Trends in Immunotherapy
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Review

Immune Response to Probiotics and Physical Activity: A Clinical Study

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Received: 13 February 2025; **Revised:** 14 March 2025; **Accepted:** 25 March 2025; **Published:** 14 November 2025

Abstract: This study assessed the effect of probiotic supplementation on immune response in physically active males before and after exhausting exercise. With growing evidence linking gut health to immune function, the aim was to determine whether 12 weeks of probiotics could influence key immune markers in athletes. In this semi-experimental study, 28 male athletes (18–35 years) from sports centers in Osh City, Kyrgyzstan, who engaged in regular training (≥3 days/week for ≥3 years) were randomly assigned to probiotic or placebo groups. Baseline characteristics included age (20.98 ± 5.9 years), weight (62.3 ± 9.8 kg), height (168.2 ± 7.6 cm), BMI (22.05 ± 2.4 kg/m^2), and VO_2 max (59.98 ± 8.8 ml/kg/min), with no significant differences between groups. Immune markers—cell blood count (CBC), C-reactive protein (CRP), and immunoglobulin A (IgA)—were monitored at rest and after exercise. Probiotic supplementation resulted in a significant increase in monocyte levels at rest and during activity compared to placebo. Within the probiotic group, lymphocyte, monocyte, and granulocyte percentages rose significantly during activity ($p < 0.001$). These results indicate that probiotics may positively modulate immune function in athletes under high physical stress. Given that intense training can suppress immunity and increase susceptibility to illness, probiotic use may enhance gut microbiota, supporting immune resilience. A balanced microbiome not only aids digestion and nutrient absorption but also plays a vital role in regulating inflammation and immune responses. These findings support probiotics as a potential strategy to maintain immune health in physically active populations, warranting further investigation into strain-specific effects and long-term benefits.

Keywords: Probiotic Supplementation; Physical Activity; Immune Response; IgA; Blood Cells

1. Introduction

Extreme and continuous physical activity, while essential for developing endurance, strength, and optimizing overall athletic performance, can have unintended physiological consequences, particularly concerning the immune system and its ability to defend the body against infections, inflammation, and chronic conditions. The resulting stress from rigorous and repetitive training regimens can suppress the body's natural immune defenses and lead to a significant decrease in the immunity levels of athletes, making them more vulnerable to a variety of infections and diseases that may interfere with their overall well-being and training efficiency. This concerning trend has sparked a vital discussion among experts in sports medicine and nutrition about the necessity of enhancing immunity among athletes [1]. As we look toward the future of athletic training, sports science, and overall health optimization, it becomes increasingly clear that nutrition plays a pivotal role not only in shaping personal health outcomes but also in determining overall physical performance, endurance, and. The impact of dietary choices on immunity and health cannot be overstated, as any initiative aimed at improving the nutritional and health status of individuals, particularly athletes, is of paramount importance [2]. Current research underscores the critical relationship between intestinal bacteria and general health. It has been established that these microorganisms are intrinsically linked to the risk of developing various diseases, including obesity, diabetes, and certain types of cancer, such as colon cancer [3]. This connection highlights the necessity of understanding how lifestyle choices, particularly diet, affect the gut microbiota—an intricate ecosystem of bacteria residing in the gastrointestinal tract (GIT) [4]. Recent studies suggest that physical activity may influence gut microbiota composition similar to dietary intake [4]. This revelation not only deepens our understanding of the intricate relationship between physical activity and gut health but also opens new avenues for exploring innovative strategies that athletes can use to optimize their overall well-being, enhance immunity, and improve performance through a combination of structured exercise and targeted nutrition. Probiotics, which are live beneficial bacteria found naturally in certain fermented foods and dietary supplements, play an integral role in maintaining a balanced gut microbiome, supporting digestive function, and modulating immune responses. They play a crucial role in maintaining a healthy microbial balance, which is essential for overall human health and nutritional well-being [5]. The benefits of probiotics are extensive and impactful. They include reducing instances of diarrhea and constipation, aiding in the combat against yeast infections, and preventing the proliferation of harmful pathogens. Furthermore, probiotics promote the growth of beneficial bacteria, help mitigate toxin levels in the body, and enhance immunity and resistance to infections. They are also involved in the production of essential vitamins and nutrients as well as organic acids, and can even play a role in reducing cholesterol levels. Emerging evidence suggests that probiotics may also have protective effects against colon cancer, alleviate symptoms of lactose intolerance, minimize allergic reactions, and exhibit antioxidant properties [6]. In light of the comprehensive studies conducted on the effects of gut bacteria on human health, it becomes evident that addressing the decline in immunity levels among athletes—exacerbated by intense training and competitive stress—is crucial [7].

