

Different diets and their effect on tuberculosis prevention in HIV patients

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ABSTRACT

Introduction: The relationship between nutrition and human immunodeficiency virus (HIV) infection, tuberculosis, and other infectious diseases is logically proven. Nutrition affects the immune system and the health of the organs. Inadequate dietary intake endangers the immune system, which itself increases susceptibility to disease and often culminates in active disease. The disease then reduces the body's appetite and ability to absorb nutrients, and the cycle continues. Considering the importance of the role of nutrition in the health of acquired immune deficiency syndrome (AIDS) patients, this current review aimed to discuss the different diets and their effects on tuberculosis (TB) prevention in HIV patients. **Method and Materials:** The present study evaluates the important points related to AIDS and the prevention and treatment of this disease by considering the diet and known scientific cases during the last 10 years, in simple terms, the prevalence of this disease. **Result:** Articles were searched by valid databases in May 2021. The findings showed that in addition to malnutrition, the high prevalence of infectious diseases can have serious consequences for public health. Many people will be safe from getting infections if there are safe and effective interventions for many of these infectious diseases. **Conclusion:** Based on the information presented herein, it is clear that TB affects the nutritional status. Many patients with active TB experience severe weight loss, and many people with the symptoms show a lack of vitamins and minerals.

Keywords: AIDS, diet, HIV, prevention, tuberculosis

Introduction

The human immunodeficiency virus (HIV), which causes AIDS, has become one of the biggest public health challenges. The virus was first identified in 1981 in Los Angeles, USA.^[1] HIV belongs to the Retroviridae family, Orthoretrovirinae subfamily of the Lentivirus genus. Based on the genetic characteristics and differences in viral antigens, HIV is classified into types 1 and 2. At present, the epidemiological and phylogenetic analyzes indicate that HIV entered the human population from 1920 to 1940. HIV-1 evolved from non-human mammalian immunodeficiency

viruses such as Central African chimpanzee (SIVcpz) and HIV-2 from the common West African monkeys (SIVsm). In terms of pathogenicity, the two types of viruses are similar.^[2-5]

HIV is usually associated with the progressive chronic destruction of the immune and nervous systems. It can lead to a possible attack and opportunistic and malignant infections if not managed. The incidence of AIDS varies widely from person to person and can range from a few months to 20 years. There is ample evidence that the incubation period is 7–10 years in 50% of the cases.^[6] Because of its ability to destroy the immune system, HIV has emerged as the most important risk factor for the development of *latent tuberculosis infection* into TB disease. In general, the development of tuberculosis infection and its transformation into tuberculosis leads to a decrease in the efficiency of the body's defenses. The HIV infection has a

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profound effect on the increase in tuberculosis worldwide, and HIV-infected people are 5–15% more likely to develop active tuberculosis annually after infection.^[7]

Malnutrition is often associated with diseases and infections such as gastrointestinal disorders, pneumonia, tuberculosis, and HIV. Food insecurity, alcohol abuse, and drug use, and a number of other conditions can be the cause of malnutrition.^[7] A person's immune system becomes very active and the body uses more energy and nutrients if that person is infected with HIV. HIV infection increases intestinal permeability and impairs the absorption of proteins, carbohydrates, fats, vitamins, minerals, and water. Malnutrition and HIV are related and exacerbate each other at the same time so that HIV disrupts the immune system of infected people and increases their vulnerability to infections leading to increased nutrient deficiencies. And it will lead to malnutrition if they are not completed. On the other hand, malnutrition leads to a defective immune system, and in turn, accelerates the progression of HIV.^[8] HIV and TB are two of the most common infections in South Africa, and both diseases have nutritional challenges that must be addressed to effectively treat these diseases. According to a nutritionist and American Dairy Science Association (ADSA) spokesperson, HIV and TB patients do not need nutrition just to maintain normal bodily functions such as muscle nutrition and heart pumping; rather, they often need extra energy and nutrients to effectively treat the disease, maintain weight, help absorb drugs, and support the body to repair the damaged cells.^[9]

