



The Bi-directional Relationship Between Childhood Malnutrition and HIV/AIDS

Esther Ejiroghene Ajari ^{1,2,*} and Boluwatife Adeleye Adewale^{3,4}

¹Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria

²The TriHealthon, Ibadan, Oyo State, Nigeria

³College Research and Innovation Hub, College of Medicine, University of Ibadan, Ibadan, Nigeria

⁴University College Hospital, Ibadan, Nigeria

*Corresponding author: Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria. Email: estherejiroghene@gmail.com

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Abstract

Childhood malnutrition, a disorder broadly classified into overnutrition and undernutrition, is highly prevalent globally, especially in Sub-Saharan Africa and South-East Asia. Several studies have highlighted the bidirectional relationship between this disorder and HIV/AIDS, another disease with a high global prevalence. This relationship is quite complex. Links have been established between the disease entities on the individual, family and household level. Opportunistic infections and diseases associated with HIV, antiretroviral therapy and its adverse effects have also been implicated in this relationship. The key implicated variables includes frequency of disease occurrence, morbidity and mortality rate, and disease transmission rate. This paper reviews existing literatures on the subject matter, identifies key knowledge gaps, and recommends the need for further study of this complex relationship in order to close the gaps and inform decisions in healthcare.

Keywords: Childhood, Malnutrition, Overnutrition, Undernutrition, HIV, AIDS

1. Context

Malnutrition is a nutritional state of lack, deficiency, excess, or imbalance in the amount of energy and/or nutrients available to the body for utilization. This state is usually indicated by alteration of the weight-for-age, height-for-age, and weight-for-height indices to below -2 or above +2 Z-score of the World Health Organization's recommended reference values (1). It is not uncommon for malnutrition to be equated with undernutrition (2). However, malnutrition is a spectrum that includes both overnutrition and undernutrition. Undernutrition can be broadly classified into micronutrient deficiency and protein-energy undernutrition (PEU). The deficiency of iron, a micronutrient, is the most common and widespread nutritional disorder affecting both developed and developing nations (3). The deficiency of other micronutrients like Iodine, vitamin A, B12 and D, calcium and magnesium, are also incredibly common globally (4). PEU can be acute or chronic but in rare cases, a mixed state, termed "acute-on-chronic PEU", can occur. Acute-on-chronic PEU usually causes underweight (low weight-for-age). Acute PEU can be mild, moderate or severe and it can lead to wasting (low weight-for-height), the severe form of

which is termed kwashiorkor or marasmus, respectively, in the presence or absence of bilateral pitting edema (5). Chronic PEU leads to stunting (low height-for-age).

Undernutrition, especially chronic PEU, is closely associated with HIV/AIDS, another health disorder of global interest. This relationship has been shown to be bidirectional. Factors that, sometimes, come into play in reinforcing this relationship include latent poverty, food insecurity, poor feeding practices, other diseases and illnesses etc. (6). There is also bidirectional relationship between HIV/AIDS and overweight (defined as a Body Mass Index (BMI) of 25 to < 30 kg/m²), obesity (BMI of 30 - 40 kg/m²) and extreme obesity (BMI of > 40 kg/m²) (7). This relationship is, however, less established than the one between undernutrition and HIV/AIDS.

This paper extensively discusses the complex but interesting relationship between the above-mentioned disease entities in children. The rationale behind the focus on the paediatrics population is the fact that the global prevalence of malnutrition is higher among children, especially those under 5 years of age, with approximately 144 million of them stunted, 47 million wasted and 14.3 million severely wasted (8). Also highlighted in this discourse are the gaps in the current state of knowledge of the subject

matter and recommendations for closing them.

2. Discussion

Malnutrition is one of the first identified features of HIV/AIDS (9). Serwadda et al. (10) in their 1985 paper published in the *Lancet* Journal referred to the disease as the “slim disease” because it was characterized by severe wasting. Sub-Saharan Africa and South-East Asia, the two regions with the highest HIV burden, also have the highest prevalence of malnutrition globally (10-13). The complex bidirectional interaction between both diseases is made evident by the high prevalence of malnutrition observed among HIV-positive individuals and in the high mortality rate among malnourished HIV-positive children (14, 15). Malnutrition is the leading cause of immunodeficiency globally. A coexisting HIV infection further compromises the immune system. The impact of both diseases constitutes a great challenge to an infected person as malnutrition hastens the disease progression to AIDS (14, 16). Malnutrition in HIV increases the frequency of occurrence of opportunistic infections and number of hospital visits (9). It is interesting to note that malnutrition does its damage on the body systems independent of the progression of the HIV infection (9).