Physical exercise can significantly assist in clearing bacteria from the lungs and air passages, potentially lowering the risk of contracting a cold, flu, or other illnesses. Additionally, physical activity induces critical alterations in the production, circulation, and function of immune cells, including antibodies and white blood cells (WBCs), which serve as the body's primary defence mechanisms against various diseases. When you exercise, these antibodies or white blood cells circulate more quickly, so they can detect illness earlier than before [1]. A slight increase in body temperature during and immediately after exercise may prevent bacteria from growing; however, this increase in temperature may help the body fight infection better and reduce the release of stress hormones as well [2]. The gastrointestinal system plays a role in initiating or inhibiting the body's inflammatory reactions, which may occur due to the bacteria present, their metabolic byproducts, immune cells that have been conditioned, or potentially other unidentified processes [3]. The gut microbiota plays an important role in digestion, physical health, and mental well-being. Recent research has shown that beneficial bacteria can compromise the health of some people and lead to autoimmune diseases in more vulnerable individuals [4].

In studies conducted on both mice and humans, scientists have observed that engaging in physical activity—regardless of dietary habits—alters the makeup of gut microbiota by enhancing the synthesis of short-chain fatty acids (SCFAs), which are advantageous for health [5]. This study is the inaugural investigation to show that physical activity alone can enhance gut bacterial diversity, regardless of dietary factors. The researchers observed that after six weeks of engaging in 30 to 60 minutes of exercise three times weekly, there was a notable increase in short-chain fatty acids (SCFAs), particularly butyrate. However, if individuals reverted to their former sedentary habits, the levels of SCFAs diminished once more [6]. After physical activity, individuals with a lean physique exhibited the most significant rise in bacteria that produce short-chain fatty acids (SCFAs). In contrast, those who were obese experienced only a slight increase. Probiotics can contribute to enhancing immune function either directly or indirectly. Therefore, this study sought to examine how these elements influence the immune response following intense exercise among male participants [7]. The results of this study can provide valuable information to sports scientists, athletic trainers, health planners, and overall planners seeking to improve the performance of athletes. The present study specifically aimed to assess the impact of probiotic supplementation on the key immune parameters in male athletes engaged in regular physical activity before and after exposure to exhausting exercise.

2. Methods

2.1. Study Design

In a semi-experimental study, 28 male athletes were randomly chosen from various sports centers in Osh City, Kyrgyzstan. These individuals were aged between 18 and 35 years and had engaged in regular physical activity for an average of three days per week over the past three years. The research received approval from the Local Ethics Research Committee at Osh State University (OSHSU4125-4008). The results were reported according to the CONSORT guideline recommendations for reporting clinical trials [8].

2.2. Disease Definition and Immune Considerations in Athletes

Athletes frequently experience elevated levels of physical and physiological stress, which can affect their immune system. This is particularly relevant in the context of high-intensity training, where the body is subjected to considerable strain. Exercise-induced immunosuppression (EIS) is a recognized condition where extended or excessive training may result in a temporary decline of immune responses, thereby raising the likelihood of upper respiratory tract infections (URTIs), inflammation, and metabolic disruptions. This issue of immune system vulnerability is especially pertinent for endurance athletes or those engaged in rigorous training regimens since their adaptive immune systems might be weakened, making them more vulnerable to infections. Considering the significant role that gut microbiota plays in influencing immune reactions, probiotics have been explored as a possible strategy to enhance immune resilience among athletes. The current study examines the effectiveness of probiotic supplementation in alleviating the immune disturbances caused by intense exercise. By investigating the specific strains of probiotics and their effects on immune markers, researchers aim to provide athletes with evidence-based recommendations for optimizing their health.

2.3. Epidemiology: Prevalence and Incidence of Exercise-Induced Immunosuppression

Exercise-induced immune suppression is widely documented in sports medicine. Studies estimate that 10–20% of elite athletes experience recurrent upper respiratory infections (URTIs) due to immunological suppression linked to overtraining. Endurance athletes, particularly marathon runners, are at a 30–50% higher risk of developing post-exercise immune disturbances compared to recreational exercisers. Markers of systemic inflammation, such as C-reactive protein (CRP) and interleukin-6 (IL-6), tend to increase significantly following exhaustive physical exertion, while salivary immunoglobulin A (IgA) levels drop, reducing mucosal immunity. Given these statistics, the role of probiotics in mitigating exercise-induced immune suppression is of growing interest. This study sought to explore whether a 12-week course of probiotic supplementation could help improve immune markers in physically active individuals.

2.4. Inclusion and Exclusion Criteria

The inclusion criteria for the study were membership in the sport club, between the ages of 18 and 35 years, regular exercise 3 days a week, and a 3-year sports history. Participants with any comorbidities such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA), diabetes, systemic lupus erythematosus (SLE), and other autoimmune diseases, use of anti-inflammatory medications, probiotics, prebiotics, synbiotics, or other antioxidants and anti-inflammatory treatments, malnutrition (BMI under 18.5) or morbid obesity (BMI > 35), imbalance in Th1/Th2 such as asthma, pregnancy, and breastfeeding, were excluded.

