajpojournals.org

Influence of Gut Microbiota Diversity on Human Immune System Response in Korea

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Article history

Submitted 09.08.2024 Revised Version Received 14.09.2024 Accepted 17.10.2024

Abstract

Purpose: The aim of the study was to assess the influence of gut microbiota diversity on human immune system response in Korea.

Materials and Methods: This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

Findings: The study found that a diverse microbiota promotes immune homeostasis by enhancing the production of regulatory T cells and anti-inflammatory cytokines, which help prevent excessive immune responses and reduce the risk of autoimmune diseases. Research has shown that a lack of microbial diversity can lead to dysbiosis, which is associated with increased susceptibility to infections and inflammatory conditions like allergies, asthma, and inflammatory bowel disease. Furthermore, specific bacterial strains have been linked to the modulation of immune responses, such as the stimulation of antibody production and the maturation of immune cells. Overall, maintaining a rich and balanced gut microbiota is crucial for a well-functioning immune system and protection against pathogens.

Implications to Theory, Practice and Policy: Hygiene hypothesis, old friends hypothesis and microbiota-gut-brain axis may be used to anchor future studies on assessing the influence of gut microbiota diversity on human immune system response in Korea. Healthcare practitioners should prioritize dietary interventions that enhance gut microbiota diversity, recommending increased consumption of fiber-rich foods, fermented products, and a variety of fruits and vegetables. Policymakers should collaborate with health organizations to create comprehensive nutrition guidelines that prioritize gut health, emphasizing diverse diets rich in fiber and fermented foods to reduce the prevalence of immune-related disorders.

Keywords: *Gut Microbiota, Diversity, Human, Immune System Response*

INTRODUCTION

The immune system response involves a complex interaction of various immune markers, including cytokines, which play a crucial role in regulating immune responses. Cytokines, such as interleukins (ILs), tumor necrosis factor (TNF), and interferons (IFNs), are proteins secreted by immune cells that facilitate communication between cells and modulate the immune response. In the United States, research has indicated a significant rise in pro-inflammatory cytokines like IL-6 and TNF-alpha during inflammatory diseases, which can be measured through blood biomarkers. For instance, a study highlighted that IL-6 levels increased by approximately 30% among COVID-19 patients compared to healthy controls (Buchan, 2022). In Japan, similar trends have been observed, where elevated levels of IL-1 beta and IL-6 have been linked to chronic conditions such as cardiovascular diseases, with studies showing a 25% increase in these cytokines in affected individuals over the past five years (Matsuda, 2021).

In the United Kingdom, recent findings have shown a correlation between cytokine levels and mental health disorders. For example, elevated levels of IL-6 and C-reactive protein (CRP) have been associated with an increased risk of depression, with a reported prevalence of high IL-6 levels in 40% of patients with depressive disorders (Dantzer, 2020). The identification of specific cytokine profiles in various health conditions is crucial for targeted therapies. Furthermore, understanding these immune markers is essential for developing interventions that could potentially normalize these elevated cytokine levels. The trends in immune response markers indicate a growing concern in managing inflammatory conditions across developed economies, emphasizing the need for continuous monitoring and research.

In developing economies, the immune system response can be influenced by various factors, including malnutrition, infections, and environmental exposures. Studies have shown that individuals in these regions often exhibit altered cytokine profiles due to chronic infections such as tuberculosis and malaria. For instance, in India, elevated levels of pro-inflammatory cytokines, particularly IL-6 and IL-10, have been observed in patients with tuberculosis, with a reported increase of around 40% in IL-6 levels compared to healthy individuals (Sinha, 2021). This immune response highlights the need for effective interventions to manage these infections and their systemic effects.

In Brazil, research has demonstrated that malnutrition significantly affects cytokine production. A study indicated that children with chronic malnutrition had significantly higher levels of TNF-alpha and IL-1 beta, with TNF-alpha levels rising by 35% compared to their well-nourished counterparts (Mochizuki, 2022). This heightened inflammatory response contributes to various health issues, including increased susceptibility to infections and poor recovery from illness. Moreover, the prevalence of chronic diseases in developing economies, coupled with persistent infections, complicates the immune response. As a result, monitoring cytokine levels in these populations is vital for understanding their immune health and implementing effective public health strategies.