The link between tuberculosis and malnutrition has long been known. Tuberculosis worsens malnutrition, and malnutrition weakens the body's immune system, increasing the likelihood of latent tuberculosis becoming active. Most people with TB are active in the catabolic state and experience weight loss, and some have symptoms of vitamin and mineral deficiency. Weight loss in people with TB can lead to a variety of consequences, including reduced food intake due to loss of appetite, nausea and abdominal pain, loss of nutrients due to vomiting and diarrhea, and metabolic changes caused by the disease. Studies show that active TB is associated with abnormalities in protein metabolism. In such conditions, the body oxidizes disproportionate amounts of protein instead of synthesizing protein. On the other hand, malnutrition weakens the immune system, and as a result, people are prone to primary infection with *M. tuberculosis*. Likewise, the risk of the initial infection progression to active disease can be increased. The examination of the molecular process shows that the nutritional deficiencies negatively affect the immune mechanisms that are important for the control of mycobacteria (function of T lymphocytes and phagocytic cell types). Therefore, nutritional deficiencies are generally associated with both an increased risk of TB infection and higher severity of the active disease.^[7] According to global statistics, tuberculosis is the second leading cause of death in HIV-positive patients. HIV-positive patients are 30 times more likely to develop TB than HIV-negative patients. Tuberculosis is also the cause of 40% of AIDS deaths in Africa and Asia, accounting for about 26% of AIDS-related deaths worldwide; 99% of which are in developing countries [Figure 1].^[10]

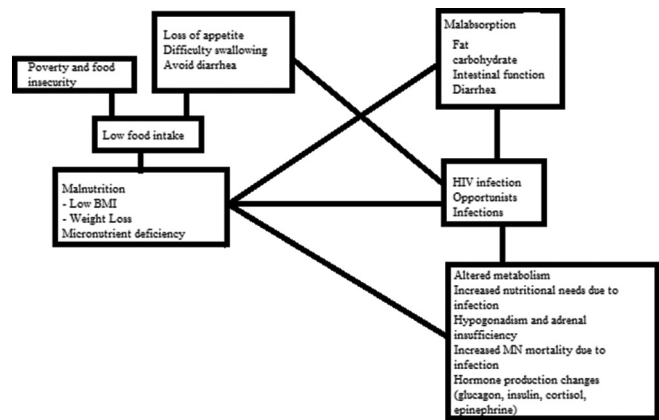


Figure 1: Relationship between HIV infection and malnutrition^[11]

The nutritional status, especially maintaining body weight and vital protein stores body composition monitor (BCM), affects a person's ability to survive while living with HIV. The loss of BCM is a characteristic of HIV-associated wasting. Micronutrient deficiencies are also very common in HIV-infected patients and may also accelerate the disease progression, which in turn leads to a further deterioration in the nutritional status. On the other hand, the emergence of multidrug-resistant tuberculosis (MDR-TB) is a global threat to health. This condition poses a very serious threat to TB control, especially in developing environments, where many TB patients are also infected with HIV.

The World Health Organization (WHO) and its international partners have formed the TB/HIV Working Group, which develops global policies to control the TB related to HIV and advises those fighting TB and HIV on how to best resolve this deadly disease,^[12] showing the importance of preventing tuberculosis in patients with AIDS.

There is a two-way and indirect relationship between the risk of tuberculosis, HIV, and nutrition. In this article, we aimed to examine the different diets and their impact on TB prevention in HIV patients.

Methods

The present study evaluates the important points related to AIDS and the prevention and treatment of this disease by considering the diet and known scientific cases during the last 10 years in a simple way. This assessment was conducted in May 2021. PubMed, Medline, WHO, Nature, NCBI, PsycINFO, and other important databases were used to access the articles.

The research on AIDS and tuberculosis was addressed by examining the aspects and issues related to the epidemiology of the virus, concerns about TB in AIDS patients, the complications of AIDS, immune responses to the infection, and the prevention and treatment of tuberculosis. To collect information on TB in terms of content, the keywords were searched in the desired databases such as AIDS, diet, world prevalence, AIDS, TB, TB prevalence, etc., Out of a total of 217 articles, 31, that

matched the subject and content coverage, were used in the main framework of this article.

