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Can Exercise Boost the Immune System? A Systematic Literature Review on the Relationship Between Physical Activity and Immune Function

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ABSTRACT: The field of sports immunology has evolved rapidly from the initial observation of infection rates in athletes to advanced mechanistic studies investigating the impact of different types, intensities, and durations of exercise on the immune system. This systematic literature review aimed to analyze the complex relationship between physical activity and immune function, examining the impact of moderate versus high-intensity exercise on immunological parameters. A systematic search was conducted on Google Scholar, PubMed, Web of Science, and Scopus databases from 2020-2025 using a combination of key terms physical activity, immune function, cytokines, lymphocytes, NK cells, and immunoglobulins with Boolean operators. Study selection based on predetermined criteria with a full-text review. An analysis of 18 studies showed a dose-response relationship of the J-curve pattern between exercise intensity and immune function. Moderate exercise has been shown to improve immune surveillance, reduce systemic inflammation, improve the function of NK cells, T lymphocytes, and B cells, and reduce the risk of infection by 31% and mortality by 37%. In contrast, excessive high-intensity exercise causes temporary immunosuppression through an "open window" phenomenon that increases susceptibility to infection. Moderate and regular exercise has consistently been shown to optimize immune function, while excessive exercise can be detrimental to the immune system.

KEYWORDS: physical activity, exercise, immune system.

I. INTRODUCTION

The interaction between physical activity and immune function has attracted significant scientific attention, especially in the context of global health challenges such as infectious diseases and chronic conditions. The immune system, which is a complex network of cells and molecules, plays an important role in protecting the body from pathogens and maintaining homeostasis [1]. Research [2] suggests that regular physical activity can modulate the immune response, potentially increase resistance to infection, increase vaccine effectiveness, and reduce chronic inflammation. This relationship is increasingly relevant in the context of the increasing prevalence of sedentary lifestyles and the accompanying spike in non-communicable diseases.

The field of sports immunology has evolved rapidly over time. Initially, this field was characterized by early observations of infection rates among athletes [3]. However, over time, this field has evolved to include sophisticated mechanistic studies. These studies investigated how different types of exercise, intensity, and duration affect the immune system, both innate and adaptive [4]. Moderate, regular exercise is now widely recognized as having the ability to improve immune surveillance, reduce systemic inflammation, and improve the function of various immune cell populations, including natural killer cells, T lymphocytes, and B cells [5]. On the other hand, excessive or unaccustomed high-intensity exercise has been shown to temporarily suppress certain immune parameters, a phenomenon known as "open window" that increases the risk of infection [6].

Recent systematic reviews and meta-analyses have provided quantitative evidence supporting the protective effects of regular physical activity against community-acquired infections and deaths from infectious diseases, as well as improvements in immune biomarkers such as immunoglobulin A and cytokine profiles [7]. The benefits mentioned above apply to a wide range of demographic groups, including the elderly, individuals with chronic illnesses, and even cancer patients, where exercise has been shown to increase responses to immunotherapy and fight imunosenesens [8]. Mechanistic insights have emerged that highlight

the key role of myokines, mitochondrial function, and redox equilibrium in the mediation of these effects. Despite the progress, some gaps still exist in our understanding. The diversity of study design, population, and practice protocols complicates the synthesis of findings and limits the generalization of recommendations. Limited research is available regarding the long-term effects of different types of exercise, the optimal dose of physical activity for immune system enhancement, and the molecular pathways underlying these adaptations. More research is needed to address this knowledge gap. In addition, the impact of exercise on immune function in specific populations such as the elderly, individuals with weakened immune systems, or those suffering from autoimmune diseases needs to be further researched.

The rationale for this systematic review is based on the urgent need to clarify the relationship between physical activity and immune function, especially in the context of global health crises, such as the pandemic of the novel coronavirus, SARS-CoV-2, also known as "covid-19." It is important to understand the potential of exercise as a non-pharmacological approach to improving immune resilience, as this understanding has profound implications for public health, disease prevention, and clinical practice. The objectives of this review are as follows: (1) to synthesize the current evidence regarding the impact of exercise on immune system parameters, (2) to identify the mechanisms by which physical activity modulates immunity, (3) to evaluate the impact of exercise on various populations and disease conditions, and (4) to highlight research gaps and future directions in this field.

