

# Changes in the nutritional status of elderly patients with HIV diagnosis undergoing antiretroviral treatment

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## Abstract

**Introduction:** Acquired immunodeficiency syndrome (AIDS) is an infectious contagious disease produced by the human immunodeficiency virus (HIV) that causes progressive immunosuppression, making individuals susceptible to infections and opportunistic diseases. Despite its benefits, antiretroviral therapy has side effects, such as insulin resistance, dyslipidemia, high blood pressure and increased risk of cardiovascular disease. **Objective:** The aim of this study was to identify metabolic alterations in elderly patients with AIDS who use antiretroviral therapy (ART). **Methods:** The study consisted of a retrospective bibliographic review, including indexed articles published over the last 10 years, written in Portuguese and English, which evaluated changes in nutritional status and metabolic changes in HIV-positive patients who used ART. **Results:** According to the Brazilian Ministry of Health, the number of people over 65 with HIV grew by 103% in the last decade. The HIV virus has a long incubation period before the onset of the first symptoms of the disease, which results in AIDS. Dyslipidemia affects approximately 70% of HIV-infected patients who use ART, and occurs due to an increase in serum cholesterol, triglycerides and/or a reduction in HDL-cholesterol. **Conclusion:** The WHO recommends that nutritional interventions form part of HIV/AIDS control and treatment programs since they improve treatment adherence and ART effectiveness. In this context, a healthy diet that is adequate for the needs of the individual contributes to increased levels of CD4 T lymphocytes and reduces the harm caused by opportunistic infections, while improving intestinal absorption, as well as decreasing muscle loss and lipodystrophy syndrome, whose symptoms can significantly reduce the survival rates of patients.

**Keywords:** HIV; AIDS; ART; Lipodystrophy syndrome (LS); Dyslipidemia; Insulin resistance.

## Introduction

Acquired immunodeficiency syndrome (AIDS) is an infectious contagious disease caused by the human immunodeficiency virus (HIV) that causes progressive immunosuppression, which makes individuals vulnerable to infections and opportunistic diseases. Clinical treatment is usually based on drugs, which can cause numerous side effects. Clinically, the disease manifests itself in a sequence of stages: acute infection,

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asymptomatic or clinical latency phase, then the early or early symptomatic phase and, finally, AIDS, which is the final stage of infection by the HIV virus.<sup>1</sup>

Malnutrition, due to metabolic changes caused by the virus, is one of the main side effects evident in these patients. In addition, antiretroviral treatment (ART) leads individuals with the human immunodeficiency virus (HIV) to develop metabolic changes resulting from the use of this treatment to fight the HIV virus.<sup>2</sup>

In 2005, HIV infection affected 42 million people all over the world. Latin America accounted for about 1.8 million of these, and Brazil was the most affected country, with about 1.2 million infected inhabitants, of which 257,780 had AIDS. The latest data presented by the Joint United Nations Program on HIV (UNAIDS), in 2008, showed an increase in the number of people infected in Latin America and Brazil.<sup>3</sup> More recent data from the Brazilian Ministry of Health (2017) found that the number of people over 65 of age with HIV rose by 103% in the last 10 years.

During the last decade, the introduction of ART in the treatment of HIV has been found to improve the condition of terminally ill patients, restore the immune system and reduce the number of deaths, while increasing the survival and quality of life of

patients infected by the virus. However, this therapy has also caused metabolic events characterized by dyslipidemia, lipodystrophy syndrome (LS), insulin resistance/glucose intolerance, and systemic arterial hypertension.<sup>4,5</sup>

As a result of the increased survival rate of patients using the treatment, the most current phenomenon of HIV is the emergence of a new vulnerable population: senior citizens. According to law n°10.741 of 1 October, 2003, this group is constituted by individuals aged over 60 years.<sup>6</sup> However, ART can cause metabolic alterations, which constitute risk factors for cardiovascular disease (CVD), with a probable association caused by HIV infection, and also due to the impact of the treatment on glucose and lipid metabolisms.<sup>7</sup>

