International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

# Effect of Probiotic Yogurt Supplementation on Intestinal Inflammation and Oxidative Stress in HIV-Positive Patients on Antiretroviral Therapy: Randomized Controlled Trials in 24 and 48 Weeks

**Kasamba Ilunga Eric[1], Balaka Ekwalanga Michel[2], Mulumba Kadiebwe David[3], Kalumba Kambote Athy[4], Ilunga Nikulu Julian[5], Lungu Anzwal[6], Kalenga Mwenze Kayamba Prosper[7], Malangu Mposhy Emmanuel Prosper[8]**

[1, 2, 5, 6, 7, 8]Department of Biomedical Sciences, Faculty of Medicine, University of Lubumbashi, R Congo

[8]Faculty of Veterinary Medicine, University of Lubumbashi, DR Congo

[3]Department of Internal Medicine, Faculty of Medicine, University of Lubumbashi, DR Congo

[4]Center of Excellence, Faculty of Medicine, University of Lubumbashi, R D Congo

**Abstract:** ***Human immunodeficiency virus (HIV) infection and antiretroviral therapy (ART) have been associated with high oxidative stress in HIV patients. The disparity in antioxidant levels and secondary inflammation due to intestinal bacterial translocation in people living with HIV is the leading cause of morbidity and mortality associated with HIV infection. Using a simple 1: 1 randomization, Efavirens (EFV) and Lopinavir (LPV) -treated antiretroviral (ARV) -treated patients were additionally supplemented with probiotic yogurt and then followed for 48 weeks and evaluated at inclusion, at mid- and at the end of the course, by the determination of markers: immunological (CD4), virological (viral load), inflammatory (soluble Hs CRP, CD14 and CD163) and oxidative stress [Superoxide dismuthase (SOD, glutathione peroxidase (GPx ) and Zinc]. The results confirm that HIV infection induces inflammation by a very significant increase in sCD14, sCD163 and HsCRP; and a collapse of the antioxidant protective system characterized by decreased levels of SOD, GPx, and Zinc. At weeks 24 and 48, a significant reversal of markers of inflammation and oxidative stress was observed under the ART + Probiotic Yogurt arm. Only the value of Zinc remained at a subnormal rate. All patients in the same arm had their undetected viral load since week 24. Although probiotic yogurt supplementation with ART has a significant impact on immunologic, virologic, inflammatory and oxidative stress markers compared to ARV only, it should be associated with Zinc for an optimal evolution of seropositive patients.***

**Keywords:** HIV, Inflammation, Oxidative Stress Probiotic

## 1. Introduction

HIV-1 induces oxidative stress by deregulation of oxidative stress pathways with increased ROS production and by inducing mitochondrial dysfunction [1, 2]. Although antiretroviral therapy can eliminate viremia and improve the immunological status of HIV-infected individuals for a prolonged period of time, both nucleoside and non-nucleoside inhibitors of Retro-Transcriptase (RT), as well as inhibitors of viral protease, trigger mass production of ROS in various cell types [3,4] also playing an important role in the development of a broad spectrum of virus-associated pathologies and is one of the factors contributing to the emergence and / or the perpetuation of chronic inflammatory syndromes. There is damage and dysfunction of the digestive system. This enteropathy due to HIV is characterized by a pronounced loss of CD4 + lymphocytes, increased intestinal permeability and microbial translocation that promotes systemic immune activation involved in the progression of the disease (5) The capitalization of these clinical observations suggests that the translocation microbial could affect the progression of HIV disease, the response to treatment, and non-AIDS comorbidities. Given its adverse effect on overall immunity, several interventions aimed at preventing or blocking microbial translocation are currently being investigated as new therapeutic agents for HIV / AIDS (6).