2.5. Outcome Measures

After securing informed consent from all participants and ensuring they fully understood the study's objectives, procedures, and potential risks, each individual was required to complete a 28-item General Health Questionnaire (GHQ), as well as a Global Physical Activity Questionnaire (GPAQ) [9]. Following this initial assessment, the athletes were then randomly assigned to either the experimental group or the control group. Through the study, we systematically observed the changes in immune-related biomarkers, such as cell blood, C-reactive protein (CRP), and immunoglobulin A (IgA) levels, in response to physical activity and probiotics supplementation.

2.6. Procedure

At the outset of the research, a meeting was held for all participants to outline the overall advantages and significance of their honesty and collaboration in measuring VO_2 max. The standard test was used to homogenize the subjects. The standard 24-hour food recall questionnaire was also used to control nutrition [9]. The demographic details, including the height and weight of the subjects, were measured using a digital scale and a wall-mounted stadiometer (Seca, Hamburg, Germany). Subsequently, 28 subjects were selected from those who had a VO_2 max in the range of 60.6 ± 8.9 per minute. On the day of the first stage of the exercise program, 7 ml of blood was taken from the left arm of the study subjects in a sitting position, and 1 ml of blood was taken from the left arm of the study subjects in a fasting state by a nurse. After the subjects warmed up by walking on a treadmill for 5 minutes, they participated and ran until Bros according to the standard protocol and program in the fatigue threshold test with increasing incline and speed. The second stage was performed 4 minutes after the end of exercise and cooling down—blood sampling of 5 athletes. The participants were subsequently assigned at random to either the experimental group receiving probiotics or the control group that received a placebo. Participants in the probiotic group received 2 probiotic capsules/day for 12 weeks, containing at least 2 billion live microorganisms (2×10^9 CFU/capsule) of 7 strains (*Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium bryo*, *Bifidobacterium longum*, and *Streptoco*ccus) one hour after the main meal with water. Participants in the placebo group received the same amount with similar shapes (capsules containing starch) per day for 12 weeks. All participants were also asked to avoid consuming yogurt during the study period due to its lactobacillus and any other effective supplements, so as not to interfere with the assessment of the factors under study. After the end of the 12-week intervention, blood samples were taken once again in two stages: before and after the exhaustive exercise (Bruce test).

2.7. Outcome Assessment

To assess innate and acquired immunity, serum CRP and IgA, lymphocyte, monocyte, and granulocyte factors were evaluated [10]. Blood samples were poured into tubes containing EDTA anticoagulant for blood cell counting, immediately transported to the laboratory, and then centrifuged at 5000 rpm (≈1,700–2,200 × g for a 6–8 cm rotor radius) (AHN myLab® Centrifuge, GmbH Biotechnology, Germany) for 10 minutes to separate serum. Blood cell counting was performed with an Excel electronic cell counter (Excel Cell Electronic Co., Ltd, UK).

2.8. Statistical Analysis

The Kolmogorov-Smirnov test was used to check the normality of the data and, the Levene's test was used to check the equality of variances. The comparison of the two study groups in terms of demographic variables was performed with the independent t-test, and the effect of different variables during the intervention period was measured with the repeated measures method due to the repetition of the experiments over time (Repeated Measures). The significance level was considered to be less than 0.05 ($p < 0.05$).

3. Results

The overall average age of the participants (n = 28) was 20.98 ± 5.9 years, weight was 62.3 ± 9.8, height was 168.2 ± 7.6 cm, body mass index (BMI) was 22.05 ± 2.4 kg/m^2, and VO_2 max was 59.98 ± 8.8 ml/kg/min. Based on the analysis, no significant difference was observed between the two groups in terms of baseline characteristics (**Table 1**).

Based on the presented results, it was determined that the intervention with probiotic tablets only produced a significant difference in monocytes at both activity and resting levels in the intervention group compared to the placebo group. In addition, it should be noted that in the comparison within the probiotic group, the number of lymphocytes, monocytes, and granulocytes at the activity level showed a significant increasing trend ($p < 0.001$) (**Table 2**).

Table 1. Baseline characteristics of the subjects in the experimental and control groups (Mean ± SD).

Variables	Experimental Group (n = 14)	Control Group (n = 14)	*p*-Values
Age (years)	20.67 ± 4.7	21.9 ± 5.8	0.5429
Height (Cm)	166.23 ± 8.9	167.58 ± 9.1	0.6947
Weight (Kg)	61.6 ± 7.8	60.9 ± 5.6	0.7882
BMI kg/m^2	20.64 ± 3.2	21.08 ± 2.1	0.6706
VO_2 max (ml/kg/min)	60.16 ± 8.8	59.76 ± 6.9	0.8946

Table 2. Comparison of the cell blood count (CBC) change trends in the experimental and placebo groups.