II. MATERIALS AND METHODS

Study Design

Systematic searches were carried out on Google scholar, PubMed, Web of Science, Scopus databases from 2020 to 2025. searches use combinations of keyword terms such as ("physical activity," OR "aerobics," OR "resistance," "HIIT") AND ("immune function," OR "cytokines," OR "lymphocytes," OR "NK cells," OR "immunoglobulins"). Boolean operators (AND/OR) connect these concepts. No language restrictions were applied at first; only studies in English are retained.

Study selection:

The selection of studies by filtering titles and abstracts based on predetermined criteria. Studies that pass the initial selection undergo a full-text review. Disagreements are resolved through discussion or by a third reviewer. Inclusion criteria: Human, Exercise intervention, discussing Imun, published 2020 to 2025. Exclusion criteria: Non-human studies, Non-English publications, unpublished books in 2020 to 2025. PRISMA flowcharts track records through identification, filtering, eligibility, and inclusion [9].

Procedure:

In Search using by selecting Google data base, PubMed, Web of Science from 2020 to 2025. The author found an article from the Google scholar database, PubMed, Web of Science: 4233 articles. Furthermore, the articles found by the author will be processed and analyzed through several screening processes based on exclusion and inclusion criteria. After meeting the criteria, only 18 articles were left. Most of the articles are unused because they do not discuss physical activity and immunity. All articles are extracted from the source and analyzed using Mendeley to eliminate duplication of articles.

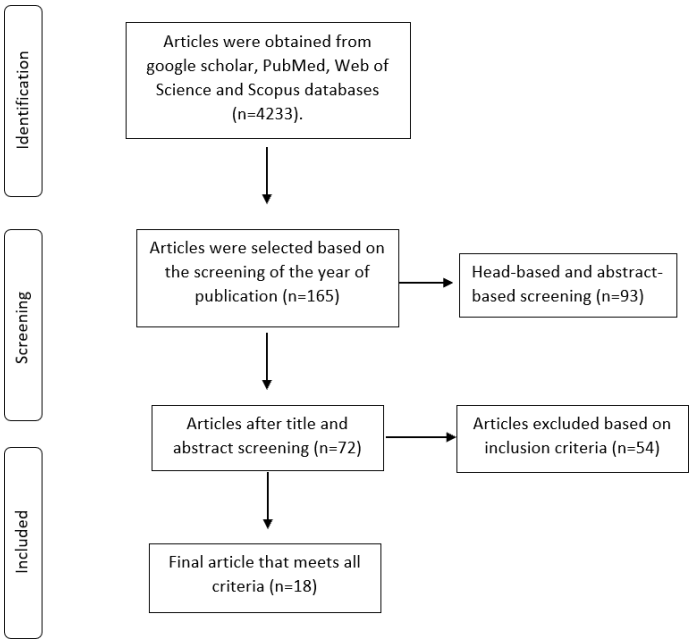


Figure 1. PRISMA Research Flowchart

III. RESULT

An analysis of the literature shows that exercise has a complex and multifaceted impact on the immune system. Research from [7] showed that regular physical activity can reduce the risk of community infectious diseases by 31% and mortality from infectious diseases by 37%. These findings are supported by [10] which identifies that moderate exercise can increase immunovigilance and reduce inflammaging through modulation of cytokine profiles and immune cell activity.

The dose-response relationship between exercise intensity and immune function following a consistent J-curve pattern has been reported in various studies. Research from [11] It shows that low- to moderate-intensity exercise improves cellular immune function, while prolonged high-intensity exercise can lead to temporary immunosuppression. [4] confirms that moderate exercise improves the function of T cells, NK cells, and neutrophils, but vigorous exercise can lead to an "open window" for susceptibility to infection.

In the elderly population, research [5] demonstrated that a 6-week functional exercise program in 29 elderly women resulted in an increase in naïve Tc cells, a decrease in memory cells, and a rebalancing of immune regulation. [12] reports that acute endurance exercise increases secretory immunoglobulin A (SIgA) and chronic exercise reduces systemic inflammation in elderly populations.

The molecular mechanisms underlying the immunomodulatory effects of exercise involve various signaling pathways. Research from [13] identified that resistance training activates the NF-κB pathway, increases natural killer cell activity (NKCA), and reduces oxidative stress. [14] suggests that exercise-induced reactive oxygen species (ROS) can be beneficial or detrimental depending on the intensity and duration of exercise. [15] identified 15 microRNAs validated in endurance exercise and miR-206 in resistance exercise as key regulators of immune response.