TB in patients with AIDS

There is an epidemiological and biological synergy between HIV and TB that affects the distribution, prevention, and outcome of both infections. The HIV epidemic is a major cause of TB regrowth as well as a major cause of TB worldwide. Reports indicate that one in eight TB cases occurs in HIV-positive patients. TB accounts for about one-fifth of HIV-related deaths. TB and HIV are most commonly reported in Africa; one-third (2.3 million people) of the HIV-positive patients were infected with TB in 2010. Meanwhile, India and Eastern Europe are among the areas affected by dual TB and HIV epidemics. The age of the TB infection in HIV-positive patients has been reported to be between 20 and 45 years.^[12]

HIV alters the pathogenesis of tuberculosis and increases the risk of developing active tuberculosis in people with latent infection as well as in people who are newly exposed to tuberculosis. In the non-HIV-infected population, only about 10% of the TB-infected people develop TB. However, in people with HIV, there is a 20–30-fold increased risk of TB from the latent disease compared to the people without HIV; an increase that reduces other risk factors such as malnutrition.

In addition, the number of CD4 T-cells decreases in HIV-positive patients. This suggests that although cellular immunosuppression as HIV progresses may be an important factor in increasing the risk of HIV-associated active TB, it is probably due to multifactorial processes. The essential role of CD4 T-cells in the production of granulomas and the reduction of these cells as the HIV disease progresses may explain the increased risk of extrapulmonary tuberculosis (EPTB) in HIV-positive patients. In addition, the lack of an increase in the CD4 T-cell population in the regulation and maintenance of granulomas is one of the mechanisms that has been proposed to increase the risk of re-infection in the recently infected patient.^[12]

Common diets of AIDS patients

The relationship between infection and nutrition has been known since the early 1900s, but the role of nutrition in medical practice and public health has changed over time. Research on the relationship between HIV infection and nutrition has focused mainly on the role and effect of the micronutrients, proteins, specific nutrients such as mixtures of specific amino acids, and dietary supplements.^[13]

Micronutrients are important for safety, mental growth, and movement because they catalyze many processes in the body and are the essential components of specific tissues. For instance,

Table 1: Documented findings between micronutrients and HIV infection. Studies show that deficiencies in vitamins B, D, A, and many essential minerals such as zinc and iron are common

Micronutrient	Low intake described in literature	Deficient status described	Deficiency associated with adverse HIV infection outcomes	RNI for 19 to 70 years olds
Vitamin A µg	x	x	Yes, but also with positive outcome in on study	600
Vitamin E mg	x	x	Yes, but one study with a negative and one with a positive outcome	10
Vitamin B ₁ mg	x		Yes, part of B-complex supplement	1.4
Vitamin B ₂ mg	x		Yes, part of B-complex supplement	1.6
Niacin mg				18
Pantothenic acid, mg				6
Folic acid, µg	x	x		400
Vitamin C, mg	x			75
Vitamin B ₆ , mg	x	x	Yes	2
Vitamin B ₁₂ , µg		x	Yes	6
Calcium, mg				1000
Magnesium, mg				
Selenium, µg		x	Yes	
Zinc, mg	x	x	Yes	15
Iron, mg	x	x		15
Iodine, µg				150
Copper, mg				2
Phosphorus, mg				1000
Potassium, mg				3500
Manganese, mg				
Vitamin D, µg		x		5
Vitamin K, µg				
Biotin, µg				30
Sodium, mg				
Chromium, µg				
Molybdenum, µg				
Chloride, mg				
Carotenoids, µg		x	Yes	

iron is the part of hemoglobin that carries oxygen in the body. Vitamin A is known as an anti-infective vitamin and is given in high doses every 6 months as an intervention in survival. Zinc tablets are recommended as adjunctive therapy for people suffering from diarrhea to improve the episode faster and reduce the risk of other infectious diseases. Because micronutrient deficiencies are higher in developing countries than in developed countries, the likelihood of inadequate micronutrient intake among HIV-infected patients in developing countries at any stage of infection is very high. Table 1 shows the micronutrients that have been reported to be low in patients with AIDS.^[13]

Low levels of vitamin E in the serum or plasma have also been reported in HIV-infected adults and lactating women in South Africa.^[14-20] This shows the role of vitamin D in boosting the immune system and the importance of studying it in populations suffering from AIDS, which can also be present in Iran.

