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Review Article

Physiology Section

Immune System and Malnutrition: The Inseparable Duo in Managing HIV: A Narrative Review

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ABSTRACT

Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) are among the greatest public health challenges around the globe. India ranks the third largest HIV epidemic in the world. People Living With HIV (PLWH) are highly susceptible to life threatening conditions as HIV destroys the body's immune system. Despite anti-retroviral treatments, tackling HIV and AIDS has been an uphill task for decades with all the countries contributing their best to decrease the incidence and mortality rate. But this has been difficult as there are problems in plenty across the globe. Loss of life, economic burden, psychological effects, stigma, discrimination are the perennial problems of HIV and AIDS. Awareness about HIV/AIDS and factors influencing the disease progression is the key to break this cycle. One of the important factors influencing the disease outcome is immune status of an individual. The immune system is highly influenced by nutrition which is an integral part in managing HIV. Nutrition has always contributed to the robust functioning of the immune system of an individual. PLWH almost always have malnutrition which, if not corrected, influences the outcome of HIV infection drastically. With people across the globe showing malnutrition, either under or excess, the immune system functioning is impaired, particularly so in PLWH. Unfortunately, nutrition has been ignored or sidelined in managing HIV/AIDs. This review gives an overview of the interrelation of nutrition and immune system and how these influence the outcomes in PLWH.

Keywords: Acquired immune deficiency syndrome, Human immunodeficiency virus, Immunology, Nutritional status

INTRODUCTION

The Human Immunodeficiency Virus (HIV) has existed since almost a century. Historically, HIV and Acquired Immune Deficiency Syndrome (AIDS) epidemic began from illness, death, and subsequent fear, as the world faced a new and unknown virus. HIV crossed from chimps to humans in the late 19th or early 20th century [1].

Types of HIV: There are two types of HIV, namely, HIV-1 and HIV-2. HIV-1 is the commonest virus infecting the population.

HIV targets White Blood Cells (WBCs) called CD4+ T lymphocytes. HIV infects these T cells by entering them and making numerous copies of itself. Later, the infected T cells are killed and the viral copies are released. The newly formed HIV copies find other uninfected T cells and the cycle continues. Thus, the important cell required for maintaining the body's defence mechanism is targeted repeatedly, causing weakening of the immune system functioning [2].

Nutrition plays a major role in the robust functioning of the immune system. There is an inherent connection between the two. It is seen that People Living With HIV (PLWH) have inadequate nutrition which is termed as malnutrition. This malnutrition in PLWH adversely affects the immune system causing rapid progression of the disease [3]. Therefore, PLWH need to make sure that they consume a balanced diet for optimal functioning of their immune system along with appropriate medications.

Immune system: Immune system is the body's defence mechanism to protect it from various pathogens. Immune system evolves from infants and continues till death. The evolving immune system continues to evolve and attain memory after exposure to multiple pathogens. The bioactivity of components of the immune system is very minimal at birth. As growth and development takes place, the bioactivity levels of various components of immune system starts to increase till adulthood [4]. The optimal functioning of the immune system is seen in adolescents and young adults. Till adulthood, the immunocompetency increases and then slowly starts declining as age advances [4].

Factors affecting immune system: Various factors influence the development and functioning of the immune system. These include genetic predisposition, maternal nutrition, infant's nutrition, exposure to environmental pathogens, and maternal stress, to name a few [5]. Studies have proved that nutritional sufficiency during the first 1000 days of life is critical for robust functioning of the immune system. Malnutrition during this period will hamper the evolving defensive capability of the immune system along with normal growth and development of the baby [5,6]. Sex hormones are known to influence the immune system. Studies have shown that women mount a better immune response than men [7,8]. This is attributed to the presence of oestrogen which is an immunomodulator. Whereas in men, testosterone has an immune inhibiting action [4].

Immune system has three levels of defence/barriers within the body.