Studies report that some patients presented LS with the use of ART, which is a worrisome problem resulting from treatments to combat the HIV virus. SL is a side effect, characterized by the redistribution of body fat. The typical manifestations of LS are represented by lipoatrophy (reduction of fat in peripheral regions); lipohypertrophy (accumulation of fat in the abdominal region, breasts and dorsocervical region); or a mixture of both.<sup>2,8</sup>

These nutritional and metabolic changes in patients with HIV should be minimized through adequate drug therapy and dietary intervention in order to control eventual changes caused in these patients.<sup>9</sup>

In this context, this study aims to assess nutritional and metabolic changes in elderly patients who use ART and how dietary intervention in these individuals can directly interfere in the improvement of the altered biochemical picture, especially in cases exhibiting mixed dyslipidemia and insulin resistance.<sup>7</sup>

## Materials and methods

This study consists of a retrospective bibliographic review, covering indexed articles written in Portuguese and English, published over the last 10 years, which evaluated changes in nutritional status and metabolic changes in HIV-positive patients who use ART.

A systematic literature review technique was used for data collection, in which articles indexed in the Scielo and *Pubmed* databases, published between 2007 and 2017, were searched, listing the scientific production by year and subsequently choosing the most relevant publications on the subject. To find

articles of interest, the following descriptors were used: AIDS, HIV, AIDS, nutritional assessment, malnutrition, lipodystrophy, dyslipidemia and metabolic alterations.

## Literatura review

### HIV epidemiology

The incidence of HIV in the Brazilian population over 50 years old increased from 3.6 to 7.1 per 100,000 inhabitants between 1996 and 2006, representing a 50% increase of new cases. The disease in this specific group has particular epidemiological relevance due to its high incidence, prevalence and lethality rates.

Of the HIV cases reported since the beginning of the epidemic in people over 50 years old, 29,393 (62%) were registered from 2001 to June 2008, suggesting underreporting before the year 2000. In this group, 37% were women and 63% were men. The HIV rate among seniors in Brazil is now higher than that of adolescents aged between 15 and 19 years.<sup>10</sup>

Epidemiologists estimate that persons newly diagnosed with HIV infection who are involved with and maintained using ART have a life expectancy of 20 years, thus allowing them to lead a normal or almost normal life, which permits those infected to reach an older age.<sup>11</sup>

The literature emphasizes knowledge about HIV in young individuals and health professionals; however, information related to HIV among seniors is lacking.<sup>12</sup>

The increase in the number of HIV cases among seniors has been associated with the aging of the Brazilian population, the increased survival of people living with HIV and access to medication for erectile disorders, a factor that has prolonged sexual activity among seniors, in combination with the demystification of sex in old age. The experience of sexuality has made the elderly more vulnerable to sexually transmitted diseases (STD), contributing to a higher incidence of these diseases in individuals over 50 years old.<sup>10</sup>

Due to lack of information, studies in this area must be developed, since knowledge is important both to promote the reduction of prejudice against HIV carriers and to introduce prevention measures.<sup>12</sup>

### Social and economic factors

The relationship between both economic and social impacts on HIV patients is closely linked to costs and the issue of education, which is the main means

for the assimilation of information and adherence to information campaigns.<sup>13</sup>

According to Okuno *et al.* (2014), low income exerts a negative influence on the quality of life of elderly people with HIV who received a minimum wage or less. Quality of life is a multifaceted issue, as mentioned above, and is related to economic issues, lifestyle, health condition, housing, among others. In addition, a high level of education has been associated with higher quality of life and longevity scores.<sup>14</sup>

Another important factor is the mental state of patients with HIV, which can interfere with their nutritional issues.<sup>15</sup> It is necessary to understand the clinical, economic and psychosocial history in which patients are inserted in order to design a therapeutic plan compatible with their lifestyle, which respects their food preferences, aversions and the relationship between food and the ART used.