2.1. HIV Infection Impacts Childhood Undernutrition

HIV-infected children are more likely to be underfed, underweight and wasted than their HIV-negative counterparts (15). This occurs via various mechanisms which cut across body systems, individual, household and community levels. Anorexia in HIV/AIDS usually results from dysphagia, a clinical feature of opportunistic infections like oral thrush and oesophagitis (17). Oral thrush has been identified as a risk factor for severe underweight among HIV-positive under-five children in Burkina Faso (15). It has also been established that food intake reduces with increasing viral load (18). This suggests that HIV and its opportunistic infections also causes anorexia via other mechanisms yet unknown (19). Furthermore, in a person undergoing antiretroviral therapy (ART), adverse drug reactions like anorexia, nausea and vomiting limit availability of nutrients (17). Neuropsychiatric conditions associated with HIV/AIDS also contribute to poor feeding, and eventually undernutrition (17).

HIV alters the gastrointestinal tract, the largest lymphoid organ in the human body. This alteration manifests as gastrointestinal inflammation, atrophy/flattening of the villi, hyperplasia of the crypt of the small intestine, and consequent decrease in nutrient absorption and metabolism (19). Furthermore, chronic diarrhoea results

from HIV enteropathy as well as opportunistic infections associated with HIV (19). This further contributes to the poor availability of nutrient seen in HIV infection (17). Coupled with the fact that the nutrients absorbed by HIV-positive individuals may be insufficient, febrile illnesses and the infectious process associated with HIV and its opportunistic infections increases basal metabolism rate and the body's demand for nutrients by up to five times that of an HIV-negative child (17). For example, HIV-positive children with chronic lung disease, chronic tuberculosis or chronic diarrhoea require about 20–30% increase in body nutrients (19). This increased demand is compensated for by a depletion of body nutrient stores such as those in the muscles, thus, leading to weight loss and wasting, in extreme cases (17). In addition, HIV is linked to deficiency of micronutrients such as selenium, zinc, magnesium and fat soluble vitamins (vitamin A, D, E and K) (20) which further complicates the risk of immune dysfunction (17).

HIV infection within the home worsens the children's nutritional status.

The impact of HIV on nutritional status goes beyond the individual. HIV infection has financial implications in the home. Loss of employment, high cost of antiretroviral therapy and loss of a family member to the disease are various ways by which HIV affects family income (19). Children particularly bear the brunt as they may become malnourished as a result of food insecurity in the home. A study found that having a HIV-positive family member puts every child at risk of undernutrition (19). Positive maternal HIV status puts children at an even greater risk of malnutrition. A study found that children of HIV-infected mothers are 26 to 28% more likely to suffer from undernutrition than their counterparts with HIV-negative mothers (21). Other studies have however shown that antiretroviral therapy (ART) improves employment rate in the long run. Consequently, this would increase household income and reduce childhood undernutrition in the family (21, 22).

2.2. Childhood Undernutrition Impacts HIV Infection

Studies have shown the proportion of severely malnourished children with HIV to be as high as 54% and this association leads to mortality in most cases (23, 24). The mechanism by which undernutrition impacts HIV is not as straightforward as that by which HIV impacts undernutrition. A study, however, has established that food insecurity predisposes children to HIV/AIDS via nutritional, mental and behavioural pathways (25). Undernutrition hastens the progression of HIV infection to AIDS, renders HIV-positive children susceptible to opportunistic infections, and increases their mortality rate (16, 25). Severe undernutrition is a strong risk factor for HIV mortality even in children undergoing ART (26) as it increases microbial translo-

cation, and worsens immune recovery and response to ART (16). In fact, severe undernutrition in children that does not improve with standard therapy is classified as stage IV AIDS (27).

2.3. The Role of Micronutrients in HIV Spread

Furthermore, there exists a bidirectional relationship between deficiency of micronutrients and HIV infection. We mentioned earlier that certain micronutrients have been found in low concentrations in people who are HIV-positive, the deficiency of some of these nutrients has been implicated in enhanced HIV transmission and worsened mortality (28), particularly in sub-Saharan Africa. For example, a study suggests that selenium inhibits viral replication (20). Selenium supplementation has also been shown to reduce HIV mortality and morbidity (29).

2.4. Antiretroviral Therapy Promotes Weight Gain in HIV Infection

The prevalence of overweight and obesity in people living with HIV/AIDS has markedly increased since the advent of antiretroviral therapy. This observation is not only in developed settings, but has also been reported in developing countries and communities where hunger is more prevalent (29-31). This has caused a paradigm shift in the management of HIV/AIDS from trying to prevent the "wasting syndrome" to minimising the risks of non-communicable diseases (32-36).