- Physical and physiological
- Innate immunity
- Adaptive immunity

Physical barriers include intact skin and mucosa, tears, saliva, gastric juice, and normal commensals in the body, to name a few. The gut microbiome plays a dynamic role in functioning of the immune system, thereby warranting the microbiome level assessment during evaluation of nutritional status [9]. Innate immunity prevents entry of pathogens in the body and in case pathogens enter, they are rapidly eliminated. Neutrophils, eosinophils, basophils, monocytes, macrophages, and Natural Killer (NK) cells are involved in innate immunity. These cells do not have any memory of the pathogens that enter the body. Any foreign body is identified as 'non self' and is destroyed immediately. Therefore, such an immune response is also known as unspecified immune response [10].

In certain conditions, this innate immune response is not sufficient. So, a more complex immune response, termed adaptive immune response is warranted. This adaptive immune response is effective only after few days of initial activation due to pathogen. This type of immune response is found to persist over a long period of time, even

after the offending pathogen has been eliminated. When the cells of adaptive immune system are exposed to a variety of pathogens, it leads to immunological memory of these pathogens [11]. On re-exposure to that pathogen, the immune response is stronger and better [12].

The two classes of adaptive immune response are humoural and cell mediated response. These are mediated by lymphocytes. Humoural response involves B lymphocytes against extracellular pathogens, and T lymphocytes are involved in cell mediated immune response involving intracellular pathogens like bacteria and virus. Both humoural and cell mediated immunity are linked together, resulting in a highly effective immune response [10].

Nutritional immunology: Nutritional immunology is a part of immunology and deals with the influence of nutrition on the immune system [13].

Immune deficiency and its type: When the immune system is incapable of mounting an appropriate response, it is called immune deficiency. According to aetiology, there are two types of immune deficiency- primary and secondary/acquired. When the immune deficiency is due to genetic or developmental defect, it is termed primary immune deficiency. When the immune deficiency is due to various extrinsic factors, it is secondary immune deficiency. Secondary immune deficiency is more common than primary immune deficiency [14]. As nutrition highly influences the immune system, qualitative or quantitative malnutrition have shown to alter the humoural and cell mediated responses to varying degrees in both mother (during pregnancy) and child, thus becoming the primary reason for secondary immune deficiency. The next reason for acquired or secondary immune deficiency is HIV/AIDS [6]. But, the main cause of immune deficiency is severe malnutrition. This affects both innate and acquired immunity wherein the functioning of the components of the immune system is compromised [4,15].

Immune System and Nutrition

"Chicken or Egg," scenario: Till date, researchers find it is difficult to ascertain among immune system dysfunction and malnutrition, which is the cause and which is the effect [16]. The consensus may be that, both being the cause and the consequence of the other. The impact of immune dysfunction has been known to be recorded in the Deoxyribonucleic Acid (DNA). This leads to a scenario wherein, if malnourished people have offspring, the children inherit an altered immune system even after multiple generations [17].

This alteration in the immune system may then cause malnutrition even when there is adequate diet. In case of infections, malnutrition is aggravated, thereby causing the immune system to lower the immune response against the pathogens [18]. Therefore, malnutrition and immune system are intricately linked to one another [16].

Components of nutrition [19]:

- Macronutrients- Carbohydrates, proteins, and fat that provide calories or energy.
- Micronutrients- Vitamins and minerals

Functions of Macro and Micronutrients

For day-to-day activities, it is recommended that a balanced nutrition should have the following:

Carbohydrates accounting for 45-65%, fats accounting for 20-35% and protein accounting for 10-35% of the diet [20].

Micronutrients are present in different types of food. So, in order to get adequate micronutrients, a variety of foodstuff need to be consumed regularly. It is recommended that locally available seasonal food are one of the best sources of nutrients [21].