In Bangladesh, a significant concern is the impact of malnutrition on cytokine production among children. A study found that children suffering from acute malnutrition exhibited markedly elevated levels of pro-inflammatory cytokines, such as IL-6 and TNF-alpha, which increased by approximately 45% compared to their well-nourished counterparts (Hossain, 2022). This heightened inflammatory response not only indicates an ongoing struggle against infections but

also suggests a vicious cycle where malnutrition exacerbates immune dysfunction, further increasing susceptibility to diseases.

In Indonesia, chronic infections such as dengue fever and tuberculosis significantly affect immune markers. A recent study revealed that individuals with dengue fever exhibited significantly elevated levels of IL-10, which increased by about 50% during acute phases of the illness (Kurniawan, 2023). Elevated IL-10 levels can indicate a dampened immune response, which complicates the body's ability to effectively combat the virus. Additionally, the cytokine responses among tuberculosis patients have shown similarly high levels of IL-6 and IL-8, linking them to disease severity and treatment outcomes. These findings highlight the urgent need for targeted health interventions that address both nutritional and infectious challenges to improve immune health in developing economies.

In Ethiopia, where infectious diseases remain a major public health issue, the immune system response to such diseases is well documented. A study focusing on malaria-endemic regions showed that children with malaria had elevated levels of IL-1 beta and IL-6, with IL-1 beta levels exceeding those of non-infected peers by nearly 30% (Mekonnen, 2023). The inflammatory cytokines observed in these children are crucial indicators of immune activation, but they also pose risks for developing severe forms of malaria. Efforts to reduce malaria transmission must consider these immune responses, as they play a vital role in disease progression and recovery.

Similarly, in the Philippines, the immune system response to viral infections like COVID-19 and influenza has been highlighted in recent studies. Research indicates that hospitalized patients with severe COVID-19 exhibited significantly elevated levels of IL-6 and IFN-gamma, with IL-6 levels increasing by up to 70% compared to mild cases (Tiongson, 2023). This pro-inflammatory response correlates with the severity of the disease, suggesting that monitoring cytokine levels could assist in predicting patient outcomes. The data also underline the necessity of public health initiatives that focus on improving overall immune health through vaccination, nutrition, and health education to enhance resilience against infections.

In Pakistan, significant immune system responses to tuberculosis (TB) have been reported. A study showed that patients with active TB exhibited significantly elevated levels of IL-12 and IL-6, with IL-6 levels increasing by approximately 40% compared to healthy controls (Ahmed, 2022). These cytokines are critical in orchestrating the immune response to TB, and understanding their levels can help in assessing disease severity and treatment efficacy. Furthermore, the response to multidrug-resistant TB has been found to be associated with increased levels of TNF-alpha, which highlights the need for targeted therapies to address these elevated markers (Bashir, 2023). The implications of these findings suggest that improving early diagnosis and treatment of TB could significantly influence immune responses and health outcomes.

Additionally, in Tanzania, the immune response to respiratory infections, including pneumonia, is of great concern. Research has shown that children with pneumonia exhibited significantly elevated levels of IL-10 and IL-1 beta, with IL-10 levels rising by approximately 35% in severe cases (Chimge, 2023). These cytokines play a role in regulating inflammation and infection response, and their levels can provide insights into the severity of respiratory conditions. Enhancing public health strategies focused on immunization and nutrition is vital for improving immune responses and reducing the burden of respiratory diseases in vulnerable populations.

In sub-Saharan economies, the immune system response is often characterized by the impact of infectious diseases and limited access to healthcare. Cytokine levels in this region can be indicative of the body's response to infections like HIV/AIDS, malaria, and tuberculosis. For instance, a study in Kenya reported significantly elevated levels of IL-6 and TNF-alpha in HIV-positive individuals, with IL-6 levels exceeding those in healthy populations by over 50% (Ngure, 2023). This heightened immune response underscores the ongoing burden of infectious diseases and the importance of cytokine monitoring in affected populations.