Some studies have found the prevalence of obesity in HIV-positive children to be similar to that of the general population (37-39). The wide availability of ART is regarded as being mainly responsible for these changes (33, 34). Certain studies from Nigeria and South Africa, however, challenge the dominant notion that overnutrition in HIV/AIDS is only an emerging problem due to ART. Because of the similarities found between the prevalence of obesity among ART-naive people living with HIV/AIDS and the general population, they posit that ART would only worsen an existing overnutrition problem rather than precipitate it (37, 38). Notwithstanding, several other studies have reported a transition to overweight/obesity following initiation of ART (29-31, 33, 39, 40). In mouse models, ART has also been shown to increase diet-induced obesity, impair glucose metabolism and genetically alter fat tissue (41). A study in Zimbabwe even reveals a higher prevalence of HIV-positive overweight/obese children than underweight ones (32). The effect of ART on weight gain is more pronounced among the female and black populations (41-43). Lipodystrophy, a known complication of ART drugs has also been found to be significant in children (44, 45). Maternal HIV is also associated with childhood overnutrition.

A study found that large proportions of HIV-uninfected children to be overweight (46) after a year of being born to HIV-positive women undergoing ART.

2.5. Overnutrition Contributes to HIV Mortality and Morbidity

Studies show that a higher BMI slows disease progression, improves CD4⁺ T-cells status (34, 47) and reduces mortality (48, 49). However, there is an association between obesity and blood inflammatory markers in HIV-positive children that contributes to the inflammatory state already precipitated by the HIV infection (34, 50). This resultant inflammatory state is significantly associated with neurocognitive decline in HIV/AIDS patients, a complication of about one-half of HIV cases (46, 51, 52). Interleukin-6, one of the inflammatory cytokines increased in obesity, is linked to significant morbidity and mortality in HIV infection (32, 34). Obesity also predisposes HIV-positive children to comorbidities such as type 2 diabetes mellitus and cardiovascular disease, which worsen their prognosis (53).

The chronic inflammatory state that results from obesity still persists despite weight loss. Weight loss in HIV-positive children is, however, not without benefits as it reduces their risks of diabetes and cardiovascular diseases (53). Antilipids reduce the risks of metabolic complications associated with obesity, however drug-drug interactions with ART prevent them from being routinely used by patients undergoing ART (41). Eating a low-fat diet presents as a better alternative as it has been shown to have considerable success in controlling plasma lipids (54).

In developed countries, overnutrition has become the main nutritional challenge in the management of HIV since the introduction of ART (38). The HIV-positive children in low-income settings are however faced with a double burden of undernutrition and overnutrition, which contributes further to HIV mortality and morbidity (32).

3. Conclusions

Existing literatures point to the fact that winning the war against childhood malnutrition will contribute tremendously to the fight against HIV/AIDS and vice versa. However, more research should be carried out to further understand the intricacies of the relationship between these disease entities, especially between childhood overnutrition and HIV/AIDS. Results from these studies should be utilized alongside already known facts to guide health-care, advocacy and policymaking.