TB and HIV infections are both independently associated with malnutrition. The coinfection with TB/HIV has additional metabolic, physical, and nutritional loads resulting in increased energy intake, absorption, nutrient deficiencies, and increased production of proinflammatory cytokines, resulting in the breakdown of body fat and proteins. A concomitant infection may lead to poor appetite with reduced nutrient intake, which may interact with the altered metabolism associated with both infections as part of the immune and inflammatory responses. A combination of coinfection with tuberculosis, HIV, and malnutrition has been termed the "triple problem."^[21,22]

To evaluate the effect of HIV on "the nutritional status in patients with active TB in a cross-sectional study, Niyongabo *et al.*^[23] compared the nutritional status of the TB patients who were HIV-negative and HIV-positive, respectively. Moderate anthropometric measures in comparison of HIV-negative TB patients with patients with TB and HIV at the same time showed that weight loss, fat mass, and fat-free mass were very important in the HIV-infected cases. Moderate anthropometric measures of HIV-negative TB patients and patients with a coinfection of TB and HIV showed that weight loss, fat mass, and fat-free mass were very important in HIV-infected cases. Also, the mean serum albumin of patients with the coinfection was significantly lower compared to the patients with HIV-negative tuberculosis. They suggested that patients with TB/HIV may have more severe malnutrition or increased inflammation and that these proteins may have a useful prognostic value in patients with TB and HIV. Paying attention to the proteins in the blood can also play an important role in recognizing malnutrition as a prognostic factor in patients with AIDS.

Studies on HIV, tuberculosis, and their relationship with nutrition

According to a study by Tekelehaimanot *et al.*, The most important factors influencing malnutrition are living in the countryside, low frequency of meals, low dietary diversity, low

hemoglobin levels, and difficult livelihoods. However, many studies, including those of Alebel and Lewis, support this view and consider malnutrition to be a factor in the progression of HIV.^[24-26] Of course, as mentioned earlier, malnutrition and HIV are related, and at the same time, exacerbate each other. As HIV disrupts the immune system of the infected people and increases their vulnerability to infections, the infections lead to an increase in nutrient deficiencies and, if not supplemented, lead to malnutrition. Table 2 summarizes the studies on the relationship between nutrition and TB and HIV.

According to the findings of Getachew *et al.*,^[27] approximately half of the TB patients were malnourished at the start of the treatment based on their body mass index (BMI) [Table 2]. There was a high mortality rate among the TB patients who were also malnourished. Getachew suggested that a larger study was needed to better understand the prognosis. To increase the nutritional status during the treatment, the government should consider supporting dietary supplements for TB patients. The findings of Isa Ma'rufi *et al.*^[29] also supported this finding, and their study showed that by taking the BMI supplements for a month, the patients with TB ascended faster than the control group and the disease improved with minimal negative effects of the disease. Therefore, to eliminate or reduce the incidence of TB in the community, further study on the use of dietary supplements in patients with TB is needed.

Some TB control programs can be implemented to improve populations. Food aid is a potentially effective tool for increasing adherence to TB treatment, reducing treatment costs for patients undergoing the treatment, and improving the nutritional status. Although most evidence suggests that dietary support affects the nutritional status, quality of life, adherence to treatment, and outcome for TB patients, it is believed that this support has direct effects on the recovery of TB-infected adults and children.^[28]

Studies by Bares *et al.*^[30] also support the claim that malnutrition has a very acute and direct effect on TB and even the transformation of TB from latent to active. However, their findings on BMI are somewhat inconsistent with those of Peggy *et al.*'s^[28] However, a study by Laura *et al.*^[31] provided evidence of a high prevalence of co-morbidities in the Filipino people with drug-sensitive TB in rural areas suggesting that the HIV infection was not significantly associated with the TB disease. However, malnutrition occurs moderately and severely in the final months of TB treatment. Anemia is also a factor that can be evaluated in patients with acute TB, which indicates the need for additional interventions to diagnose and treat this condition. For the effective management of several diseases, health care programs should move toward the integration of services, and support for nutrition management and appropriate lifestyle changes are among the most important factors.