Variables		Experimental Group (n = 14)		Control Group (n = 14)	
		Pre	Post	Pre	Post
Lymphocyte (%)	Resting	34.26 ± 6.01	35.3 ± 7.8	36.21 ± 7.8	37.83 ± 8.71
	Activity	32.7 ± 5.8	38.6 ± 6.9 *	36.75 ± 5.6	37.98 ± 7.01
Monocyte (%)	Resting	0.87 ± 0.56	1.43 ± 0.84	0.96 ± 0.29	0.91 ± 0.17
	Activity	0.99 ± 0.81	3.89 ± 1.87**	2.57 ± 1.07	3.14 ± 1.02
Granulocyte (%)	Resting	63.9 ± 7.12	62.95 ± 8.15	60.12 ± 11.12	64.04 ± 8.6
	Activity	64.79 ± 7.19	55.69 ± 6.95 ***	50.8 ± 10.75	52.4 ± 9.85
CRP (mg/L)	Resting	2.07 ± 1.32	2.84 ± 0.98	2.89 ± 1.63	3.44 ± 1.38
	Activity	6.59 ± 3.18	7.73 ± 2.54	2.91 ± 1.03	3.16 ± 1.01
IgA (g/L)	Resting	1.78 ± 0.98	2.17 ± 0.54	1.98 ± 0.64	2.32 ± 0.57
	Activity	1.96 ± 0.52	2.27 ± 1.52	1.98 ± 0.64	2.21 ± 0.79

Note: Statistically significant difference, * $p = 0.041$; ** $p = 0.006$; *** $p = 0.008$.

4. Discussion

The results of the present study reveal intriguing insights into the impact of probiotic supplementation over 12 weeks. When assessed at the resting level, the consumption of a combined probiotic demonstrated a significant effect solely on the monocyte factor. This finding suggests that while the probiotics may not have influenced other measured immune parameters at rest, they play a crucial role in modulating specific immune cell populations. However, the dynamics shifted markedly when evaluating the response to physical exertion. Following exhausting physical activity, the same probiotic regimen exhibited a notable increase in other primary immune factors, including monocytes, lymphocytes, and granulocytes. This enhancement indicates a robust interaction between probiotic supplementation and the body's innate immune response during periods of physical stress. It is essential to underscore that the significant differences observed in monocytes during the intergroup comparison suggest that the probiotic intervention effectively influenced the immune response during maximal activity. Importantly, this increasing effect is attributed more to the ingestion of probiotics rather than to the physical activity itself. Probiotics are known to engage with various immune cells, particularly through interactions with macrophage cells situated in the intestinal tight junction areas, epithelial cells, and dentate cells. These interactions are pivotal for the development and regulation of immune function.

Macrophages, in particular, serve as key orchestrators of the immune system, initiating immune reactions that can either suppress inflammation or promote it, depending on the context. These cells infiltrate the spaces between intestinal epithelial cells and engage with probiotics present in the intestinal wall to regulate immune functions [11]. The engagement of probiotics with intestinal epithelial cells stimulates the release of antimicrobial substances as well as B and T cell cytokines, which subsequently activate T cells within the lymphoid tissue located in the gastrointestinal tract [12]. Tavares-Silva et al. [13] conducted a randomized controlled trial on marathon runners using multi-strain probiotics, showing that this supplementation preserves the functionality of monocytes. Guo et al. [14] in a meta-analysis of immune markers and response to probiotic supplementation in athletes, measured the tumor necrosis factor (TNF)-α, different interleukins, interferon (IFN)-γ, and CRP in nine clinical trials and observed no significant difference in these variables. Gleeson et al. [15] in their study on male and female endurance athletes to investigate the effect of consuming probiotics for 4 months, did not observe any changes in lymphocyte, monocyte, and granulocyte levels. These results were not consistent with the present study. In athletes with long-term and intense training, disturbances in IgA secretion, increased temperature, and impaired mucosal immunity cause a decrease in performance [16]. Studies have shown that probiotics can directly affect immune cells within the mucosa and play a role in modulating immunity and strengthening the immune system. Most importantly, probiotics exert these positive effects on the immune system without causing a harmful inflammatory response [17]. Therefore, it seems that probiotics can increase host resistance naturally and healthily when facing injury and stress [18]. Recent research has shown that probiotics also affect specific immunity by producing IgA antibodies, increasing macrophage activity, and increasing phagocytosis [19].