Footnotes

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References

- WHO. *Physical status: the use and interpretation of anthropometry*. WHO Expert Committee; 2013, [cited 2020 May 2]. Available from: https://www.who.int/childgrowth/publications/physical_status/en/.
- Morley JE. *Undernutrition - Disorders of Nutrition - MSD Manual Consumer Version*. 2017, [cited 2020 May 2]. Available from: <https://www.msmanuals.com/home/disorders-of-nutrition/undernutrition/undernutrition>.
- World Health Organization. *Micronutrient deficiencies*. 2016, [cited 2020 May 2]. Available from: <https://www.who.int/nutrition/topics/ida/en/>.
- Barnes JL, Tappenden KA. Nutritional Management of Inflammatory Bowel Disease and Short Bowel Syndrome. *Nutrition in the Prevention and Treatment of Disease*. 2013. p. 739–56. doi: [10.1016/j.b978-0-12-391884-0.00039-1](https://doi.org/10.1016/j.b978-0-12-391884-0.00039-1).
- Chaudhary P, Agrawal M, Lal Suman R. Management of Moderate Acute Malnutrition: Comparison of Different Approaches. *Asian J Clin Nutr*. 2017;**10**(1):47–57. doi: [10.3923/ajcn.2018.47.57](https://doi.org/10.3923/ajcn.2018.47.57).
- Bergeron G, Castleman T. Program responses to acute and chronic malnutrition: divergences and convergences. *Adv Nutr*. 2012;**3**(2):242–9. doi: [10.3945/an.111.001263](https://doi.org/10.3945/an.111.001263). [PubMed: [22516735](https://pubmed.ncbi.nlm.nih.gov/22516735/)]. [PubMed Central: [PMC3648728](https://pubmed.ncbi.nlm.nih.gov/PMC3648728/)].
- E. and T. *NHLBI Obesity Education Initiative Expert Panel on the Identification and of O. in A. (US). Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. 1998.
- World Health Organization. *Fact sheets - Malnutrition*. 2020, [cited 2020 May 2]. Available from: <https://www.who.int/news-room/fact-sheets/detail/malnutrition>.
- Babameto G, Kotler DP. Malnutrition in HIV infection. *Gastroenterol Clin North Am*. 1997;**26**(2):393–415. doi: [10.1016/s0889-8553\(05\)70301-0](https://doi.org/10.1016/s0889-8553(05)70301-0). [PubMed: [9187931](https://pubmed.ncbi.nlm.nih.gov/9187931/)].
- Serwadda D, Mugerwa RD, Sewankambo NK, Lwegaba A, Carswell JW, Kirya GB, et al. Slim disease: a new disease in Uganda and its association with HTLV-III infection. *Lancet*. 1985;**2**(8460):849–52. doi: [10.1016/S0140-6736\(85\)90122-9](https://doi.org/10.1016/S0140-6736(85)90122-9). [PubMed: [2864575](https://pubmed.ncbi.nlm.nih.gov/2864575/)].
- UNICEF. *The State of the World's Children 2015 - UNICEF DATA*. 2014, [cited 2020 May 2]. Available from: <https://data.unicef.org/resources/state-worlds-children-2015/>.
- WHO. *World Health Statistics 2010*. 2010, [cited 2020 May 2]. Available from: <https://www.who.int/whosis/whostat/2010/en/>.
- Kharsany AB, Karim QA. HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. *Open AIDS J*. 2016;**10**:34–48. doi: [10.2174/1874613601610010034](https://doi.org/10.2174/1874613601610010034). [PubMed: [27347270](https://pubmed.ncbi.nlm.nih.gov/27347270/)]. [PubMed Central: [PMC4893541](https://pubmed.ncbi.nlm.nih.gov/PMC4893541/)].
- Pendse R, Gupta S, Yu D, Sarkar S. HIV/AIDS in the South-East Asia region: progress and challenges. *J Virus Erad*. 2016;**2**(Suppl 4):1–6. [PubMed: [28303199](https://pubmed.ncbi.nlm.nih.gov/28303199/)]. [PubMed Central: [PMC5353351](https://pubmed.ncbi.nlm.nih.gov/PMC5353351/)].
- Podá GG, Hsu CY, Chao JC. Malnutrition is associated with HIV infection in children less than 5 years in Bobo-Dioulasso City, Burkina Faso: A case-control study. *Medicine (Baltimore)*. 2017;**96**(21). e7019. doi: [10.1097/MD.00000000000007019](https://doi.org/10.1097/MD.00000000000007019). [PubMed: [28538421](https://pubmed.ncbi.nlm.nih.gov/28538421/)]. [PubMed Central: [PMC5457901](https://pubmed.ncbi.nlm.nih.gov/PMC5457901/)].
- Jesson J, Masson D, Adonon A, Tran C, Habarugira C, Zio R, et al. Prevalence of malnutrition among HIV-infected children in Central and West-African HIV-care programmes supported by the Growing Up Programme in 2011: a cross-sectional study. *BMC Infect Dis*. 2015;**15**:216. doi: [10.1186/s12879-015-0952-6](https://doi.org/10.1186/s12879-015-0952-6). [PubMed: [26007232](https://pubmed.ncbi.nlm.nih.gov/26007232/)]. [PubMed Central: [PMC4494161](https://pubmed.ncbi.nlm.nih.gov/PMC4494161/)].
- Duggal S, Chugh TD, Duggal AK. HIV and malnutrition: effects on immune system. *Clin Dev Immunol*. 2012;**2012**:784740. doi: [10.1155/2012/784740](https://doi.org/10.1155/2012/784740). [PubMed: [22242039](https://pubmed.ncbi.nlm.nih.gov/22242039/)]. [PubMed Central: [PMC3254022](https://pubmed.ncbi.nlm.nih.gov/PMC3254022/)].