Macronutrient status reflects the total mass of the body and micronutrient status reflects the relative level of the body's cellular functions. Trace amounts of these micronutrients are highly essential for developing efficient immune system [22]. Micronutrient deficiency may exist without macronutrient deficiency, whereas macronutrient deficiency is commonly associated with micronutrient deficiencies. Irrespective of age, each person may have single or multiple micronutrient deficiencies. Micronutrients play a vital role in every step of the immune response. The quantity of micronutrients required for sustained optimal functioning of the immune response is more than the recommended dietary intake. Micronutrient deficiencies may be due to other factors like stress, anxiety, pollution, socioeconomic status, lifestyles, co-morbidities, seasons which depletes the body's reserve of micronutrients. [Table/Fig-1] gives us the overview of the role of micronutrients in each step of the immune response. Deficiency in macronutrients and/or micronutrients causes impairment of immune function, which usually can be reversed by nutrient repletion to some extent [13]. Therefore, it is imperative to provide adequate and balanced nutrition from birth and continue throughout life [23].

Zinc	• Weakens the barrier mucosa and facilitates penetration of pathogens • Associated with chronic inflammation • Impaired phagocyte and lymphocyte activity • Thymic atrophy • Increases the risk of infection • Decreased antiviral activity
Iron	• Depresses cellular immunity
Selenium	• Hastens disease progression in PLWH • Decreased antiviral activity
Vitamin A	• Compromised development of neutrophils, macrophages and Natural Killer (NK) cells leading to impairment of both innate immunity and adaptive immune response to infection
Vitamin C (Ascorbic acid)	• Weakens the mucosal barrier and facilitates penetration of pathogens • Delay in wound healing
Vitamin D	• Altered immunoregulatory effects on Immune cells like B cells, T cells, monocytes, Dendritic Cells (DCs) • Immunomodulatory effect • Higher susceptibility to infections • Defect in antigen-specific cellular immune response
Vitamin B12	• Significant decrease in the absolute number of CD8+ cells and suppressed NK cell activity
Vitamin B complex (B1, B2, B3, B5, B6, B9, B12)	• Dysregulation of the immune system and modifications in the function and production of neurotransmitters

[Table/Fig-1]: Deficiency of micronutrients and their effects [4,12,18,24-29].

Malnutrition

According to World Health Organisation (WHO), malnutrition refers to deficiencies, excesses, or imbalances in a person's intake of energy and/or nutrients. Malnutrition is a result of a deficiency of both macronutrients and micronutrients that is essential for physical and mental development, disease prevention, and general well-being [19].

Cause and effects of malnutrition: Malnutrition contributes in the alteration of physiological, psychological, and functional aspects [19]. It is especially severe in PLWH. Qualitative and quantitative inadequate diet over a long period of time, unhealthy lifestyle, unavailability of healthy food, consumption of low nutritive value foods, poor food habits, low socioeconomic status, poverty, insufficient education, chronic infections and improper utilisation of nutrition programme, are few causes of malnutrition [15].

Malnutrition can be divided into two groups, undernutrition and overnutrition. Both, under- and overnutrition are major factors in health and disease. It affects both children and adults.

1. Undernutrition: This is clinically seen as following in children [30]:

- Stunting (low height for age)
- Wasting (low weight for height)
- Underweight (low weight for age)
- Micronutrient deficiencies or insufficiencies (lack of important vitamins and minerals)

2. Excess/Overnutrition: This is clinically seen as following [30]:

- Overweight
- Obesity
- Diet-related non-communicable diseases (such as heart disease, stroke, diabetes, and cancer to name a few)

In 2021, 1.9 billion adults were obese, 462 million were underweight. In 2020, globally 149 million children under 5 years were stunted, 45 million were wasted, 38.9 million were obese [30].

Types of malnutrition: Immune deficiency is a hallmark of malnutrition. Immune dysfunction directly drives the pathological processes in malnutrition and contributes to a destructive interplay with global dimensions. There are 2 types of malnutrition-primary and secondary [6].

In primary malnutrition, organs involved in formation of components of the immune system are affected, thereby leading to a compromised defence system. This predisposes an individual to opportunistic infections as well as new pathogens [6].