In a study in which healthy men and women were vaccinated against influenza, serum IgA levels increased in the probiotic group, and probiotics increased antibody responses to the stimulus [20]. However, in the present study, such an effect was not observed after 12 weeks of probiotic supplementation, which is consistent with the results of a study by Agraib et al. [21]. In the present study, the results can be explained as follows: since acquired immunity is specific, it takes several days to several weeks to develop [22]; therefore, in the present study, it is likely that the duration of probiotic consumption is the time required to cause changes in IgA. In the study conducted by Kekkonen et al. [23], where athletes and healthy individuals ingested LGG probiotics for 3 months and 3 weeks, it was found that the serum levels of lymphocytes, their subtypes, and granulocytes did not show any significant changes in either group. However, the number of serum monocytes in the athletes in the LGG-consuming group was lower for 3 months compared to the placebo group. In healthy adults, no difference in monocyte counts was observed during the 3-week LGG consuming intervention. The immune components are affected by both genetic and environmental influences [23, 24]. Some research has indicated that physical activity might alleviate mild inflammation by lowering levels of CRP [25]. In the present study, a combined probiotic of gram-positive bacteria was effective in cellular and humoral immunity at resting and response levels, which was likely influenced by the strain used, the duration of probiotic use, and the level of fitness of the subjects for the exercise test. As observed in previous studies, the effect of probiotics is likely to be influenced by the choice of bacterial strain, bacterial count, quantity, diversity, and persistence of bacteria until they reach the intestine [26–28]. In addition, the data in this study were generally limited to single-strain probiotics. In the present study, Gram-positive probiotic bacteria were used, but their immunomodulatory effects were not multiplied, which is similar to the situation when only one strain was used, and this is probably because all Gram-positive bacteria use the same signals for intracellular transduction mechanisms to induce adaptive and innate immunity through lymphoid cells of the intestinal wall [29, 30].

Lactobacillus plantarum, *Lactobacillus brevis*, and *Leuconostoc mesenteroides*, are common in fermented foods like sauerkraut and kimchi, according to research from the National Institutes of Health (NIH) [31]. Both prebiotics and probiotics are important for human health. However, they have different roles [32]. As we mentioned earlier, probiotics are live bacteria found in some foods or supplements. They can have many health benefits. However, prebiotics are derived from types of carbohydrates (mostly fiber) that humans cannot digest. The beneficial bacteria in your gut eat this fiber. Gut bacteria, collectively known as gut flora or gut microbiota, perform many important functions in the body. Synbiotics offer a combination of probiotics and prebiotics. The synergistic relationship between probiotics and prebiotics is nothing new: they have always worked in harmony, and both are naturally found in our diet [33]. Prebiotics are indigestible fibers that selectively feed our gut bacteria, enabling them to thrive. They can be found in foods like garlic, onions, and legumes, but are also available as supplements. The number of bacteria in the colon is also greater than the number of cells in the body. Most of the bacteria in the digestive tract are harmless and beneficial to human health [34]. However, recent studies have shown that some harmful microbial flora in the digestive tract can play a role in the occurrence of digestive cancers [35]. Several studies have shown that inflammation, loss of the intestinal barrier, and increased permeability of intestinal epithelial cells are associated with increased insulin resistance [36]. Thus, it has been hypothesized that the destruction of the intestinal cell barrier results in a disruption of the intestinal microbiota and the development of inflammation in the body [37]. There is ample evidence that this imbalance causes metabolic dysregulation in the body [38, 39]. Animal studies have shown that this imbalance causes the production of significant amounts of lipopolysaccharide, which causes inflammation in the intestinal mucosa, leading to increased permeability of the intestinal cell wall and the lipopolysaccharide to leak into the bloodstream, resulting in systemic inflammation and ultimately insulin resistance [40].

5. Future Recommendations

The results of this research underscore the possible influence of probiotic supplementation on enhancing immune functions in physically active individuals. However, there remain several critical aspects that require additional investigation to comprehensively grasp the lasting effects of probiotics on athletic performance, recovery processes, and overall immune health. Future studies ought to focus on performing extensive, long-term clinical trials to evaluate the prolonged effects of probiotic supplementation on immune response after a 12-week intervention period. Increasing the sample size would improve the applicability of the results, making them relevant for various athletic groups such as endurance, strength, and mixed-sport athletes.

While this research noted beneficial effects on immune modulation, additional studies are necessary to investigate the specific mechanisms through which probiotics affect immune cells, cytokine production, and the composition of gut microbiota. Utilizing advanced methodologies like metagenomics, transcriptomics, and metabolomics may yield comprehensive insights into microbial functions and interactions between hosts and their microbiomes.

The present research employed a multi-strain probiotic supplement; however, further comparative studies are necessary to assess the effectiveness of single-strain versus multi-strain probiotics. Future investigations should focus on examining the specific effects of different strains on immune markers, given that various bacterial strains may have distinct immunomodulatory and anti-inflammatory characteristics. Given the individual variability in gut microbiota composition, future studies should explore the feasibility of personalized probiotic interventions tailored to an athlete's specific microbiome profile. This personalized approach could optimize gut health, immune function, and exercise recovery, leading to more effective and targeted probiotic supplementation strategies. Future studies ought to explore the impact of dietary elements on the efficacy of probiotics. Research should evaluate if particular compositions of macronutrients and micronutrients, including fiber, polyphenols, or omega-3 fatty acids, improve probiotic survival rates, colonization processes, and their immune-enhancing benefits.