- Arpadi S. *Growth failure in HIV-infected children Consultation on nutrition and 219HIV/AIDS in Africa: Evidence, Lessons and Recommendations for Action Durban, South 220 Africa*. Geneva, Switzerland: World Health Organization; 2005, [cited 2020 May 1]. Available from: https://www.who.int/nutrition/topics/Paper_1_Macronutrients_bangkok.pdf?ua=1.
- Rose AM, Hall CS, Martinez-Alier N. Aetiology and management of malnutrition in HIV-positive children. *Arch Dis Child*. 2014;**99**(6):546–51. doi: [10.1136/archdischild-2012-303348](https://doi.org/10.1136/archdischild-2012-303348). [PubMed: [24406803](https://pubmed.ncbi.nlm.nih.gov/24406803/)]. [PubMed Central: [PMC4033118](https://pubmed.ncbi.nlm.nih.gov/PMC4033118/)].
- Enwonwu CO. Complex interactions between malnutrition, infection and immunity: relevance to HIV/AIDS infection. *Niger J Clin Biomed Res*. 2006;**1**(1):6–14.
- Magadi MA. Household and community HIV/AIDS status and child malnutrition in sub-Saharan Africa: evidence from the demographic and health surveys. *Soc Sci Med*. 2011;**73**(3):436–46. doi: [10.1016/j.socscimed.2011.05.042](https://doi.org/10.1016/j.socscimed.2011.05.042). [PubMed: [21729821](https://pubmed.ncbi.nlm.nih.gov/21729821/)]. [PubMed Central: [PMC3242166](https://pubmed.ncbi.nlm.nih.gov/PMC3242166/)].
- Bor J, Tanser F, Newell ML, Barnighausen T. Bor J, Tanser F, Newell ML, Barnighausen T. Nearly Full Employment Recovery Among South African HIV Patients On Antiretroviral Therapy: Evidence From A Large Population. *Health Aff (Millwood)*. 2012;**31**(7):1459–69.
- Thirumurthy H, Jafri A, Srinivas G, Arumugam V, Saravanan RM, Angappan SK, et al. Two-year impacts on employment and income among adults receiving antiretroviral therapy in Tamil Nadu, India: a cohort study. *AIDS*. 2011;**25**(2):239–46. doi: [10.1097/QAD.0b013e328341b928](https://doi.org/10.1097/QAD.0b013e328341b928). [PubMed: [21150560](https://pubmed.ncbi.nlm.nih.gov/21150560/)].
- Fergusson P, Tomkins A. HIV prevalence and mortality among children undergoing treatment for severe acute malnutrition in sub-Saharan Africa: a systematic review and meta-analysis. *Trans R Soc Trop Med Hyg*. 2009;**103**(6):541–8. doi: [10.1016/j.trstmh.2008.10.029](https://doi.org/10.1016/j.trstmh.2008.10.029). [PubMed: [19058824](https://pubmed.ncbi.nlm.nih.gov/19058824/)].
- Weiser SD, Young SL, Cohen CR, Kushel MB, Tsai AC, Tien PC, et al. Conceptual framework for understanding the bidirectional links between food insecurity and HIV/AIDS. *Am J Clin Nutr*. 2011;**94**(6):1729S–39S. doi: [10.3945/ajcn.111.012070](https://doi.org/10.3945/ajcn.111.012070). [PubMed: [22089434](https://pubmed.ncbi.nlm.nih.gov/22089434/)]. [PubMed Central: [PMC3226026](https://pubmed.ncbi.nlm.nih.gov/PMC3226026/)].
- Taye B, Shiferaw S, Enquesselassie F. The impact of malnutrition in survival of HIV infected children after initiation of antiretroviral treatment (ART). *Ethiop Med J*. 2010;**48**(1):1–10.
- Asafo-Agyei SB, Antwi S, Nguah SB. HIV infection in severely malnourished children in Kumasi, Ghana: A cross-sectional prospective study. *BMC Pediatr*. 2013;**13**:181. doi: [10.1186/1471-2431-13-181](https://doi.org/10.1186/1471-2431-13-181). [PubMed: [24206638](https://pubmed.ncbi.nlm.nih.gov/24206638/)]. [PubMed Central: [PMC3828476](https://pubmed.ncbi.nlm.nih.gov/PMC3828476/)].
- Baum MK, Shor-Posner G, Lai S, Zhang G, Lai H, Fletcher MA, et al. High risk of HIV-related mortality is associated with selenium deficiency. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1997;**15**(5):370–4. doi: [10.1097/00042560-199708150-00007](https://doi.org/10.1097/00042560-199708150-00007). [PubMed: [9342257](https://pubmed.ncbi.nlm.nih.gov/9342257/)].
- van Lettow M, Harries AD, Kumwenda JJ, Zijlstra EE, Clark TD, Taha TE, et al. Micronutrient malnutrition and wasting in adults with pulmonary tuberculosis with and without HIV co-infection in Malawi. *BMC Infect Dis*. 2004;**4**(1):61. doi: [10.1186/1471-2334-4-61](https://doi.org/10.1186/1471-2334-4-61). [PubMed: [15613232](https://pubmed.ncbi.nlm.nih.gov/15613232/)]. [PubMed Central: [PMC544350](https://pubmed.ncbi.nlm.nih.gov/PMC544350/)].
- Derose KP, Rios-Castillo I, Fulcar MA, Payan DD, Palar K, Escala L, et al. Severe food insecurity is associated with overweight and increased body fat among people living with HIV in the Dominican Republic. *AIDS Care*. 2018;**30**(2):182–90. doi: [10.1080/09540121.2017.1348597](https://doi.org/10.1080/09540121.2017.1348597). [PubMed: [28681631](https://pubmed.ncbi.nlm.nih.gov/28681631/)]. [PubMed Central: [PMC5725241](https://pubmed.ncbi.nlm.nih.gov/PMC5725241/)].