In most conditions, the nutritional status can predict the clinical outcome of the disease [4].

In secondary malnutrition, when the primary cause of malnutrition is treated, functioning of the immune system improves when adequate and essential nutrition is supplemented above and beyond the requirement to compensate for the nutritional deficiency till balance is achieved. Diagnosis of immune deficiency must include other factors which influence immune system, such as age, comorbidities, medication, trauma, stress, etc., [4,14].

Malnutrition involving macronutrients like proteins, carbohydrates, and fat lead to protein-energy deficiencies/Protein Energy Malnutrition (PEM) and are seen exclusively in children. Malnutrition involving micronutrients like electrolytes, minerals and vitamins leads to specific micronutrient deficiencies [Table/Fig-1] [15].

PEM is seen as the following [31]:

- Kwashiorkor is seen as malnutrition with oedema wherein there is sufficient calorie intake but, deficient protein intake
- Marasmus, wherein severe wasting is seen due to deficient calorie intake
- Marasmic Kwashiorkor, wherein severe wasting and oedema is seen together due to marked protein deficiency and marked calorie insufficiency

Consequence of malnutrition: Physical barriers like skin, mucosa, gut environment is severely affected. The cornerstones of cellular immunity are phagocytosis and lymphocyte-mediated phenomena. Functioning of the immune system is altered in case of malnutrition, which includes cell survival ability, cellular proliferation, and function, leading to altered response to infection. B lymphocytes, macrophages and DCs are Antigen Presenting Cells (APC) which are required for both humoural and cell mediated immunity. These cells are significantly affected by malnutrition. Cell mediated immune response is more affected than humoural immunity. Of the macronutrients, deficiency of proteins impairs proliferation and activation of antigen specific T cells [15]. Altered cellular immunity and increased risk of autoimmunity is seen in obesity [32]. Delayed hypersensitivity reaction is affected. There is reduction in the phagocytosing capabilities, motility, chemotaxis, and bactericidal functions. In case of protein malnutrition, the body is unable to repair the immune system.

The integrity of the body's mechanical barriers against infection depends on good nutritional status. The primary immune response reflects the degree of malnutrition. Severe malnutrition causes fat degeneration of various organs [10]. Gut is the primary interface between diet and the immune system. Atrophy of intestine is observed in malnutrition, leading to suboptimal digesting capacity. In PEM, atrophy of thymus and bone marrow is commonly noted in infants, leading to inability of the immune system to function optimally as these are the source of cells involved in immune response, especially T and B cells [18]. The quality and quantity of the components of the immune system is altered according to nutritional status, leading to devastating results. Malnutrition increases susceptibility to infection. In case of infections, the nutritional demand increases which becomes a vicious downward cycle. Infections adversely affect nutritional status and malnutrition adversely affects the host's ability to withstand infection. Infections can also precipitate malnutrition. In case of malnourished mothers, there is reduction in the transfer of protective maternal immune factors and increase susceptibility to infections and poorer outcome in infections [16,33].

Microbiota and Malnutrition

Microbiota is thought to act as a sensor of dietary change as it is in direct contact with the ingested food. The microbiota sends signals to the human gut, thereby influencing the immune system. In turn the immune system sends signals that influence the composition of the microbiota in the gut [16]. The bacterial and viral microbiome also influences the systemic metabolism and vice versa [32]. When there is parasitic infestation, malnutrition is accentuated. Malnutrition in turn increases the susceptibility of infections.