#### Physiological changes related to aging

Although aging is a normal process inherent to human beings, this process promotes physiological changes. These modifications can progress differently in each individual and depend on factors such as genetics, diseases, socioeconomic status and lifestyle. In the aging process, changes in the body composition of these individuals are common. These modifications are characterized by an increase in fat mass and visceral fat and a reduction in lean mass. In many cases, malnutrition is prevalent.<sup>16</sup> In addition, sarcopenia can be found, which is characterized by a reduction in muscle mass, strength and function, thus contributing to a worsening in the quality of life of the elderly and possibly increasing the risk of falls.<sup>15</sup>

Another very important change is related to taste and smell. Sensory losses are closely related to a declining appetite and reduced nutrient intake. The changes can be due to aging itself, but in some cases are the consequence of the use of medications and pathologies. Because of this, many seniors can overdo spices, especially those with added salt, causing a negative effect on health.<sup>15</sup>

Hearing loss affects 25 to 40% of elderly Americans, mainly due to presbycusis, although it can also be caused by the cumulative effect of sounds throughout life, such as construction work, exposure to music and noises, among others. Vision changes, such as age-related macular degeneration, glaucoma and cataracts, promote poor vision that interferes with shopping, cooking and eating.<sup>15</sup>

Very frequent changes that can compromise the nutritional status of elderly patients occur due to the absence of teeth, the presence of dentures and the occurrence of dry mouth, which can impair the chewing and swallowing of certain foods, such as fruits, vegetables and vegetables and, as a consequence, worsen digestion.<sup>16</sup> This exacerbates the condition of hypochlorhydria (insufficient acid production) that is already expected in these patients. In addition to these changes in the gastrointestinal tract, one should also mention constipation, which is quite frequent in the elderly population as a result of reduced fluid intake, medication, low fiber intake and physical inactivity.<sup>15</sup>

#### Assessment methods and nutritional screening of elderly patients

Several simple and easy-to-apply tools for nutritional screening are available in the literature, including NRS (Nutritional Risk Screening) 2002, MNA SF (Mini Nutritional Assessment Short Form),<sup>17</sup> MUST (Universal Malnutrition Screening Tool) and NRS (Nutritional Risk Score). These are sensitive to nutritional risk and the nutritional profile of the patient.

On the other hand, the nutritional screening of elderly patients can lose sensitivity to the physical and metabolic changes that occur in the aging process. These include height, in which the individual may have problems with the spine, inability to stand upright and being bedridden, as well as the replacement of muscle by fatty fat.<sup>15</sup>

Therefore, it is important to choose the best screening method for the profile of the elderly person who will be evaluated, taking into account the limitations and the method with the best sensitivity for that patient. For example, the MNA-SF includes the alternative of using the circumference of the calf, which is a sensitive measure of muscle mass in the elderly.<sup>17</sup>

#### Malnutrition in elderly patients with HIV

The HIV virus is characterized by a long period of incubation before the onset of the first symptoms of the disease, which results in AIDS.<sup>18</sup>

HIV-infected individuals also present other complications, such as cardiorespiratory, anthropometric (wasting syndrome), muscle (muscle wasting- sarcopenia) and psychiatric (depression) diseases, which may be associated with the worsening of their clinical condition and cause a decrease in their functional independence.

It must be borne in mind that sarcopenia is a predictor of morbidity and mortality, since it promotes a decrease in muscle strength, making individuals physically debilitated and thus contributing to the progression of HIV infection.<sup>19</sup>

Although ART is associated with an improvement in the quality of life of HIV patients, it is also linked to cardiovascular events, since there has been a frequent increase in the number of cases of coronary events related to increased survival of these patients and to the toxicity of therapy. The use of ART and protease inhibitors has been connected with dyslipidemia, insulin resistance and *diabetes mellitus*, which are risk factors for the development of cardiovascular diseases.<sup>7</sup>

The gastrointestinal tract (GIT) is one of the areas most susceptible to damage in these patients, especially in the part that integrates the immune tissue. The nutritional status of HIV/AIDS patients becomes a concern, due to reduced appetite and insufficient energy intake associated with increased energy expenditure at rest. Weight loss typically occurs in 95 to 100% of AIDS patients. In addition, most have nausea, bloating and vomiting, which further impair their nutritional status.<sup>20</sup>

A significant minority also reports diarrhea and oral moniliasis, in which the appearance of gastrointestinal symptoms, mainly due to opportunistic diseases, is cause for frequent hospitalization. This makes the immediate nutritional assessment of hospitalized patients essential to diagnose the risks of malnutrition and the presence of gastrointestinal symptoms that directly interfere with their nutritional status.<sup>20</sup>