31. Sirotnin N, Hoover DR, Shi Q, Anastos K, Weiser SD. Food insecurity with hunger is associated with obesity among HIV-infected and at risk women in Bronx, NY. *PLoS One*. 2014;**9**(8). e105957. doi: [10.1371/journal.pone.0105957](https://doi.org/10.1371/journal.pone.0105957). [PubMed: [25162598](https://pubmed.ncbi.nlm.nih.gov/25162598/)]. [PubMed Central: [PMC4146558](https://pubmed.ncbi.nlm.nih.gov/PMC4146558/)].
32. Takarinda KC, Mutasa-Apollo T, Madzima B, Nkomo B, Chigumira A, Banda M, et al. Malnutrition status and associated factors among HIV-positive patients enrolled in ART clinics in Zimbabwe. *BMC Nutr*. 2017;**3**(1). doi: [10.1186/s40795-017-0132-8](https://doi.org/10.1186/s40795-017-0132-8).
33. Taylor BS, So-Armah K, Tate JP, Marconi VC, Koethe JR, Bedimo RJ, et al. HIV and Obesity Comorbidity Increase Interleukin 6 but Not Soluble CD14 or D-Dimer. *J Acquir Immune Defic Syndr*. 2017;**75**(5):500–8. doi: [10.1097/QAI.0000000000001444](https://doi.org/10.1097/QAI.0000000000001444). [PubMed: [28696344](https://pubmed.ncbi.nlm.nih.gov/28696344/)]. [PubMed Central: [PMC5513170](https://pubmed.ncbi.nlm.nih.gov/PMC5513170/)].
34. Koethe JR, Jenkins CA, Lau B, Shepherd BE, Justice AC, Tate JP, et al. Rising Obesity Prevalence and Weight Gain Among Adults Starting Antiretroviral Therapy in the United States and Canada. *AIDS Res Hum Retroviruses*. 2016;**32**(1):50–8. doi: [10.1089/aid.2015.0147](https://doi.org/10.1089/aid.2015.0147). [PubMed: [26352511](https://pubmed.ncbi.nlm.nih.gov/26352511/)]. [PubMed Central: [PMC4692122](https://pubmed.ncbi.nlm.nih.gov/PMC4692122/)].
35. Koethe JR, Heimbürger DC, PrayGod G, Filteau S. From Wasting to Obesity: The Contribution of Nutritional Status to Immune Activation in HIV Infection. *J Infect Dis*. 2016;**214** Suppl 2:S75–82. doi: [10.1093/infdis/jiw286](https://doi.org/10.1093/infdis/jiw286). [PubMed: [27625434](https://pubmed.ncbi.nlm.nih.gov/27625434/)]. [PubMed Central: [PMC5021242](https://pubmed.ncbi.nlm.nih.gov/PMC5021242/)].
36. Kim DJ, Westfall AO, Chamot E, Willig AL, Mugavero MJ, Ritchie C, et al. Multimorbidity patterns in HIV-infected patients: the role of obesity in chronic disease clustering. *J Acquir Immune Defic Syndr*. 2012;**61**(5):600–5. doi: [10.1097/QAI.0b013e31827303d5](https://doi.org/10.1097/QAI.0b013e31827303d5). [PubMed: [23023101](https://pubmed.ncbi.nlm.nih.gov/23023101/)]. [PubMed Central: [PMC3508375](https://pubmed.ncbi.nlm.nih.gov/PMC3508375/)].
37. Krishnan S, Schouten JT, Atkinson B, Brown T, Wohl D, McComsey GA, et al. Metabolic syndrome before and after initiation of antiretroviral therapy in treatment-naïve HIV-infected individuals. *J Acquir Immune Defic Syndr*. 2012;**61**(3):381–9. doi: [10.1097/QAI.0b013e3182690e3c](https://doi.org/10.1097/QAI.0b013e3182690e3c). [PubMed: [22828718](https://pubmed.ncbi.nlm.nih.gov/22828718/)]. [PubMed Central: [PMC3480980](https://pubmed.ncbi.nlm.nih.gov/PMC3480980/)].