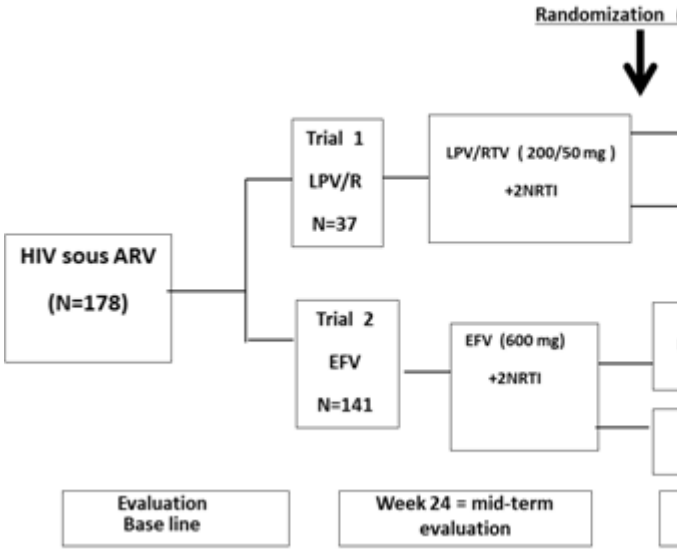
Thus, in the search for new therapeutic approaches to restore antioxidant defense systems and inhibit microbial translocation and / or attenuate chronic immune activation in HIV-infected individuals, in order to complement treatments aimed at the direct suppression of viral replication. We conducted a study to evaluate the effect of probiotic yoghurt supplementation on intestinal wall inflammation and oxidative stress on disease progression

## 2. Methods

A simple 1: 1 randomization, selecting 229 HIV-positive patients on ART, of whom only 178 were elected and included in the study because of 141 under Bras Efavirens (68 under ART and 73 under ART + probiotic yogurt) and 37 under LPV / r ( 18 on ART and 19 HAART + Probiotic Yogurt) combined with Tenofovir (TDF) and Lamuvidine (3TC) according to the following criteria: written informed consent, age ≥ 18 years, patient on antiretroviral therapy for more than 6 months, meet criteria following, negative pregnancy test at the selection visit (♀ of childbearing age) and the non-inclusion criteria are defined as follows:

presence of Grade 4 laboratory abnormalities at the selection visit, ALT or AST> 3X limit Sup of normal, hemoglobin <8.5 g% (♀), <9.0g% (♂), estimated creatinine clearance <50ml / min, according to the Cockcroft-Gault formula suspicion of TBC at X-ray thorax . And followed for 48 weeks.

The parameters of interest were as follows: age, sex; therapeutic regimen, CD4 count (s) count, sCD14 (Enzo life science), sCD163 (Avisera Biosciences) (Hypersensitive CRP (Enzo life science), Glutathione peroxidase (Randox), sulfoxide dismuthase (Randox), Zinc (Randox)), the viral load (Roche CAPCTM) The data collected at inclusion, in weeks 24 and 48 were analyzed using the software Epi Info version 7.2.2.2, and Excel 2010.




## 3. Results and Discussion

**Table 1:** Randomization: Patient Status at Inclusion and Week 24 and 48ko

| *Parameters* | *n* |
|---|---|
| Selected patients | 229 |
| Eligible patients | 178 |
| Ineligible patients | 51 |
| Pregnacy | 19 |
| Tuberculis(TBC) | 23 |
| Refusal consent | 9 |
| Randomization | EFV-TDF-3TC |

| | ARV | ARV+Probiotic Yogurt | ARV | ARV+Probiotic Yogurt |
|---|---|---|---|---|
| | n | n | n | n |
| Inclusion | 68 | 73 | 18 | 19 |
| Week 24 | 58 | 69 | 11 | 18 |
| **Withdrawals:** | | | | |
| • Death | 3 | 0 | 4 | 0 |
| • TBC | 1 | 0 | 3 | 0 |
| • Lost from view | 6 | 4 | 0 | 1 |
| • Week 48 | 52 | 67 | 10 | 16 |
| **Withdrawal:** | | | | |
| • Death | 2 | 0 | 0 | 0 |
| • TBC | 0 | 0 | 0 | 0 |
| • Lost from view | 4 | 2 | 1 | 2 |

77.7% of eligible patients were included in our study, tuberculosis (10.0%) and pregnancy (8.29%) were the main causes of non-eligibility with a refusal of consent of 3.93% or 9 patients of the selected group. After 24 and 48 weeks of follow-up, 7 deaths in week 24 and 2 in week 48, ie 3.92% of cases, the lost were respectively divided again: 11 in week 24 set 9 in week 48 or 20 cases in total (11.23% ); 4 cases of tuberculosis occurring during our cohort, ie 2.31% of patients included. Most of our patients are female, ie 71.9% with an average age of 30 (28-45).