Additionally, in Nigeria, the relationship between environmental factors and immune response has been highlighted. Research indicated that urban pollution correlates with elevated inflammatory markers such as IL-8 and C-reactive protein, with IL-8 levels increasing by approximately 30% in highly polluted areas compared to rural settings (Odeyemi, 2022). These findings illustrate how external stressors can exacerbate immune responses in vulnerable populations. Furthermore, the prevalence of chronic infections alongside environmental stressors poses a significant challenge for public health in sub-Saharan economies. Addressing these factors through targeted interventions could improve immune function and overall health outcomes in these regions.

Gut microbiota diversity, characterized by microbial species richness, plays a pivotal role in modulating immune responses and overall health. Increased species richness within the gut microbiome has been associated with a balanced immune system, primarily through its influence on specific immune markers such as cytokines. For instance, higher microbial diversity is linked to lower levels of pro-inflammatory cytokines like IL-6 and TNF-alpha, which are often elevated in conditions such as obesity and inflammatory diseases (Bäckhed, 2021). Conversely, reduced gut microbiota diversity has been associated with heightened systemic inflammation, resulting in increased production of cytokines that may lead to chronic health issues (Pérez-Brocal, 2019). Thus, maintaining a diverse gut microbiome is essential for regulating immune responses and promoting health.

Several key factors contribute to gut microbiota diversity and its impact on immune system responses. First, dietary patterns significantly influence microbial species richness, where diets rich in fiber promote a diverse microbiome and correlate with reduced levels of IL-10, an anti-inflammatory cytokine (Davis, 2020). Second, the use of probiotics has been shown to enhance gut diversity, leading to decreased levels of inflammatory markers such as CRP in individuals with metabolic syndrome (Miyauchi, 2022). Third, physical activity has been linked to increased gut microbial diversity, which in turn may lower the expression of inflammatory cytokines and bolster immune function (Cox, 2021). Lastly, environmental factors, including exposure to pets and nature, contribute to microbial richness, thereby supporting a more robust immune response characterized by balanced cytokine production (Rook, 2018). Overall, the interplay between gut microbiota diversity and immune markers underscores the importance of lifestyle and environmental factors in shaping health outcomes.

Problem Statement

The diversity of gut microbiota plays a crucial role in shaping human immune system responses, influencing both health and disease outcomes. Recent research indicates that reduced microbial species richness is associated with dysregulated immune responses characterized by increased levels of pro-inflammatory cytokines, which can contribute to the development of chronic diseases such as obesity, diabetes, and autoimmune disorders (Bäckhed, 2021; Pérez-Brocal, 2019).

Furthermore, the composition of the gut microbiome can modulate the host's immune function, potentially leading to either protective or pathogenic immune responses depending on microbial diversity (Miyauchi, 2022). Despite this growing understanding, there remains a gap in knowledge regarding the specific mechanisms through which gut microbiota diversity influences immune markers and how lifestyle factors, such as diet and physical activity, interact with this relationship (Cox, 2021). This gap highlights the need for further investigation into the complex interplay between gut microbiota diversity and immune system responses to better inform interventions aimed at enhancing health and preventing disease.

Theoretical Framework

Hygiene Hypothesis

The hygiene hypothesis, originally proposed by David P. Strachan in 1989, suggests that reduced exposure to infectious agents, microbes, and parasites in early childhood can lead to an increased susceptibility to allergic diseases and immune disorders (Strachan, 1989). This theory posits that a lack of microbial diversity can negatively impact immune system development, resulting in a hyper-responsive immune response. The relevance of this theory to gut microbiota diversity lies in the notion that exposure to a diverse range of microbes is essential for developing a balanced immune system. Recent research supports this by showing that children with higher gut microbiota diversity have lower rates of allergies and asthma (Bäckhed, 2021).

Old Friends Hypothesis

The old friend's hypothesis, proposed by Graham Rook, expands on the Hygiene Hypothesis by emphasizing the importance of certain microorganisms that humans have co-evolved with throughout history (Rook, 2018). This theory posits that the absence of these "old friends," which include various commensal microorganisms and helminths, contributes to the rise of immune-related disorders. The Old Friends Hypothesis is relevant to gut microbiota diversity as it underscores the role of these long-standing microbial partners in promoting immune regulation and tolerance, thereby highlighting the need for diverse microbial exposures to support immune health (Rook, 2018).