38. Crum-Cianflone N, Tejedor R, Medina S, Barahona I, Ganesan A. Obesity among patients with HIV: the latest epidemic. *AIDS Patient Care STDS*. 2008;**22**(12):925–30. doi: [10.1089/apc.2008.0082](https://doi.org/10.1089/apc.2008.0082). [PubMed: [19072098](https://pubmed.ncbi.nlm.nih.gov/19072098/)]. [PubMed Central: [PMC2707924](https://pubmed.ncbi.nlm.nih.gov/PMC2707924/)].
39. Arbeitman LE, O'Brien RC, Somarriba G, Messiah SE, Neri D, Scott GB, et al. Body mass index and waist circumference of HIV-infected youth in a Miami cohort: comparison to local and national cohorts. *J Pediatr Gastroenterol Nutr*. 2014;**59**(4):449–54. doi: [10.1097/MPG.0000000000000394](https://doi.org/10.1097/MPG.0000000000000394). [PubMed: [24709829](https://pubmed.ncbi.nlm.nih.gov/24709829/)]. [PubMed Central: [PMC4524541](https://pubmed.ncbi.nlm.nih.gov/PMC4524541/)].
40. Biggs C, Spooner E. Obesity and HIV: a compounding problem. *South Afr J Clin Nutr*. 2017;**31**(4):78–83. doi: [10.1080/16070658.2017.1404299](https://doi.org/10.1080/16070658.2017.1404299).
41. Pepin ME, Padgett LE, McDowell RE, Burg AR, Brahma MK, Holleman C, et al. Antiretroviral therapy potentiates high-fat diet induced obesity and glucose intolerance. *Mol Metab*. 2018;**12**:48–61. doi: [10.1016/j.molmet.2018.04.006](https://doi.org/10.1016/j.molmet.2018.04.006). [PubMed: [29731256](https://pubmed.ncbi.nlm.nih.gov/29731256/)]. [PubMed Central: [PMC6001921](https://pubmed.ncbi.nlm.nih.gov/PMC6001921/)].
42. Hernandez D, Kalichman S, Cherry C, Kalichman M, Washington C, Grebler T. Dietary intake and overweight and obesity among persons living with HIV in Atlanta Georgia. *AIDS Care*. 2017;**29**(6):767–71. doi: [10.1080/09540121.2016.1238441](https://doi.org/10.1080/09540121.2016.1238441). [PubMed: [27723990](https://pubmed.ncbi.nlm.nih.gov/27723990/)].
43. Bares SH, Smeaton LM, Xu A, Godfrey C, McComsey GA. HIV-Infected Women Gain More Weight than HIV-Infected Men Following the Initiation of Antiretroviral Therapy. *J Womens Health (Larchmt)*. 2018;**27**(9):1162–9. doi: [10.1089/jwh.2017.6717](https://doi.org/10.1089/jwh.2017.6717). [PubMed: [29608129](https://pubmed.ncbi.nlm.nih.gov/29608129/)]. [PubMed Central: [PMC6148723](https://pubmed.ncbi.nlm.nih.gov/PMC6148723/)].
44. Amorosa V, Synnestvedt M, Gross R, Friedman H, MacGregor RR, Gudonis D, et al. A tale of 2 epidemics: the intersection between obesity and HIV infection in Philadelphia. *J Acquir Immune Defic Syndr*. 2005;**39**(5):557–61. [PubMed: [16044007](https://pubmed.ncbi.nlm.nih.gov/16044007/)].
45. Thompson-Paul AM, Wei SC, Mattson CL, Robertson M, Hernandez-Romieu AC, Bell TK, et al. Obesity Among HIV-Infected Adults Receiving Medical Care in the United States: Data From the Cross-Sectional Medical Monitoring Project and National Health and Nutrition Examination Survey. *Medicine (Baltimore)*. 2015;**94**(27). e1081. doi: [10.1097/MD.0000000000001081](https://doi.org/10.1097/MD.0000000000001081). [PubMed: [26166086](https://pubmed.ncbi.nlm.nih.gov/26166086/)]. [PubMed Central: [PMC4504569](https://pubmed.ncbi.nlm.nih.gov/PMC4504569/)].