Table 1. Characteristics of Studies on Physical Activity and the Immune System

Author & Year	Research Methods and Types	Samples and Population	Interventions or Variables
[10]	Narrative review	General population and the elderly	Physical activity and dietary interventions
[13]	Systematic review	Adult Humans	Resistance training
[12]	Critical review	Elderly population	Acute and chronic exercise
[7]	Systematic review dan meta-analysis	General population	Regular physical activity
[4]	Narrative review	General population	Moderate and vigorous exercise
[16]	Narrative review	General population	Physical exercise
[5]	Experimental study	29 elderly women (67.03 ± 3.74 years)	6-week functional training program
[17]	Narrative review	General population with a COVID-19 focus	Physical activity and fitness
[18]	Review article	Athletes and active population	Exercise of different intensities
[19]	Systematic review	Adult population	Acute and chronic exercise
[20]	Narrative review	Patients of hematological malignancies	Sports
[21]	Comprehensive review	General population and aging	Physical exercise
[11]	Perspective article	General population	Low to high intensity sports
[22]	Experimental study	32 students	Aerobic and Pilates training for 14 weeks
[23]	Narrative review	General population	Exercise in hypoxia conditions
[24]	Systematic review (secondary data)	General population	Physical activity of various intensities
[14]	Review article	General population	Sports and ROS
[15]	Systematic review	Healthy adult human	Physical activity

Table 2. Results of Synthesis of Objectives and Key Findings of Physical Activity Research on the Immune System

Author & Year	Research Objectives	Key Findings
[10]	Examining the role of exercise and diet in shaping the immune system during aging	Moderate exercise boosts immunity, reduces inflammation, and improves vaccine response
[13]	Analyzing the effects of resistance training on immune cell function	Resistance training activates the NF-κB pathway, increases NK cell activity, and reduces oxidative stress
[12]	Examining the impact of exercise on immunoglobulins and cytokines in the elderly	Acute endurance exercise increases SIgA, chronic exercise reduces systemic inflammation
[7]	Evaluating the relationship between physical activity and infectious disease risk	Physical activity reduces the risk of infectious diseases by 31% and mortality by 37%
[4]	Analyze the impact of exercise on immunity, metabolism, and atherosclerosis	Moderate exercise improves immune function, vigorous exercise can cause temporary immunosuppression
[16]	Examining the sport-induced anti-inflammatory response	Exercise induces an anti-inflammatory response through cytokine modulation and activation of the Nrf2 pathway
[5]	Evaluating changes in lymphocyte subtypes after regular exercise	Navigable Tc cell increase, memory cell decline, and immune regulation rebalancing
[17]	Analyzing the relevance of physical activity to immune defense in the context of COVID-19	Physical activity increases immunovigilance and reduces the risk of severe infections
[18]	Examine the effect of exercise intensity on immune response and susceptibility to infection	Moderate exercise is beneficial, strenuous exercise can increase the risk of infection
[19]	Analyzing the impact of exercise on B-cell-related immunity	Exercise increases CD4 cell count, IgA concentration, and vaccination efficiency
[20]	Examining the impact of exercise on the immune system and outcomes on hematological malignancies	Exercise improves T, NK, and neutrophil cell function and reduces inflammation
[21]	Analyze the relationship between immunosenescence, exercise, and tumor immunity	Exercise can mitigate immunosenescence and improve antitumor response
[11]	Examining the effects of exercise intensity on cellular immunity	Moderate exercise improves immune function, strenuous exercise causes immunosuppression
[22]	Comparing the effects of aerobic exercise and Pilates on the adaptive immune system	Both types of exercise reduce regulatory T cells, aerobic exercise is more impactful
[23]	Examining the immune consequences of exercise in hypoxia	The combination of exercise and hypoxia can synergize or interfere with immune function
[24]	Analyze the modulation of the immune response through physical activity	Moderate exercise increases immunovigilance, excessive exercise can impair immune function
[14]	Analyze the role of ROS in modifying innate and adaptive immune responses during exercise	Exercise-induced ROS can be beneficial or detrimental depending on intensity
[15]	Identify ncRNAs involved in exercise-induced immune modulation	15 miRNAs are validated in endurance exercise, miR-206 is validated in resistance exercise

IV. DISCUSSION

These findings confirm that physical activity acts as a powerful modulator of the immune system through complex and interrelated mechanisms. The concept of "exercise immunology" developed from these studies suggests that the immune response to exercise is biphasic – with acute effects that can differ from chronic adaptations.

Research [16] emphasizing that exercise induces an anti-inflammatory response through cytokine modulation and activation of the Nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. This mechanism involves the release of myokines such as IL-6, IL-10, and IL-1ra which play a role in reducing low-level chronic inflammation. Research [22] Comparing aerobic exercise with Pilates suggests that both exercise modalities may reduce regulatory T cells, although aerobic exercise shows a more pronounced impact.