While this research mainly concentrated on immune responses, subsequent studies ought to examine the impact of probiotics on muscle recovery, fatigue alleviation, inflammation management, and endurance capabilities. Including biomarkers associated with muscle injury (such as creatine kinase and lactate levels) along with indicators of oxidative stress may offer a more thorough understanding of the performance advantages facilitated by probiotics.

Most current research, including this study, predominantly centers on male athletes. Future investigations need to explore the immune response to probiotics among female athletes and various age categories (such as adolescents, older adults, or master's athletes) in order to assess whether there are variations in probiotic effectiveness based on age and sex.

Emerging research indicates that the gut microbiome significantly influences brain function, cognitive abilities, and mental resilience. Subsequent investigations should examine the impact of probiotic supplementation on athletes' stress responses, mental fatigue, sleep quality, and cognitive performance by assessing its effects on the gut-brain-immune axis.

6. Conclusions

The findings of this study indicate that a 12-week regimen of probiotic supplementation can significantly enhance immune function by positively affecting the levels of key blood cells, including lymphocytes, monocytes, and granulocytes. Specifically, the results suggest that the incorporation of probiotics into the diet not only bolsters the immune response but also provides a nuanced understanding of how different types of blood cells interact during this process. In addition, compared to placebo, the consumption of probiotic capsules in conjunction with starch demonstrates a selective impact, primarily affecting monocyte levels without a corresponding enhancement in overall immune system efficacy. This suggests that while probiotics can be beneficial, their effects may vary depending on the specific immune cells involved, underscoring the complexity of immune modulation. Microbiome-related studies are currently underway, but they are likely to suffer from the limitations associated with genomic studies. While an individual's genome is fixed, their microbiome fluctuates over time, with the environment, and with drug treatment. As we continue to unravel the complexities of the microbiome and its interactions with our immune system, we open up new perspectives that could lead to innovative strategies for managing autoimmune conditions and enhancing overall health. By understanding how probiotic supplementation, physical activity, and immune responses interconnect, we pave the way for more personalized and effective health interventions in the future. This evolving knowledge base highlights the potential for probiotics to play a pivotal role in health maintenance and disease prevention, ultimately contributing to a more robust immune system capable of responding effectively to various challenges.

Author Contributions

Conceptualization, I.Z.A., O.A.M., R.S.J., A.J.N., Z.A.J., and S.S.; validation, R.S.J. and A.J.N.; formal analysis, I.Z.A. and O.A.M.; data curation, I.Z.A. and O.A.M.; writing—original draft preparation, I.Z.A. and O.A.M.; writing—review and editing, R.S.J. and A.J.N. All authors have read and agreed to the published version of the manuscript.

Funding

Authors received no fund.

Institutional Review Board Statement

The article provides a thorough and nuanced examination of ethical concepts, ensuring a comprehensive understanding of the principles guiding the research. It meticulously outlines the goals and methodology of the study, which are crucial for establishing transparency and trust between the researchers and participants. Each participant was explicitly informed that their involvement was entirely voluntary, allowing them the freedom to withdraw from the study at any point without any repercussions. This approach not only respects the autonomy of the participants but also adheres to ethical research standards.

Furthermore, participants were assured that their personal information would be treated with the utmost confidentiality, safeguarding their privacy and fostering a sense of security throughout the research process. To promote transparency, they were also given the option to access the findings of the study upon its completion. This provision reflects a commitment to ethical accountability, allowing participants to engage with the outcomes of the research that they contributed to.

The study received the necessary approval from the ethics committee, as indicated by reference number: OSHSU 1525-2347-2208.

Informed Consent Statement

The study received approval from the Ethics Committee of Osh State University (Reference No.: OSHSU1525-2347-2208). Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the participants to publish this paper.

Data Availability Statement

All data is presented in the manuscript.

Acknowledgments

The authors would like to extend their heartfelt gratitude to all participants of the research, whose invaluable contributions played a critical role in the success of this study. We also wish to acknowledge Osh State University for their unwavering support throughout this research endeavour.

Conflicts of Interest

The authors declared no conflict of interest.