In their Cameroon series Dimala CA et al (7) found that the mean age was 40.2 ± 8.0 years and 70% of them were women, which is close to our observation; In addition, Woldemedhin B et al., Studying the reason for the change of regimen in HIV / AIDS patients who initiated highly active first-line antiretroviral therapy in southern Ethiopia found that the majority of patients ( 69.29%) were women (8), same observation made by Abo Y et al (9) in West Africa where their series consisted of 67% women, with a median age of 35 years. As for the mortality rate, it is lower compared to the estimates of Farahani M and all (10) which report a mortality rate in sub-Saharan countries of 18.5% (95% confidence interval). 13.8 to 23.7). But, our rate is similar to that found in Kenya by Onyango, DO et al (11) where it is estimated at 6% with a tuberculosis incidence of 10% as in our study.

### 1) Immunological marker monitoring

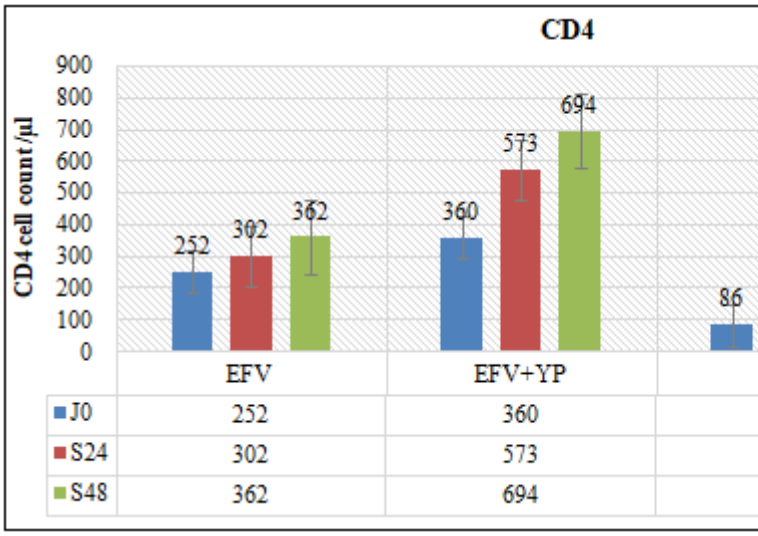



**Figure 1:** Variation in CD4 count

The CD4 follow-up results during randomization show that a significant difference in variation between the two arms, ART + Yogurt significantly improved CD4 count, an increase of 92.7% and 396.6% respectively under supplementation. in probiotic yogurt and EFV (p = 0.00206) and LPV (p = 0.00278) versus 43.6% and 46.5% respectively under EFV and LPV only. The results under ART only approximate those of Roul H et al who showed a cumulative incidence of CD4 recovery after 6 years of virological control was 69.7% with CD4 recovery as the main factor. their rate at the beginning of treatment (12); and Kroezes S et al who observed CD4 CD4 incidence rates were 12.5 times higher for AIDS (13); But the results of the CD4 level obtained with ART alone are far lower than those

obtained with ART and probiotic yogurt supplementation, which is confirmed by Irvine SL et al who found in their study that the introduction of probiotic yogurt , made by local women in a low-income community in Tanzania, was significantly associated with an increase in CD4 count among consumers living with HIV (14), the same observation was made by Anukam KC (15) in his study on Yogurt containing Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 probiotics that helped treat moderate diarrhea and increase CD4 counts in HIV / AIDS patients.

**2) Tracking markers of inflammation**

Generally, within 48 weeks, high levels of macrophage activation markers, such as sCD163, sCD14 in the blood, as well as inflammatory biomarkers, such as Hs-CRP, were observed under ARV treatment. and decreases non-significantly under ART only. And a very significant decrease was found under the ARV + Probiotic Yogurt arm and this regardless of the ARV base.