The context of the clinical application of these findings is particularly relevant, especially in the era of the COVID-19 pandemic. [17] Analyzes that physical activity can increase immunovigilance and reduce the risk of severe infections through improved mucosal barrier function and optimization of adaptive immune responses. [19] complements this perspective by showing that exercise increases CD4 cell count, IgA concentration, and vaccination efficiency.

In special populations such as patients with hematological malignancies, [20] shows that exercise can improve the function of T cells, NK cells, and neutrophils and reduce inflammation, providing evidence for the therapeutic application of exercise oncology. [21] Expanding this discussion by analyzing the relationship between immunosenescence, exercise, and tumor immunity, demonstrates the potential of exercise in immunosenescence mitigation.

The implications of these findings are far-reaching for clinical practice and public health policy. First, evidence-based exercise prescriptions can be developed as non-pharmacological interventions to improve immune function. [18] suggests that exercise guidelines should consider optimal intensity to maximize immune benefits while minimizing the risk of immunosuppression.

In the context of an aging population, these findings support the implementation of structured physical activity programs to prevent immunosenescence and reduce the risk of infection in the elderly. Research [24] emphasizing that modulating the immune response through physical activity can be a cost-effective strategy to increase healthspan and reduce the burden on the health system. For specific clinical settings, as analyzed by [23] Regarding exercise in hypoxia, special consideration is needed for the optimization of exercise protocols that can provide synergistic benefits without interfering with immune function.

The contribution of this study to the body of knowledge in exercise immunology is significant in several aspects. First, this synthesis provides a comprehensive framework for understanding the relationship between physical activity and immune function. Second, the identification of specific molecular mechanisms, including the role of microRNAs and signaling pathways such as NF-κB and Nrf2, provides a foundation for the development of new biomarkers and therapeutic targets. Third, evidence for specific clinical applications, ranging from healthy populations to patients with pathological conditions, expands the applicability of research findings. Fourth, understanding the variability of responses based on age, gender, and health status provides the basis for personalized exercise medicine.

Several significant limitations are identified in this body of literature. First, the heterogeneity of methodology between studies, including variations in exercise protocols, measured immune parameters, and study populations, makes generalizing findings challenging. Second, the majority of studies were observational or used relatively short duration interventions, so the long-term effects still require further investigation. Third, standardization in measuring immune parameters still varies between studies, which can affect the comparability of results. Fourth, confounding factors such as nutrition, sleep status, stress level, and genetic predisposition were not always adequately controlled in the studies analyzed.

Then based on this comprehensive analysis, some recommendations for future research can be formulated as follows:

1. Large-scale randomized controlled trials with standardized protocols are needed to establish optimal exercise prescriptions for various populations.
2. Longitudinal research with long-term follow-up is needed to understand the sustainability of exercise-induced immune adaptation.
3. A more in-depth investigation of molecular mechanisms, especially the role of epigenetic regulation and personalized medicine approaches based on genetic profiling.
4. development and validation of practical biomarkers for monitoring immune response to exercise interventions.
5. Research on optimal combination of exercise modalities (aerobic, resistance, flexibility) to maximize immune benefits.
6. Investigation of exercise immunology in the context of emerging health challenges, including environmental stressors and novel pathogens.

V. CONCLUSIONS

Based on a systematic review of 18 studies from 2020-2025, it was conclusively proven that physical activity has a profound impact on the immune system by following a J-curve dose-response pattern. Moderate exercise consistently improved immunovigilance, reducing the risk of infectious diseases by 31% and mortality due to infection by 37%, while also improving vaccination responses and reducing inflammation in the elderly population. Underlying molecular mechanisms include activation of the NF-κB pathway, increased activity of natural killer cells (NK cells), modulation of pro and anti-inflammatory cytokine profiles, and rebalancing of T and B lymphocyte populations. Highly relevant findings suggest that resistance and aerobic exercise are equally effective in optimizing immune function, with resistance training in particular increasing the activity of T cells, neutrophils, and reducing oxidative stress. Clinical implications suggest that moderate and regular exercise is not only an effective disease prevention strategy, but also a non-pharmacological therapeutic approach that can be applied to a wide range of populations,

including patients with hematological malignancies and individuals with immunodeficiency conditions. This study confirms that proper physical activity is a fundamental long-term health investment to optimize the body's defenses against pathogens and degenerative diseases.

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