The literature has indicated that food supplementation in HIV-positive individuals, especially males, whether or not they use a protease inhibitor (PI), preferentially promotes the gain of fat mass at the expense of lean mass, probably as a result of a marginal testosterone deficiency observed in such patients.<sup>21</sup>

Nutritional interventions are important to control the progression of metabolic syndromes that affect patients with HIV/AIDS. Since nutritional risk is a predominant factor in these patients, continuous nutritional assessment and periodic biochemical tests become relevant to identify and set goals for the avoidance of possible nutritional deficiencies. This helps nutritionists to define the exact moment to start providing supplements to the HIV-positive patient and thereby minimizes and reverses possible nutritional damage caused by the side effects of ART.<sup>22</sup>

## Most common micronutrient deficiencies in elderly HIV patients

Nutritional deficiencies are common in these patients, many of which are closely related to the immune function. Many of these deficiencies are caused by gastrointestinal changes, such as malabsorption, drug-nutrient interactions and changes in the intestinal barrier. Some nutrients that may occur in lower concentration in the body are vitamin A, zinc, selenium and vitamin D. Reduced levels of these nutrients are associated with faster progression of the disease. While data on these deficiencies exist, uncertainty still prevails as to whether this is in fact a deficiency or an acute response to the virus. Therefore, attention must be paid to the supplementation of multivitamins.<sup>23</sup>

## Diet therapy for the elderly and/or adult patients with HIV

The WHO recommends that nutritional interventions be included in all HIV control and treatment programs since, in addition to improving adherence to treatment, they make ART therapy more effective, as well as contribute to the improvement of metabolic abnormalities. According to the Brazilian Ministry of Health, healthy and adequate food for the needs of each individual contributes to increased levels of CD4 T lymphocytes and reduces harm caused by opportunistic infections, as well as improving intestinal absorption, muscle loss, and SL.<sup>24</sup>

According to a study on the importance of nutrition in adults with HIV, the association of drug therapies with nutrition favors their health status and reduces the mortality rate. However, despite the use of (medicament-nutrition) treatment to bring benefits to people with HIV, the patient's body continually develops viral resistance, which impairs the action of the medication.<sup>24</sup>

Furthermore, studies have shown a close link between adequate nutrition and the strengthening of the immune system, which improve the nutritional status of the patients as well as achieve more favorable results in the treatment.<sup>25</sup>

In this context, diet therapy works mainly with the objective of: protecting muscle mass, which reduces the chances of developing malnutrition; recovering or maintaining nutritional status; providing adequate amounts of nutrients; and reducing the complications, opportunistic infections

and side effects of ART that may interfere with nutrient intake and absorption.<sup>24</sup>

In other words, the role of nutrition education should be to lead patients to adopt healthy eating habits, related to quality, quantity, harmony and nutritional adequacy, and to improve the quality of life of these individuals, who should be made aware of the importance of nutrition in the context of the disease.<sup>24</sup>

Furthermore, recent studies demonstrate that the adoption of a Mediterranean dietary pattern (characterized mainly by the intake of plant foods, such as whole grains, fruits, vegetables, legumes and olive oil; a moderate intake of fish and dairy products; and a low intake of red meat, saturated fats and sweets) has been associated with decreased mortality, as well as with improved health conditions and cardiovascular risk factors associated with aging. Increased blood triglyceride levels have been observed especially among individuals with HIV treated with ART containing a protease inhibitor (PI). Such increases can be observed a few weeks after the start of treatment. And supplementation with omega-3 fatty acids has been shown to be effective in reducing drug-induced elevated triglyceride levels.<sup>26</sup>

In the case of interventions aimed at dyslipidemia, the presence of symptoms, the clinical picture, the type and duration of use of nutritional therapy, in addition to the presence of cardiovascular risk factors, are fundamental conditions for monitoring and nutritional treatment aimed at this guy.<sup>24</sup>

The Brazilian Ministry of Health states that a healthy diet, adequate for the individual needs of each patient, contributes to an increase in the levels of CD4 T lymphocytes, improves intestinal absorption, reduces the problems caused by diarrhea, improves muscle wasting, SL, and all other symptoms that, in one way or another, can be minimized or reversed through a balanced diet. In this context, proper nutritional guidance is extremely important as an integral part of the treatment of HIV-positive patients who use ART.<sup>26</sup>