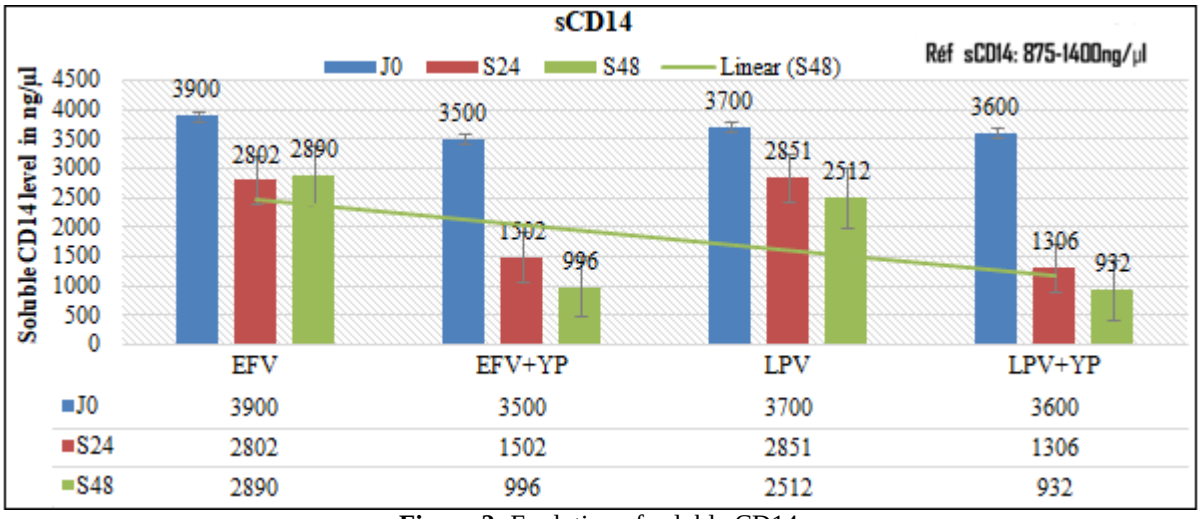



**Figure 2:** Evolution of soluble CD14

The figure above shows a high level of soluble CD14 for all patients on ART at the inclusion of randomization under EFV [3560 (2300-5980)] and under LPV [3500 (2210-5840)], which translates persistent inflammation despite ART. This persistence of high sCD14 levels was also observed by Macatangay BJ et al (16) who noted among study participants who started antiretroviral therapy in the first six months of HIV infection, high levels of sCD14 and CRP and remained similar to levels seen prior to antiretroviral therapy, suggesting that immune lesions occurring during the early stages of infection persist despite short-term virological suppression; Sereti I et al (17) also observed that sCD14 levels decreased during antiretroviral treatment, but remained high compared to non-HIV infected participants. ; Negi N et al also noted in their results that elevated levels of sCD14, Endo Cab and IgM LPS in HIV-1 infected individuals are potent predictors of disease progression and could be considered Candidate biomarkers for disease surveillance (18). Sereti at al (17) suggest that additional interventions to reduce inflammation may be necessary to optimize clinical outcomes in HIV-infected individuals. Thus, under probiotic yogurt and HAART, our results show a significant decrease in the level of sCD14. Indeed, Pei R (19) et al claim that yogurt consumption after nine weeks showed that ΔAUC ratios of YO and YN LY / SCD14 ratios were less than half those of control groups (P = 0, 0093). Similarly, Kong LC et al (20) in their study of dietary habits associated with inflammation and gut microbiota in overweight and obese subjects, found that the group with the healthiest eating behaviors (lower consumption of sweets and sugary drinks, and higher fruit consumption, but also yogurts and soups) had the lowest inflammatory markers (sCD14).