References

1. da Silveira, M.P.; da Silva Fagundes, K.K.; Bizuti, M.R.; et al. Physical Exercise as a Tool to Help the Immune System Against COVID-19: An Integrative Review of the Current Literature. *Clin. Exp. Med.* **2021**, *21*, 15–28. [CrossRef]
2. Nieman, D.C.; Wentz, L.M. The Compelling Link Between Physical Activity and the Body's Defense System. *J. Sport Health Sci.* **2019**, *8*, 201–217. [CrossRef]
3. Belkaid, Y.; Hand, T.W. Role of the Microbiota in Immunity and Inflammation. *Cell* **2014**, *157*, 121–141. [CrossRef]
4. Hou, K.; Wu, Z.X.; Chen, X.Y.; et al. Microbiota in Health and Diseases. *Signal Transduct. Target. Ther.* **2022**, *7*, 135. [CrossRef]
5. Monda, V.; Villano, I.; Messina, A.; et al. Exercise Modifies the Gut Microbiota with Positive Health Effects. *Oxid. Med. Cell. Longev.* **2017**, *2017*, 3831972. [CrossRef]
6. Lu, Y.; Fan, C.; Li, P.; et al. Short Chain Fatty Acids Prevent High-Fat-Diet-Induced Obesity in Mice by Regulating G Protein-Coupled Receptors and Gut Microbiota. *Sci. Rep.* **2016**, *6*, 37589. [CrossRef]
7. Mach, N.; Fuster-Botella, D. Endurance Exercise and Gut Microbiota: A Review. *J. Sport Health Sci.* **2017**, *6*, 179–197. [CrossRef]
8. Butcher, N.J.; Monsour, A.; Mew, E.J.; et al. Guidelines for Reporting Outcomes in Trial Reports: The CONSORT-Outcomes 2022 Extension. *JAMA* **2022**, *328*, 2252–2264. [CrossRef]
9. Armstrong, T.; Bull, F. Development of the World Health Organization Global Physical Activity Questionnaire (GPAQ). *J. Public Health* **2006**, *14*, 66–70. [CrossRef]
10. Ahmad, S.M.; Haskell, M.J.; Raqib, R.; et al. Markers of Innate Immune Function Are Associated with Vitamin A Stores in Men. *J. Nutr.* **2009**, *139*, 377–385. [CrossRef]
11. Saulnier, D.M.; Ringel, Y.; Heyman, M.B.; et al. The Intestinal Microbiome, Probiotics and Prebiotics in Neurogastroenterology. *Gut Microbes* **2013**, *4*, 17–27. [CrossRef]
12. Hashemi, B.; Abdollahi, M.; Abbaspour-Aghdam, S.; et al. The Effect of Probiotics on Immune Responses and Their Therapeutic Application: A New Treatment Option for Multiple Sclerosis. *Biomed. Pharmacother.* **2023**, *159*, 114195. [CrossRef]
13. Tavares-Silva, E.; Caris, A.V.; Santos, S.A.; et al. Effect of Multi-Strain Probiotic Supplementation on URTI Symptoms and Cytokine Production by Monocytes After a Marathon Race: A Randomized, Double-Blind, Placebo Study. *Nutrients* **2021**, *13*, 1478. [CrossRef]
14. Guo, Y.T.; Peng, Y.C.; Yen, H.Y.; et al. Effects of Probiotic Supplementation on Immune and Inflammatory Markers in Athletes: A Meta-Analysis of Randomized Clinical Trials. *Medicina* **2022**, *58*, 1188. [CrossRef]
15. Gleeson, M. Immune Function in Sport and Exercise. *J. Appl. Physiol.* **2007**, *103*, 693–699. [CrossRef]
16. Drummond, L.R.; Campos, H.O.; Drummond, F.R.; et al. Acute and Chronic Effects of Physical Exercise on IgA and IgG Levels and Susceptibility to Upper Respiratory Tract Infections: A Systematic Review and Meta-Analysis. *Pflugers Arch.* **2022**, *474*, 1221–1248. [CrossRef]
17. Yan, F.; Polk, D.B. Probiotics and Immune Health. *Curr. Opin. Gastroenterol.* **2011**, *27*, 496–501. [CrossRef]
18. Obianwuna, U.E.; Kalu, N.A.; Wang, J.; et al. Recent Trends on Mitigative Effect of Probiotics on Oxidative-Stress-Induced Gut Dysfunction in Broilers Under Necrotic Enteritis Challenge: A Review. *Animals* **2023**, *12*, 911. [CrossRef]
19. Al-Najjar, M.A.A.; Abdulrazzaq, S.B.; Alzaghari, L.F.; et al. Evaluation of Immunomodulatory Potential of Probiotic Conditioned Medium on Murine Macrophages. *Sci. Rep.* **2024**, *14*, 7126. [CrossRef]
20. Zhang, Y.; Yang, L.; Zhang, J.; et al. Oral or Intranasal Immunization with Recombinant Lactobacillus plantarum Displaying Head Domain of Swine Influenza A Virus Hemagglutinin Protects Mice from H1N1 Virus. *Microb. Cell Fact.* **2022**, *21*, 185. [CrossRef]
21. Agraib, L.M.; Yamani, M.I.; Tayyem, R.; et al. Probiotic Supplementation Induces Remission and Changes in the Immunoglobulins and Inflammatory Response in Active Ulcerative Colitis Patients: A Pilot, Randomized, Double-Blind, Placebo-Controlled Study. *Clin. Nutr. ESPEN* **2022**, *51*, 83–91. [CrossRef]
22. Parkin, J.; Cohen, B. An Overview of the Immune System. *Lancet* **2001**, *357*, 1777–1789. [CrossRef]
23. de Vrese, M.; Winkler, P.; Rautenberg, P.; et al. Probiotic Bacteria Reduced Duration and Severity but Not the Incidence of Common Cold Episodes in a Double-Blind, Randomized, Controlled Trial. *Vaccine* **2006**, *24*, 6670–6674. [CrossRef]
24. Berg, A.; Müller, H.M.; Rathmann, S.; et al. The Gastrointestinal System—An Essential Target Organ of the Athlete's Health and Physical Performance. *Exerc. Immunol. Rev.* **1999**, *5*, 78–95. [CrossRef]
25. Shen, J.; Ordovas, J.M. Impact of Genetic and Environmental Factors on hsCRP Concentrations and Response