#### Insulin resistance in elderly patients with AIDS

Insulin resistance (IR) can be caused by weight gain, changes in the distribution of body fat and the use of retroviral protease inhibitors.<sup>5</sup>

In this context, IR, glucose intolerance and type 2 *diabetes mellitus* (DM2) show significant increases in seropositive patients after the introduction of ART. Furthermore, the clinical picture of DM2 and IR has

been reported in 3% to 17% of those who receive the treatment, as a function of alterations in glucose homeostasis.<sup>7</sup>

The clarification of the factors involved in the process of alterations in glucose homeostasis, especially insulin resistance, still remains a major challenge for improving the quality of life of patients. Among users of protease inhibitors, an increased occurrence of insulin resistance has been observed without the development of diabetes mellitus.<sup>7</sup>

Hyperglycemia in patients using ART has a prevalence of 46% to 54%, and is caused by selective inhibition of the GLUT-4 receptor. This leads to loss of sensitivity to insulin from the major glucose transporter present in skeletal muscle, liver and adipocytes, and causes IR. When not treated correctly and quickly, this can lead to the development of *diabetes mellitus*. Thus, it is essential to identify those who have this metabolic change, and start treatment immediately.<sup>27</sup>

#### Dyslipidemia in elderly patients with AIDS

Dyslipidemia associated with ART is characterized by an increase in the levels of VLDL (greater triglyceride transporter), LDL, lipoprotein (a) and a reduction in HDL. In individuals without HIV, the accumulation of these substances in the plasma is associated with the development of atherosclerosis and its complications, such as myocardial infarction and peripheral vascular disease.

It has not yet been established whether dyslipidemia is a direct effect of ART or a result of the interaction of several elements, such as antiretroviral treatment, genetic predisposition, environmental factors (such as diet and exercise), or other factors, such as the host's response to infection by HIV.<sup>7</sup>

Insulin resistance increases the release of free fatty acids, while in the liver it determines a lower suppression of VLDL synthesis. This results in an excess of large, triglyceride-rich VLDL particles which, in turn, generate a cascade of switch events that result in a reduction in HDL cholesterol levels.<sup>7</sup>

The mechanisms that lead to these changes are not yet fully understood, but some hypotheses have been raised. One of these is that lipid complications arise or are aggravated as a result of ART, which leads to an increase of lipids in the bloodstream and a reduction in the peripheral storage of these molecules. When accumulated in the plasma and associated with the arterial inflammation itself resulting from the infection by the HIV, these lipids may clog arteries and facilitate

the formation of fatty plaques, which can lead to the development of CVD.<sup>28</sup>

Two main hypotheses have been raised about the mechanisms of interference in the lipid metabolism. The first would be the similarity between the viral active site where the binding of protease inhibitors (PI) occurs, leading to an increase in triglycerides and the freeing of fatty acids, combined with a reduction in plasma hydrolysis and uptake of triglycerides by the liver. The second hypothesis would be a proposed mechanism that would lead to dyslipidemia, due to the competition between PI and remnant chylomicrons (QR) by liver receptors, which prevent the removal of QR from the plasma and result in an increase in circulating triglycerides.<sup>28</sup>

## Conclusion

The present review study shows that, despite the high importance of the use of antiretroviral

treatment by HIV-positive patients, which lead to increased survival rates and higher quality of life for these patients, antiretroviral therapy has a significant pathophysiological impact on patients undergoing treatment. The relationship between the type and duration of therapy used, more common in elderly patients, can lead to metabolic syndrome resulting from the use of these drugs, and cause the development of DM2 and CVD.

This treatment highlights the importance of the intervention of nutritionists, who should direct patients towards an adequate food intake, significantly intervening in the metabolic changes caused by the use of therapy. Nutritional therapy plays a fundamental role in the recovery of these patients by conserving muscle mass and reducing the risk of malnutrition and opportunistic diseases. Nutritional guidance and consequent healthy eating habits alleviate the organic changes caused by the use of ART and improve the quality of life of patients with HIV.

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