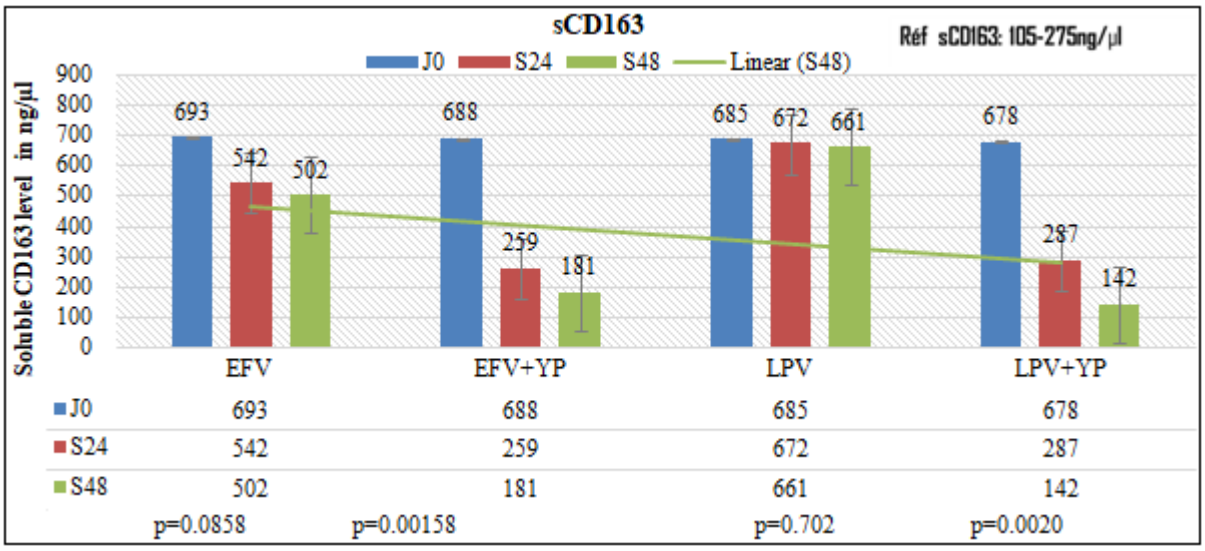



**Figure 3:** Evolution of soluble CD163

In the analysis of Figure 3, we note that the level of sCD163 mono-macrophage activation marker remains high in patients on antiretroviral therapy, which is consistent with the statement of Castley A et al (16). who report that HIV status was associated with a significant increase in the expression of CD64, CD143 and CD163 on CD16 + monocytes regardless of the virologic response to HIV treatment. This finding is also that of Burdo TH (21) who observed that the sCD163 rate was high in the plasma of people suffering from chronic HIV infection (> 1 year in duration), compared to HIV -séronégative. And under effective antiretroviral therapy, the sCD163 level decreased in parallel with the level of RNA-HIV viral load without equaling the level of seronegative subjects, suggesting the presence of residual monocyte / macrophage activation, even with viral loads. plasma levels below the limit of detection. And recently, Generoso M et al (22) confirmed in a child study that high plasma levels of sCD163 in HIV-infected children correlate with disease progression and T-cell activation and that initiation of antiretroviral therapy normalizes sCD163 levels and can reduce HIV-related morbidity and improve long-term outcomes. Ticona E et al (23) evaluating the biomarker of inflammation during antiretroviral suppressive therapy, found that prior to antiretroviral therapy, soluble CD163 concentrations were higher and remained higher after 24 months of suppressive therapy. Knudsen TB et al (24) associate rate increase sCD163 was an independent marker of all-cause mortality in a cohort of HIV-infected individuals, suggesting that activation of monocytes / macrophages may play a role in pathogenesis of HIV and be a target for intervention. While in our study, the rate of sCD163 decreased significantly in patients receiving antiretroviral therapy combined with probiotic yogurt supplementation.