Nutritional Assessment and Interventions

Nutritional deficits can be prevented through early, regular screening, assessment, and intervention. Nutrition screening tool, called the Patient-Generated Subjective Global Assessment (PG-SGA) may be used to check the nutritional status. Assessing micronutrient levels can determine deficiency state [5]. There is not a single parameter that can be used as a gold standard to assess the influence of nutritional status on immune system. Various biomarkers are assessed to study nutritional deficiency [10]. Not all macronutrients and micronutrients, are abnormal at a time. After assessment of the nutritional status, specific diet is prescribed to an individual based on the requirements. Malnutrition is reversible to some extent with nutritional rehabilitation, depending on the degree of severity. The quantity of the macro- or micronutrients generally is above the normal recommended dose in the beginning and continues till a correct or balanced nutritional status is achieved. These specific diet may modulate the activity of the immune system or the consequence of the activation of immune system [4,34]. In case of an undernourished child, the period between birth and two years of life is the golden period of opportunity for nutritional intervention. It is imperative to educate parents and caretakers about the importance of adequate and balanced diet of the child and also make them aware of the consequences of malnutrition [16].

HIV and Malnutrition

Nutritional assessment should begin when a patient is first diagnosed as HIV positive. The emphasis should be on avoiding malnutrition. Co-existence of malnutrition and infection has serious consequences and poorer outcomes. Infection causes an increase in the demand for nutrients. Conditions like tuberculosis, AIDS and other chronic infections cause anaemia and cachexia. Malnutrition in people with HIV compounds the already existing immune deficiency and hastens the disease progression. It also complicates treatment regimens [15].

Infection with HIV leads to poor nutrition. In PLWH, inadequate diet leading to malnutrition is associated with unsuppressed viral loads. PEM in PLWH leads to HIV associated 'wasting syndrome' wherein the symptoms are identified as "acquired immune deficiency syndrome defining" conditions. These include chronic diarrhoea, chronic weakness, fever for over a month, involuntary weight loss of more than 10% from baseline etc., [15]. These findings are not explained by other concurrent illnesses except for HIV infection. PEM acts as a cause of secondary immune deficiency, leading to increased risk and severity of opportunistic infection. Both decreases the quality of life as well as increase the mortality rate [19].

HIV eventually causes nutritional decline in most of the patients. In such cases, the outcome depends on the nutritional status of PLWH. A well-nourished HIV positive person with a controlled viral load is more likely to be able to withstand the effects of HIV infection [35].

Tackling Malnutrition in PLWH

To achieve optimal health in PLWH, the following protocol needs to be applied consistently. Educating, coaching, teaching, reinforcing behaviours, strengthening social support, and modelling will go a long way in improving the overall well-being of PLWH [36].

A multidisciplinary team approach is required for proper management of PLWH. Immuno-nutrition is an interdisciplinary subject, encompassing nutrition, immunity, infection, inflammation, and injury or tissue damage [10]. The prime focus in PLWH is tackling malnutrition as it influences all the above said areas. A specifically designed food containing the required nutrients in specified amounts can be developed to ensure balanced nutrition [37]. It is commonly seen that PLWH base their diet on the preference of family members leading to consumption of low value nutritive foods. PLWH are found to be ignorant regarding the ill effects of malnutrition [38]. They need to be educated as to why adequate nutrition is mandatory for their better health. They need to know the cause and consequence of malnutrition on viral loads. They need to be educated regarding the influence of nutrition on the immune system in fighting HIV. This leads to a better management of HIV symptoms and complications [38]. PLWH must be trained along with their family members on nutritional management. Diet should include all the components of macronutrients and micronutrients. Conscious effort should be made to stay away from processed foods and animal foods. Wholesome food of plant origin has shown to improve immune system. This strengthens and equips the immune system to defend the body better [39,40].

Despite potential effects of nutritional therapies in HIV infection, there are major limitations in the ability to provide effective nutritional support. One of the most important aspects is the socioeconomic status of PLWH. PLWH from low socioeconomic background who cannot afford nutritious food are at higher risk of their condition deteriorating. Appropriate treatment for malnutrition is essential for altering the existing deterioration and improve a patient's quality of life.

Physical Activity/Exercise and Immune System

Another vital area of focus in PLWH is physical activity. Exercise has been found to produce an immunomodulatory effect. The quantity of immune cells increases following physical activity. The intensity and duration of physical activity along with adequate nutrition have a strong influence on the immune system [41]. Regular physical activity is beneficial to the immune system which in turn boosts the quality of life [4,42]. For optimal immune function, good quality sleep, regular physical activity, adequate and balanced nutrition, maintaining good hygiene along with lowering stress levels will lead to a better and healthy lifestyle that will make the immune system stronger [43].