Various studies have reported an increase in malnutrition in women with TB and AIDS living in poor and developing countries.^[24,32-35] The findings show that in addition to nutrition, the most effective factor in the outcome of patients was receiving antiretrovirals, which is an important issue in these patients along

Table 2: Some studies on the relationship of TB and HIV with nutrition

Authors and years	Target	Society	Results
HIV and nutrition			
Alebel, A., <i>et al.</i> (2021) ^[24]	A systematic review of the effects of malnutrition on the mortality and morbidity in HIV-infected adults in sub-Saharan Africa	Adults living with HIV in sub-Saharan Africa	Malnutrition significantly increases the risk of mortality among adults with HIV, while adults with severe malnutrition are at a higher risk of death than the adults with malnutrition living with HIV. In addition, estimates collected from 10 group studies showed that malnutrition significantly increased the risk of tuberculosis among HIV-infected adults
Louise Houtzager. 2009 ^[25]	A review of the nutrition-related issues for people with HIV and an overview of the potential benefits of nutritional interventions for people with HIV	People with HIV	Nutrition plays a vital role in everyone's immune system, including PLHIV. Proper nutrition strengthens the immune system, while patients with HIV are more vulnerable than the general population, and the nutritional status can be a document of the death time. Malnutrition in HIV often occurs in the context of poverty and lack of access to food. Inadequate food intake, increased need, and malabsorption are the main reasons for weight loss in HIV. Asymptomatic adults with HIV infection need 10% more energy and symptomatic HIV patients need 20-30% more energy than the general population. There is insufficient evidence to increase protein and micronutrient intake in healthy HIV patients. Nutrition education should be an essential component of HIV care and treatment as it can help HIV-infected patients cope with the symptoms of the disease, prevent weight loss, and manage the side effects of medication. Limited resource settings have shown that in addition to nutrition support, food support programs are needed to optimize nutritional status and health outcomes in HIV patients with food insecurity
Aderajew Nigusse Tekelehaimanot, <i>et al.</i> , 2020 ^[26]	Predictors of malnutrition and its implications for the ongoing HIV care	Adults living with HIV in public hospitals in the Jima area of southwestern Ethiopia	Rural housing, unsustainable livelihoods, low number of meals, poor variety of foods, and advanced clinical stage of HIV are some of the factors that lead to malnutrition, especially in women. Despite the advanced clinical stage, they did not have any level of social support and unstable livelihoods negatively affected the nutritional status of these patients
Tuberculosis and nutrition			
Getachew Seid, <i>et al.</i> , 2020 ^[27]	Malnutrition and mortality in adult tuberculosis patients in Addis Ababa, Ethiopia	Evaluated adults with tuberculosis in Addis Ababa, Ethiopia	Of the patients with malnutrition, 54 (19.0%) had severe malnutrition and 78 (27.5%) had moderate malnutrition. At the end of the 2-month intensive treatment period, the prevalence of malnutrition decreased to 38.7%. Of the 284 patients, 17 (6.0%) died before completing the anti-tuberculosis treatment. The mortality rate due to the nutritional status at the time of treatment initiation among the patients with normal, moderate, and severe acute malnutrition was 1.3, 8.9, and 16.3%, respectively
Peggy Papatthakis, <i>et al.</i> , 2010 ^[28]	The effect of nutrition on tuberculosis	Evaluation and implementation of tuberculosis control program in the African populations	Tuberculosis affects the nutritional status. Many patients with active tuberculosis experience severe weight loss and some symptoms of vitamin and mineral deficiency
Isa Ma'rufi <i>et al.</i> , 2020 ^[29]	Improving nutritional status in patients with tuberculosis by supplementation	A real experimental study in Indonesia	The mean BMI of all TB patients increased during the month. A rapid change occurred in the treatment group, the change from severe weight loss to a higher BMI level is highest in the treatment group. Based on the statistical test, no difference was found in the BMI between the treatment and control groups. However, the change in the nutritional status was faster in the treatment group than in the control group. In addition, no difference was observed in their health status between the treatment and control groups
HIV, tuberculosis, and nutrition			
Bares, S.H. <i>et al.</i> , 2020 - ^[30]	Tuberculosis prevention with screening and treatment of latent tuberculosis infection (LTBI)	People with latent TB who are at risk for HIV	People living with HIV (PWH) are 15-22 times more likely to develop active TB than people without HIV worldwide. To reduce the global burden of tuberculosis, the cascade of latent tuberculosis treatment must be improved. Antiretroviral therapy (ART) and TB-preventive therapy are essential components of the LTBI treatment, and both ART and TPT regimens can be optimized to prevent drug interactions, reduce pill intake, shorten treatment duration, and minimize the side effects to increase adherence and treatment