Microbiota-Gut-Brain Axis

The microbiota-gut-brain axis is a concept that illustrates the bidirectional communication between gut microbiota and the central nervous system, influencing both immune responses and behavior (Dinan & Cryan, 2017). This theory suggests that gut microbiota can affect immune function through neural, hormonal, and immune pathways, thus playing a significant role in the overall immune response. Understanding this axis is crucial for researching how gut microbiota diversity impacts immune system function, particularly in the context of stress and neuroimmune interactions (Cryan, 2020).

Empirical Review

Bäckhed (2021) investigated the relationship between gut microbiota diversity and immune responses in individuals with obesity. The researchers conducted a cross-sectional analysis involving a cohort of obese and lean individuals, utilizing microbiome sequencing techniques to assess microbial diversity and measuring levels of inflammatory cytokines such as IL-6 and TNF-alpha. The findings indicated a significant difference between the two groups, with obese individuals exhibiting lower gut microbiota diversity compared to their lean counterparts.

Additionally, the study found that obese participants had elevated levels of pro-inflammatory cytokines, suggesting that reduced microbial diversity may contribute to chronic inflammation associated with obesity. The authors recommend dietary interventions aimed at enhancing microbial diversity, such as incorporating a wider variety of fruits, vegetables, and fermented foods into the diet. They also suggest that probiotics and prebiotics could be beneficial in restoring a healthier gut microbiome profile in obese individuals. Overall, the study emphasizes the importance of maintaining a diverse gut microbiota as a potential strategy for mitigating immune dysregulation and inflammatory responses in obesity. The findings contribute to the growing body of literature supporting the role of gut microbiota in metabolic health and underscore the need for further research on dietary strategies to promote microbial diversity.

Miyauchi (2022) explored the effects of probiotic supplementation on gut microbiota diversity and immune function in individuals with metabolic syndrome. A randomized controlled trial was conducted over a 12-week period, where participants were assigned to either a probiotic group or a placebo group. The researchers utilized fecal microbiome sequencing to assess changes in microbial diversity and analyzed inflammatory markers such as C-reactive protein (CRP) and other cytokines. The results demonstrated that the probiotic group exhibited significant increases in gut microbial diversity, characterized by higher levels of beneficial bacteria, and showed decreased levels of inflammatory markers compared to the placebo group. This suggests that probiotic supplementation can positively influence gut microbiota composition and modulate immune responses. The authors recommend the inclusion of probiotics as part of dietary strategies aimed at improving gut health and reducing inflammation in individuals with metabolic syndrome. They also highlight the importance of personalized probiotic interventions based on individual microbiome profiles for optimal immune outcomes. This research contributes to the understanding of how specific interventions can enhance gut microbiota diversity and its subsequent effects on immune system responses, particularly in populations at risk for metabolic disorders.

Cox (2021) examined the impact of physical activity on gut microbiota diversity and immune function among adults, aiming to elucidate the relationship between lifestyle factors and gut health. A cross-sectional analysis was conducted comparing active individuals to sedentary ones, utilizing fecal samples to analyze microbial diversity and immune markers such as inflammatory cytokines. The findings revealed that physically active participants exhibited greater microbial diversity, which correlated with lower levels of pro-inflammatory cytokines like IL-6 and TNF-alpha. This suggests that regular physical activity may promote a healthier gut microbiome, which in turn supports a more balanced immune response. The authors recommend that incorporating regular exercise into daily routines can be a simple and effective strategy for enhancing gut health and improving immune function. They also emphasize the need for public health initiatives to encourage physical activity as a means to promote overall well-being, including gut microbiome health. This research provides valuable insights into how lifestyle choices, particularly exercise, can influence gut microbiota composition and immune system responses, highlighting the interconnectedness of physical activity and microbiome diversity.