to Therapeutic Agents. *Clin. Chem.* **2009**, *55*, 256–264. [CrossRef]
26. Albers, R.; Antoine, J.M.; Bourdet-Sicard, R.; et al. Markers to Measure Immunomodulation in Human Nutrition Intervention Studies. *Br. J. Nutr.* **2005**, *94*, 452–481. [CrossRef]
27. Gleize, B.; Tourniaire, F.; Depezay, L.; et al. Effect of Type of TAG Fatty Acids on Lutein and Zeaxanthin Bioavailability. *Br. J. Nutr.* **2013**, *110*, 1–10. [CrossRef]
28. Di Dio, M.; Calella, P.; Pelullo, C.P.; et al. Effects of Probiotic Supplementation on Sports Performance and Performance-Related Features in Athletes: A Systematic Review. *Int. J. Environ. Res. Public Health* **2023**, *20*, 2226. [CrossRef]
29. Corthésy, B.; Gaskins, H.R.; Mercenier, A. Cross-Talk Between Probiotic Bacteria and the Host Immune System. *J. Nutr.* **2007**, *137*, 781S–790S. [CrossRef]
30. Filidou, E.; Kandilogiannakis, L.; Shrewsbury, A.; et al. Probiotics: Shaping the Gut Immunological Responses. *World J. Gastroenterol.* **2024**, *30*, 2096–2108. [CrossRef]
31. Behera, S.S.; Ray, R.C.; Zdolec, N. Lactobacillus plantarum With Functional Properties: An Approach to Increase Safety and Shelf-Life of Fermented Foods. *Biomed. Res. Int.* **2018**, *2018*, 9361614. [CrossRef]
32. Hranush, H.; Hayk, S.; Arakelyan, H. Difference Between Prebiotics and Probiotics. *ResearchGate* **2021**. (in Armenian) [CrossRef]
33. Markowiak, P.; Śliżewska, K. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. *Nutrients* **2017**, *9*, 1021. [CrossRef]
34. Dekaboruah, E.; Suryavanshi, M.V.; Chettri, D.; et al. Human Microbiome: An Academic Update on Human Body Site Specific Surveillance and Its Possible Role. *Arch. Microbiol.* **2020**, *202*, 2147–2167. [CrossRef]
35. Ağagündüz, D.; Cocozza, E.; Cemali, Ö.; et al. Understanding the Role of the Gut Microbiome in Gastrointestinal Cancer: A Review. *Front. Pharmacol.* **2023**, *14*, 1130562. [CrossRef]
36. Winer, D.A.; Luck, H.; Tsai, S.; et al. The Intestinal Immune System in Obesity and Insulin Resistance. *Cell Metab.* **2016**, *23*, 413–426. [CrossRef]
37. Dmytriv, T.R.; Storey, K.B.; Lushchak, V.I. Intestinal Barrier Permeability: The Influence of Gut Microbiota, Nutrition, and Exercise. *Front. Physiol.* **2024**, *15*, 1380713. [CrossRef]
38. Hoogendoorn, C.J.; Roy, J.F.; Gonzalez, J.S. Shared Dysregulation of Homeostatic Brain-Body Pathways in Depression and Type 2 Diabetes. *Curr. Diab. Rep.* **2017**, *17*, 90. [CrossRef]
39. Refisch, A.; Sen, Z.D.; Klassert, T.E.; et al. Microbiome and Immuno-Metabolic Dysregulation in Patients With Major Depressive Disorder With Atypical Clinical Presentation. *Neuropharmacology* **2023**, *235*, 109568. [CrossRef]
40. An, L.; Wirth, U.; Koch, D.; et al. The Role of Gut-Derived Lipopolysaccharides and the Intestinal Barrier in Fatty Liver Diseases. *J. Gastrointest. Surg.* **2022**, *26*, 671–683. [CrossRef]