Do's and don'ts for HIV patients [44,45]:

- Have balanced diet
- Do not skip meals
- Do not skip medications
- Do not miss exercise or any physical activity
- Change to a better lifestyle
- Keep immune system healthy by avoiding risky behaviours
- Avoid low value nutrient foods

CONCLUSION(S)

The deadly interplay trio of HIV, immune system and malnutrition leads to many long-lasting devastating impacts. Immune system and nutrition are inter-related. Deficiency of one influences the other in a negative way and thus becomes a vicious cycle. Each becomes the cause and effect of the other. Generally, worldwide there is an increase in malnutrition which is precipitating infections. Malnutrition is a complex process, causing overlapping effects in PLWH. They must be educated regarding the influence of nutrition on their overall wellbeing as well as their ability of their immune system to deal with HIV related symptoms and complications. Based on age and specific needs, supplements must be tailor-made for PLWH for optimal immune function. This eases the disease burden and alleviates the overall impact of malnutrition. Strained health system resources cause difficulty to provide cost-efficient health care. A balanced diet is a positive way of responding to the illness and will help people to live longer, better, and lead more comfortable lives. Improving nutrition will undeniably recover the health and well-being of the patient in spite of HIV.

Future Directions

First and foremost, a better tool for identifying malnutrition needs to be designed that can be used worldwide. Then comes various other factors, the interplay of which needs to be studied further. For example, along with HIV, malnutrition, and immunity, the interplay of comorbidities, aging, lifestyle, sleep patterns, mental well-being, socioeconomic status, gender, and social acceptance, also need to be studied. Short and long-term randomised controlled trials are to be conducted and the resultant data should be evaluated for better understanding of their influence on each other. These results will point us to the future areas of research.

REFERENCES

[1] Wikipedia contributors. History of HIV/AIDS [Internet]. USA: Wikipedia, The Free Encyclopedia; 2023 Jun 3 [cited 2023 Aug 1]. Available from: https://en.wikipedia.org/w/index.php?title=History_of_HIV/AIDS&oldid=1158391283.
[2] Balasubramaniam M, Pandhare J, Dash C. Immune control of HIV. J Life Sci. 2019;1(1):04-37.
[3] Calder PC, Jackson AA. Undernutrition, infection, and immune function. Nutr Res Rev. 2000;13:03-29.
[4] Maggini S, Pierre A, Calder PC. Immune function and micronutrient requirements change over the life course. Nutrients. 2018;10(10):1531.
[5] Pai UA, Chandrasekhar P, Carvalho RS, Kumar S. The role of nutrition in immunity in infants and toddlers: An expert panel opinion. Clin Epidemiol Glob Health. 2018;6(4):155-59.
[6] Cantani A. In: Pediatric Allergy, Asthma and Immunology. Malnutrition and the Immune System. Springer, Berlin, Heidelberg. 2008, Chapter 21, pp 1243-1264. https://doi.org/10.1007/978-3-540-33395-1_21.
[7] Fink AL, Klein SL. The evolution of greater humoral immunity in females than males: Implications for vaccine efficacy. Curr Opin Physiol. 2018;6:16-20.
[8] Kovacs EJ, Messingham KA. Influence of alcohol and gender on immune response. Alcohol Res Health. 2002;26(4):257-63.
[9] Putignani L, Chierico FD, Petrucca A, Vernocchi P, Dallapiccola B. The human gut microbiota: A dynamic interplay with the host from birth to senescence settled during childhood. Pediatr Res. 2014;76(1):02-10.
[10] Zapatera B, Prados A, Gómez-Martínez S, Marcos A. Immunonutrition: Methodology and applications. Nutr Hosp. 2015;31(3):145-54.
[11] Netea MG, Schlitzer A, Placek K, Joosten LAB, Schultze JL. Innate and adaptive immune memory: An evolutionary continuum in the host's response to pathogens. Cell Host Microbe. 2019;25(1):13-26.
[12] Calder PC. Nutrition, immunity and COVID-19. BMJ Nutr Prev Health. 2020;0:01-19.
[13] Newsholme P. Cellular and metabolic mechanism of nutrient actions in immune function. Eur J Clin Nutr. 2021;75(9):1328-31.
[14] Chinen J, Shearer W. Secondary immunodeficiencies, including HIV infection. J Allergy Clin Immunol. 2008;121(2):S388-92.
[15] França T, Ishikawa L, Zorzella-Pezavento S, Chiuso-Minicucci F, da Cunha M, Sartori A. Impact of malnutrition on immunity and infection. J Venom Anim Toxins incl Trop Dis. 2009;15(3):374-90.
[16] Bourke CD, Berkley JA, Prendergast AJ. Immune dysfunction as a cause and consequence of malnutrition. Trends in Immunol. 2016;37(6):386-98.
[17] Cell Press. Why malnutrition is an immune disorder. America: ScienceDaily; 2016 May [July 26, 2023]. Available from: https://www.sciencedaily.com/releases/2016/05/160526124552.htm.
[18] Somech R. Malnutrition, vitamin deficiencies, the immune system, and infections: Time to revisit our knowledge. [Internet]. Washington DC: Allen Institute for AI; 2014 Feb. Available from: https://www.semanticscholar.org/paper/Malnutrition%2C-Vitamin-Deficiencies%2C-the-immune-and-Somech/fb805ae6d5cb79270da59338cb01ec172f07895c.
[19] Hong H, Budhathoki C, Farley JE. Effectiveness of macronutrient supplementation on nutritional status and HIV/AIDS progression: A systematic review and meta-analysis. Clin Nutr. 2018;27:66-74.