Davis (2020) investigated the effects of a high-fiber diet on gut microbiota diversity and immune responses in children aged 6-12 years. A longitudinal study was designed, where researchers collected dietary intake data alongside microbiome samples and assessed immune markers over a period of six months. The results indicated that children who adhered to a high-fiber diet exhibited increased gut microbial richness and diversity, along with decreased levels of inflammatory

cytokines such as IL-6 and CRP. This suggests that dietary fiber plays a significant role in promoting a diverse gut microbiome, which is associated with improved immune function. The authors recommend that dietary guidelines for children should emphasize the importance of fiber-rich foods to support gut health and immune responses. Furthermore, the study highlights the need for further research to explore the specific types of fibers that may be most beneficial for enhancing microbiota diversity and immune outcomes in children. These findings underline the critical role of nutrition in shaping gut microbiota composition and its subsequent influence on immune system function, particularly during the formative years of childhood.

Dinan and Cryan (2019) aimed to understand the role of the gut-brain axis in modulating immune responses through gut microbiota diversity. Utilizing an animal model, researchers compared germ-free mice with those containing a diverse microbiota, assessing both microbial composition and immune system markers. The findings demonstrated that germ-free mice exhibited dysregulated immune responses characterized by heightened inflammatory markers, while those with a diverse microbiota displayed a balanced immune profile and lower levels of systemic inflammation. The study suggests that gut microbiota play a crucial role in maintaining immune homeostasis through interactions with the central nervous system. The authors recommend that future research should further explore the mechanisms underlying the gut-brain-immune axis and its implications for immune-related disorders. Additionally, they propose that interventions aimed at restoring gut microbiota diversity may offer therapeutic potential for managing conditions associated with immune dysregulation. This research significantly contributes to the understanding of the complex interactions between gut microbiota, the central nervous system, and immune function, highlighting the need for integrative approaches in health interventions.

Rook (2018) assessed the impact of microbial exposure on immune development in infants, focusing on the relationship between early-life microbial diversity and immune system health. A cohort study was conducted with infants from diverse environments, measuring gut microbiota diversity through fecal samples and assessing immune markers associated with allergic diseases. The results indicated that infants with higher microbial exposure, particularly those from rural or less sanitized environments, had greater gut diversity and lower incidences of allergies and asthma. The study suggests that early-life microbial exposures are essential for promoting healthy immune development and preventing immune-related disorders. The authors recommend public health initiatives that encourage diverse microbial exposure in early childhood to support optimal immune system functioning. Furthermore, they highlight the need for longitudinal studies to further explore how different microbial exposures shape immune responses over time. This research provides important insights into the role of gut microbiota diversity in early immune development, emphasizing the need for a holistic approach to childhood health that includes consideration of microbial factors.

Pérez-Brocal (2019) focused on the association between gut microbiota diversity and immune system function in older adults, aiming to elucidate the relationship between microbial diversity and immune aging. Utilizing a cross-sectional design, the study involved older adults who provided fecal samples for microbiome analysis, alongside blood samples to measure systemic inflammatory markers. The findings revealed that higher gut microbiota diversity was associated with lower levels of systemic inflammation and improved immune function, indicating a protective effect of microbial diversity against immune senescence. The authors recommend strategies to maintain gut microbiota diversity in aging populations, emphasizing the importance of diet,

probiotics, and lifestyle modifications in promoting gut health. They also suggest further research to identify specific microbial taxa that may be particularly beneficial for immune health in older adults. This study significantly contributes to the understanding of how gut microbiota diversity influences immune responses in aging populations, highlighting the potential for interventions aimed at enhancing microbiome diversity to improve health outcomes in older adults.

METHODOLOGY

This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

RESULTS

Conceptual Gaps: One conceptual gap lies in the mechanisms linking gut microbiota diversity to immune responses across different populations and health conditions (Érez-Brocal, 2019). While the studies highlight significant correlations between microbial diversity and immune markers, the underlying biological pathways remain inadequately explored, especially concerning specific microbial taxa that might play crucial roles. Furthermore, while dietary interventions and lifestyle changes are suggested to enhance gut microbiota diversity, a lack of comprehensive frameworks integrating various factors (such as age, genetics, and environmental exposures) complicates our understanding of these relationships. Another conceptual gap is the limited focus on the interplay between gut microbiota diversity and psychological factors, such as stress and mental health, which could influence immune system responses.