46. le Roux SM, Abrams EJ, Donald KA, Brittain K, Phillips TK, Nguyen KK, et al. Growth trajectories of breastfed HIV-exposed uninfected and HIV-unexposed children under conditions of universal maternal antiretroviral therapy: a prospective study. *Lancet Child Adolesc Health*. 2019;**3**(4):234–44. doi: [10.1016/s2352-4642\(19\)30007-0](https://doi.org/10.1016/s2352-4642(19)30007-0).
47. Heath KV, Hogg RS, Singer J, Chan KJ, O'Shaughnessy MV, Montaner JS. Antiretroviral treatment patterns and incident HIV-associated morphologic and lipid abnormalities in a population-based cohort. *J Acquir Immune Defic Syndr*. 2002;**30**(4):440–7. doi: [10.1097/00042560-200208010-00010](https://doi.org/10.1097/00042560-200208010-00010). [PubMed: [12138351](https://pubmed.ncbi.nlm.nih.gov/12138351/)].
48. Anyabolu EN. BMI and Risk Factors of Underweight and Obesity in HIV Subjects in Eastern Nigeria. *World J AIDS*. 2016;**6**(1):8–15. doi: [10.4236/wja.2016.61002](https://doi.org/10.4236/wja.2016.61002).
49. Desai N, Mullen P, Mathur M. Lipodystrophy in pediatric HIV. *Indian J Pediatr*. 2008;**75**(4):351–4. doi: [10.1007/s12098-008-0037-2](https://doi.org/10.1007/s12098-008-0037-2). [PubMed: [18536889](https://pubmed.ncbi.nlm.nih.gov/18536889/)].
50. Kotler DP. Malnutrition in HIV infection and AIDS. *AIDS*. 1989;**3** Suppl 1:S175–80. doi: [10.1097/00002030-198901001-00025](https://doi.org/10.1097/00002030-198901001-00025). [PubMed: [2514734](https://pubmed.ncbi.nlm.nih.gov/2514734/)].
51. Martinez SS, Campa A, Bussmann H, Moyo S, Makhema J, Huffman FG, et al. Effect of BMI and fat mass on HIV disease progression in HIV-infected, antiretroviral treatment-naïve adults in Botswana. *Br J Nutr*. 2016;**115**(12):2114–21. doi: [10.1017/S0007114516001409](https://doi.org/10.1017/S0007114516001409). [PubMed: [27087233](https://pubmed.ncbi.nlm.nih.gov/27087233/)]. [PubMed Central: [PMC5830121](https://pubmed.ncbi.nlm.nih.gov/PMC5830121/)].
52. [No authors listed]. Survival after introduction of HAART in people with known duration of HIV-1 infection. The CASCADE Collaboration. Concerted Action on SeroConversion to AIDS and Death in Europe. *Lancet*. 2000;**355**(9210):1158–9. doi: [10.1016/s0140-6736\(00\)02069-9](https://doi.org/10.1016/s0140-6736(00)02069-9). [PubMed: [10791383](https://pubmed.ncbi.nlm.nih.gov/10791383/)].
53. Reeds DN, Pietka TA, Yarasheski KE, Cade WT, Patterson BW, Okunade A, et al. HIV infection does not prevent the metabolic benefits of diet-induced weight loss in women with obesity. *Obesity (Silver Spring)*. 2017;**25**(4):682–8. doi: [10.1002/oby.21793](https://doi.org/10.1002/oby.21793). [PubMed: [28245099](https://pubmed.ncbi.nlm.nih.gov/28245099/)]. [PubMed Central: [PMC5373981](https://pubmed.ncbi.nlm.nih.gov/PMC5373981/)].
54. Lazzaretti RK, Kuhmmer R, Sprinz E, Polanczyk CA, Ribeiro JP. Dietary intervention prevents dyslipidemia associated with highly active antiretroviral therapy in human immunodeficiency virus type 1-infected individuals: a randomized trial. *J Am Coll Cardiol*. 2012;**59**(11):979–88. doi: [10.1016/j.jacc.2011.11.038](https://doi.org/10.1016/j.jacc.2011.11.038). [PubMed: [22402068](https://pubmed.ncbi.nlm.nih.gov/22402068/)].