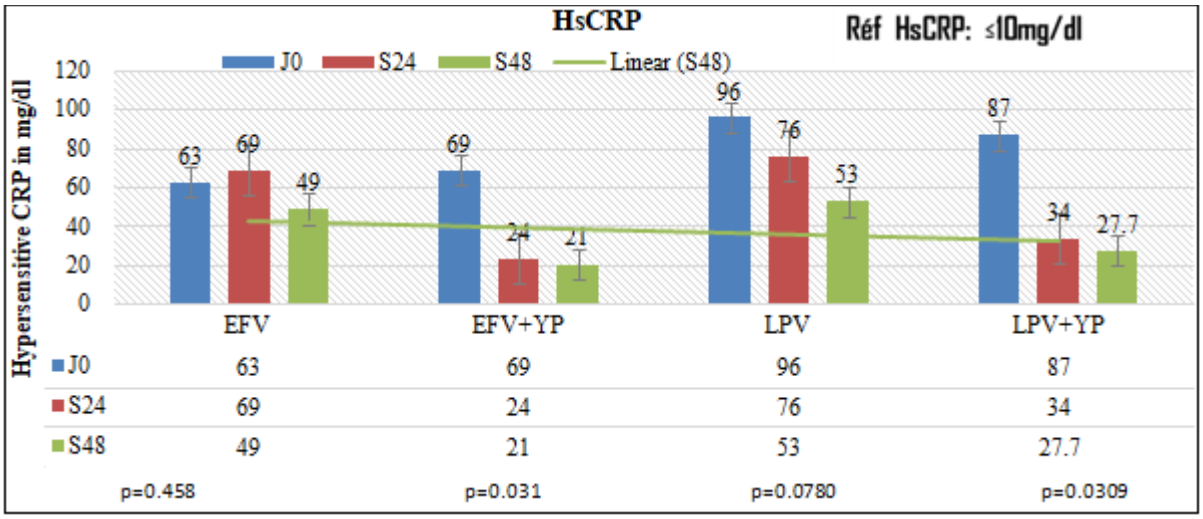



**Figure 4:** Evolution of HsCRP

Figure 4 shows the evolution of the hypersensitive CRP level; which in patients with inclusion have high values as found by Borato DC et al (25) who has significantly elevated levels of Hs - CRP were observed only in the TARV group which indicates a predictor of events cardiovascular in HIV positive patients, same finding made by Muswe R et al (26), Kozić Dokmanović S et al (27). Hattab S et al (28) investigating the impact of various antiretroviral regimens on markers of immune activation and inflammation, found that levels of hs-CRP and sCD14 remained stable and no difference was found between LPV / r and EFV as in our study. Naomi Trupper (29) measured in HIV-positive post-

ART patients and extra-virgin olive oil HsCRP at lower levels due to the effect of hydroxytyrosol concentration, a potent antioxidant found in olives with antiviral and anti-inflammatory properties and acts as a microbicide and reduces HIV transmission.

**3) Tracking markers of Oxidative Stress**

Inflammation during HIV infection contributes to the development of cancer, mainly by causing oxidative stress and DNA damage. And thus disrupting the system of enzymatic and non-enzymatic antioxidant defenses, in our study, we observe a decrease in the activity and Superoxide dismuthase and glutathione peroxidase as well as a decrease in the Zinc rate. This situation showed no significant change under ART and very significant under ART with probiotic yogurt supplementation.