[20] Wikipedia contributors. Nutrient [Internet]. USA: Wikipedia, The Free Encyclopedia; 2023 Jul 30 [cited 2023 Aug 1]. Available from: https://en.wikipedia.org/w/index.php?title=Nutrient&oldid=1167861547.
[21] Wikipedia contributors. Micronutrient [Internet]. USA: Wikipedia, The Free Encyclopedia; 2023 Jul 25 [cited 2023 Aug 1]. Available from: https://en.wikipedia.org/w/index.php?title=Micronutrient&oldid=1167022996.
[22] Mitra S, Paul S, Roy S, Sutradhar H, Bin Emran T, Nainu F, et al. Exploring the immune-boosting functions of vitamins and minerals as nutritional food bioactive compounds: A comprehensive review. Molecules. 2022;27(2):555.
[23] Gombart AF, Pierre A, Maggini S. A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients. 2020;12(1):236.
[24] Ibrahim KS, El-Sayed EM. Potential role of nutrients on immunity. Int Food Res J. 2006;23(2):464-74.
[25] Huang Z, Rose AH, Hoffmann PR. The role of selenium in inflammation and immunity: From molecular mechanisms to therapeutic opportunities. Antioxid Redox Signal. 2012;16(7):705-43.
[26] Marques CDL, Dantas AT, Fragoso TS, Duarte ALBP. The importance of vitamin D levels in autoimmune diseases. Rev Bras Reumatol. 2010;50(1):67-80.
[27] Ao T, Kikuta J, Ishii M. The effects of vitamin D on immune system and inflammatory diseases. Biomolecules. 2021;11(11):1624.
[28] Tamura J, Kubota K, Murakami H, Sawamura M, Matsushima T, Tamura T, et al. Immunomodulation by vitamin B12: Augmentation of CD8+ T lymphocytes and natural killer (NK) cell activity in vitamin B12-deficient patients by methyl-B12 treatment. Clin Exp Immunol. 1999;116(1):28-32.
[29] Mikkelsen K, Stojanovska L, Prakash M, Apostolopoulos V. The effects of vitamin B on the immune/cytokine network and their involvement in depression. Maturitas. 2017;96:58-71.
[30] Wikipedia contributors. Nutrient [Internet]. USA: Wikipedia, The Free Encyclopedia; 2019 Aug. Available from:https://en.wikipedia.org/wiki/Malnutrition.
[31] Wikipedia contributors. Protein–energy malnutrition [Internet]. USA: Wikipedia, The Free Encyclopedia; 2022 Dec [cited 2023 Aug 1]. Available from: https://en.wikipedia.org/w/index.php?title=Protein%E2%80%93energy_malnutrition&oldid=1124947662. https://en.wikipedia.org/wiki/Protein - energy_malnutrition.
[32] Karlsson EA, Beck MA, MacIver NJ. Nutritional aspects of immunity and immunometabolism in health and disease. Front Immunol. 2020;11:595115.
[33] Calder PC. Nutrition and immunity: Lessons for COVID-19. Nutr Diabetes. 2021;11(1):19.
[34] Grimble RF. Basics in clinical nutrition: Immunonutrition– Nutrients which influence immunity: Effect and mechanism of action. E Spen Eur E J Clin Nutr Metab. 2009;4(1):e10-13.