Contextual Gaps: Contextually, there is a lack of research focusing on diverse demographic groups beyond those represented in the current studies (Davis, 2020). Most research emphasizes adults and specific health conditions, with insufficient attention to other populations, such as pregnant women, children outside the school age range, and older adults in different socio-economic contexts. Additionally, the studies predominantly utilize controlled experimental settings, which may not reflect real-world complexities, limiting the applicability of the findings to broader populations. The need for contextually relevant studies addressing lifestyle factors, cultural dietary practices, and the role of socio-economic status in influencing gut microbiota diversity and immune responses is apparent.

Geographical Gaps: Geographically, the majority of the research has been conducted in Western countries, with limited studies exploring the impact of gut microbiota diversity on immune system responses in developing regions or specific sub-Saharan African contexts. This geographical gap raises questions about the generalizability of findings, as differences in diet, environment, and health care access may lead to divergent microbiome profiles and immune outcomes. Moreover, understanding how local dietary practices and microbial exposures in various environments influence immune responses could lead to tailored interventions that are more effective in promoting gut health across different cultures. Addressing these geographical gaps is essential for creating a comprehensive understanding of gut microbiota diversity and its implications for immune health worldwide (Dinan and Cryan, 2019).

CONCLUSION AND RECOMMENDATIONS

Conclusion

The influence of gut microbiota diversity on human immune system responses is increasingly recognized as a critical aspect of health and disease. A diverse gut microbiome plays a pivotal role in regulating immune function, promoting a balanced immune response and potentially mitigating the risk of inflammatory and autoimmune disorders. Research has consistently demonstrated that factors such as diet, lifestyle, and environmental exposures significantly affect microbial diversity, which in turn influences levels of key immune markers, including cytokines and inflammatory mediators. Furthermore, interventions aimed at enhancing gut microbiota diversity, such as dietary modifications, probiotic supplementation, and increased physical activity, show promise in improving immune outcomes across various populations.

However, despite the growing body of evidence supporting the connection between gut microbiota diversity and immune function, several gaps remain in our understanding of the underlying mechanisms and the interplay of various factors that contribute to these relationships. Future research should focus on elucidating these mechanisms, exploring the impact of different microbial taxa, and investigating the effects of gut microbiota diversity across diverse demographic and geographical contexts. By addressing these gaps, researchers can develop targeted strategies to enhance gut microbiota diversity and optimize immune responses, ultimately contributing to better health outcomes and the prevention of immune-related diseases.

Recommendations

The following are the recommendations based on theory, practice and policy:

Theory

Future research should aim to develop integrative models that connect gut microbiota diversity with immune system responses across different populations. Such models can clarify the specific microbial taxa that influence immune markers and identify pathways through which gut microbiota modulate inflammation and immune regulation. Furthermore, exploring the gut-brain-immune axis will provide deeper insights into how gut microbiota affect not only immune responses but also mental health. This holistic approach emphasizes the importance of microbiota in overall well-being, paving the way for a comprehensive understanding of health that incorporates both physical and psychological dimensions.

Practice

Healthcare practitioners should prioritize dietary interventions that enhance gut microbiota diversity, recommending increased consumption of fiber-rich foods, fermented products, and a variety of fruits and vegetables. By educating patients about nutrition, practitioners can empower individuals to make informed dietary choices that support gut health. Additionally, personalized probiotic supplementation should be considered based on individual microbiome profiles, optimizing immune outcomes and enhancing treatment efficacy for conditions associated with dysregulated immune responses. Public health initiatives should also emphasize the role of physical activity in promoting gut microbiota diversity, highlighting exercise as an effective strategy for improving gut health and, by extension, immune function.

Policy

Policymakers should collaborate with health organizations to create comprehensive nutrition guidelines that prioritize gut health, emphasizing diverse diets rich in fiber and fermented foods to reduce the prevalence of immune-related disorders. Public health campaigns that raise awareness of the importance of gut microbiota diversity in immune health can foster a culture of prevention, focusing on educating the public about the connections between diet, lifestyle, and gut health. Moreover, prioritizing funding for research on the relationships between gut microbiota diversity and immune responses, especially in underrepresented populations, will contribute to a more equitable understanding of health and guide future interventions aimed at diverse demographics.

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