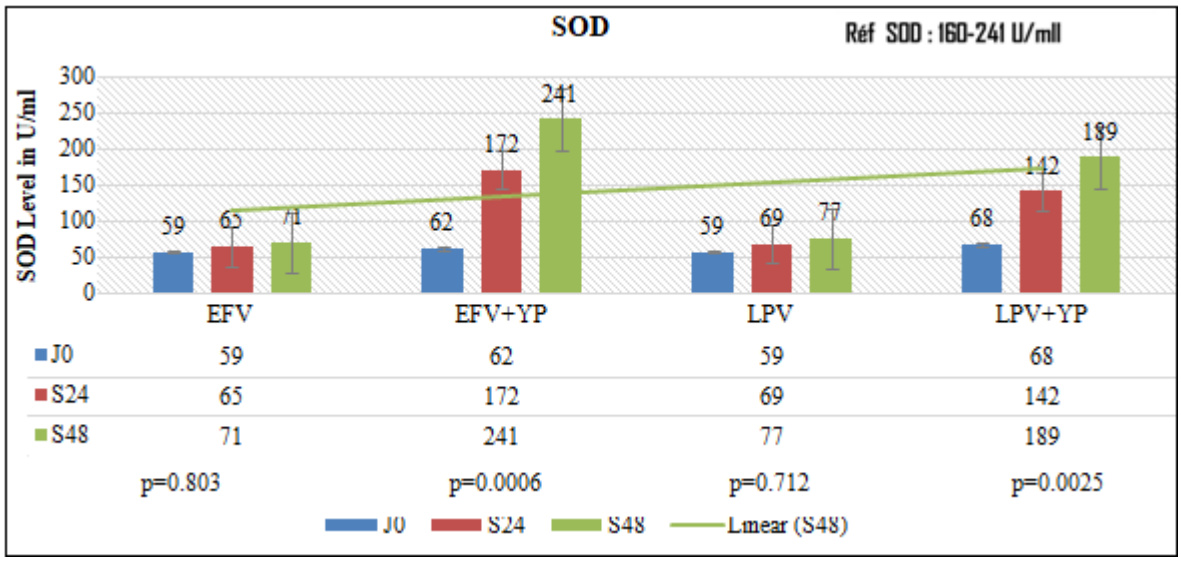



**Figure 5:** Profile of Superoxide dismuthase

The SOD level is significantly decreased on ART at baseline and the rest on ART only at week 48, this observation is also that of Makinde O et al (30) who after vitamin A supplementation in HIV-positive people on ART. , the SOD rate in its series has remained low. Similarly, Suresh et al (31) evaluating total antioxidant capacity and a new biochemical early marker of oxidative stress in HIV-infected individuals, found a significant decrease in vitamin E, vitamin C and SOD levels. . What Quaye O et al (32) also note in Ghana among HIV-infected patients was that SOD activity was significantly reduced in antiretroviral-treatment-naive patients compared to those on antiretroviral therapy and the control group. In addition, our results demonstrate that antiretroviral therapy combined with probiotic yogurt supplementation improves SOD activity and restores oxidative stress defense activity.

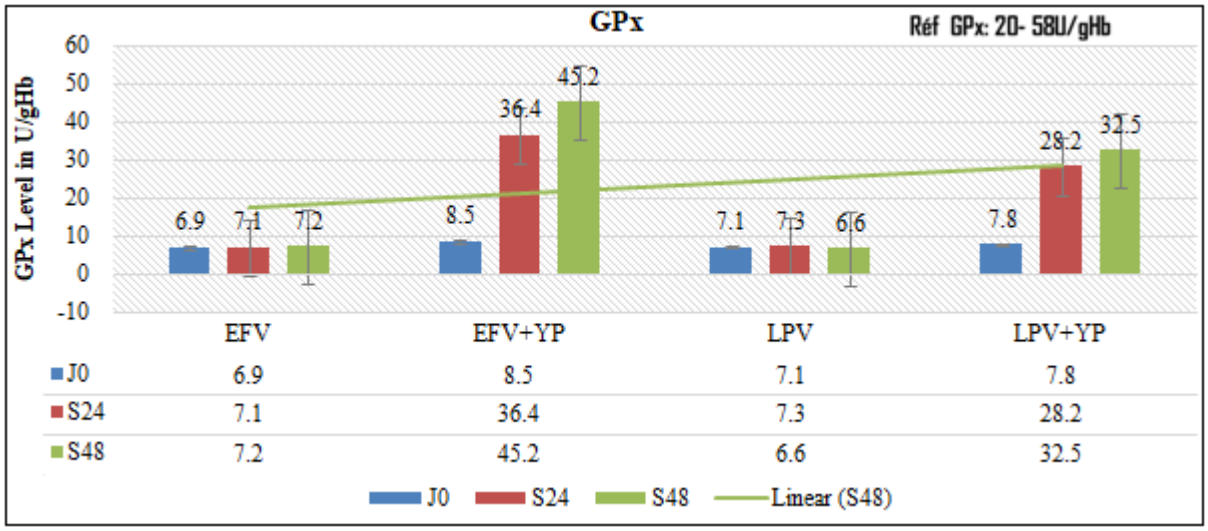



**Figure 6:** Glutathione peroxidase profile

Figure 6 high, shows a low activity of Glutathione peroxidase under ART that significantly improves with ART and probiotic yogurt. What Look MP1 et al (33) have also noted in evaluating the various antioxidant markers in people living with HIV that stages I to III of HIV disease are characterized by significant alterations in the antioxidant defenses provided by selenium, GSH-Px, SH groups and GSH. Ogunro PS et al (34), who studies the correlation