[35] Gebru TH, Mekonen HH, Kiros KG. Undernutrition and associated factors among adult HIV/AIDS patients receiving antiretroviral therapy in eastern zone of Tigray, Northern Ethiopia: A cross-sectional study. Arch Public Health. 2020;78:100.
[36] Sikkema KJ, Dennis AC, Watt MH, Choi KW, Yemeke TT, Joska JA. Improving mental health among people living with HIV: A review of intervention trials in low- and middle-income countries. Glob Ment Health (Camb). 2015;2:e19.
[37] Chandra RK. Nutrition and the immune system: An introduction. Am J Clin Nutr. 1997;66(2):460S-63S.
[38] Tafadzwa D, Gashema P, Michael H, Rosemary O. Nutrition and HIV/AIDS: A qualitative study on perceived factors affecting feeding practices among adult people living with HIV/AIDS in Kigali, Rwanda. Nutri Food Sci Int J. 2019;9(4):555767.
[39] Chand V. Nutrition as a key weapon in strengthening immune system relative to pandemic novel coronavirus disease (COVID-19): A review. Int J Health Sci Res. 2020;10(8):96-104.
[40] Calder P, Carr A, Gombart A, Eggersdorfer M. Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. Nutrients. 2020;12(4):1181.
[41] Batatinha HAP, Biondo LA, Lira FS, Castell LM, Rosa-Neto JC. Nutrients, immune system, and exercise: Where will it take us? Nutrition. 2019;61:151-56.
[42] Shao T, Verma HK, Pande B, Costanzo V, Ye W, Cai Y, et al. Physical activity and nutritional influence on immune function: An important strategy to improve immunity and health status. Front Physiol. 2021;12:751374.
[43] Theresa "Sam" Houghton. How does nutrition affect the immune system? [Internet]. New York: Colin Campbell Center for Nutrition Studies; 2022 Dec. Available from: https://nutritionstudies.org/how-does-nutrition-affect-the-immune-system/.
[44] US Department of Veterans Affairs. Nutrition and Exercise [Internet]. Washington DC: U.S. Department of Veterans Affairs; 2022 Feb. Available from: https://www.hiv.va.gov/patient/daily/diet/index.asp.
[45] Centers for Disease Control and Prevention. Can HIV affect my diet and nutrition? [Internet]. USA; Centers for Disease Control and Prevention; 2021 May. Available from: https://www.cdc.gov/hiv/basics/livingwithhiv/healthy-living.html.

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- Manual Googling: Jul 19, 2023
- iThenticate Software: Oct 10, 2023 (11%)

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- Financial or Other Competing Interests: None
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- Was informed consent obtained from the subjects involved in the study? NA
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