Contd...

Table 2: Contd...

Authors and years	Target	Society	Results
Matilda <i>et al.</i> , 2017 ^[11]	Evaluation of tuberculosis characteristics in HIV/AIDS patients	77 HIV/AIDS patients with pulmonary complications	A study of tuberculosis patients showed that the disease is a common respiratory complication with a high mortality rate in the HIV/AIDS patients. The CD4+ count levels are a predictor of clinical manifestations and prognosis.
Laura <i>et al.</i> , 2020 ^[31]	Evaluation of several non-communicable diseases (simultaneous two or more cases) in outpatients of Philippine tuberculosis, focusing on malnutrition and diabetes	A cross-sectional study of the people enrolled in TB-DOTS clinics in the Philippines	The prevalence of diabetes was 2.9%, of which 52% were newly diagnosed. Malnutrition was moderate/severe. Forty percent of the participants had at least one common disease. The HIV infection was not associated with other diseases. Centrally assessed obesity was associated with a higher waist-to-hip ratio than BMI with diabetes. Malnutrition is less common in men and has been linked to a previous history of tuberculosis and a recent reduction in food intake. The prevalence of several of the above complications showed that HIV is not a risk factor for the increase of several non-communicable diseases

with nutrition and drug treatment because, with the increase of inflammation in the body of the patients, their appetite decreases and their nutrition is affected.^[36-39]

Studies in Iran have shown that the most effective factor in increasing the survival of TB patients with AIDS was receiving antiretrovirals and attention to the antiviral drug treatment is of great importance in reducing patient mortality.^[39]

Drug resistance and nutrition

Drug resistance in patients with tuberculosis is another important issue that kills many people every year.^[40,41] Drug resistance has been proven in many cases of infectious diseases. In tuberculosis and AIDS, drug resistance is one of the therapeutic problems and reduces recovery in these patients.^[42-44] Studies show that nutrition is effective in reducing bacterial and viral resistance by affecting the immune system. Bacteria and viruses in many patients with chronic infections cause resistance, and empowering the immune system of the patients against these pathogens is one of the treatment strategies because the elimination of microbes by the immune system is one of the best strategies to reduce inflammation in these patients.^[45-48] Due to the effect of nutrition on the immune system and reducing drug resistance, it is very important and necessary to pay attention to the nutrition of the patients.

Conclusion

Based on the information presented herein, it is clear that TB affects the nutritional status. Many patients with active TB experience severe weight loss, and many people with the symptoms show a lack of vitamins and minerals. Patients with a coinfection of TB/HIV have an even worse nutritional status. Mineral deficiencies directly affect the immune system of the patients, and this issue should be considered. The evidence for the selection of the best nutrition management practices is very limited, and awareness-raising practices should be reported through the national media. Many parts of the world need more research to improve malnutrition in the coinfection of TB/HIV. In addition, research in Iran can help clarify the extent of the deficiency in these patients. Our review study suggests that diverse and cost-effective models aimed at

recognizing the role of nutrition in reducing TB in HIV patients should be considered by health organizations. It is hoped that it will be effective in reducing morbidity and mortality in such patients.

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Conflicts of interest

There are no conflicts of interest.

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