between the concentration of selenium and glutathione peroxidase, have also confirmed that selenium and glutathione peroxidase are reduced to scavenging antioxidants, and that their concentration decreases significantly with evolution. of the disease. This is exactly what Wanatabe et al (35) state that HIV infection was associated with increased oxidative stress and appears to affect the protective activity of Glutathione Peroxidase. While Stephensen CB et al (36) insist on the relationship between Glutathione peroxidase activity and good nutrition because in their conclusion, they specify that the GPX activity seems to have been induced by the oxidative stress associated with the infection. HIV and antiretroviral therapy. Thus, young and well-nourished subjects can develop a compensatory antioxidant response to HIV infection.

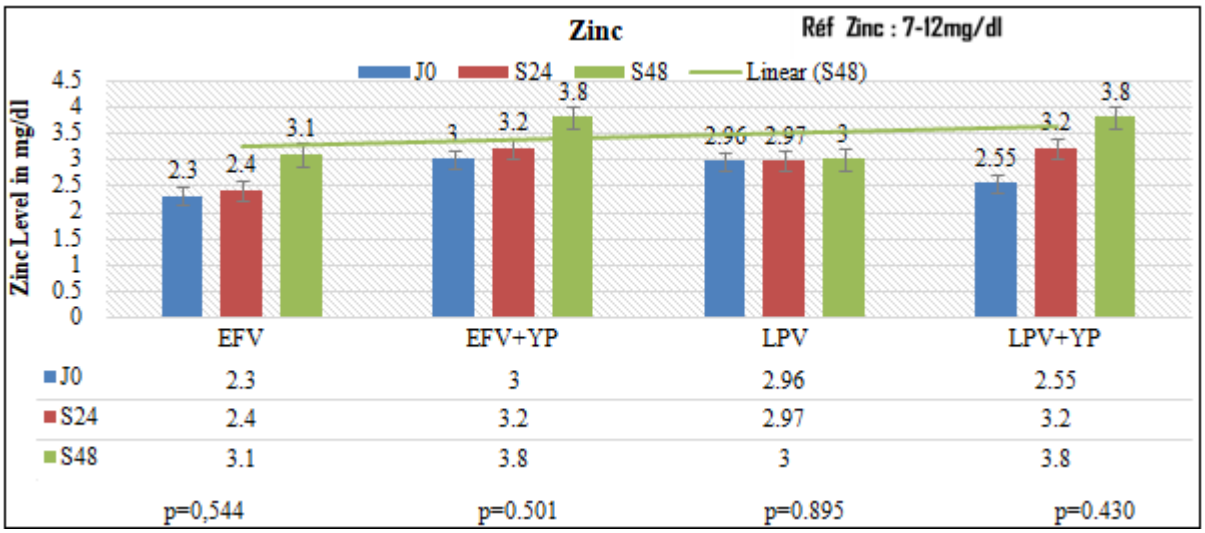



**Figure 7:** Evolution u Zinc rate

The Zinc rate remains low in our series throughout 48 weeks of treatment with ART or ART supplemented with Probiotic Yogurt. Shivakoti R et al (37), in their studies, found that despite increasing micronutrient levels, the prevalence of individual deficiencies remained virtually unchanged after 48 weeks of antiretroviral therapy and noted that antiretroviral therapy alone is not sufficient to improve micronutrient deficiency. In addition, low levels of zinc and chronic inflammation are known to be common in persons infected with the human immunodeficiency virus (HIV) (38) and zinc deficiency may promote systemic inflammation. (39), which is confirmed by Mburu AS et al (40) in a study in Kenyan adults living with HIV showing that plasma zinc levels were lower in those with inflammation. Similarly Osuna-Padilla I et al (41) found frequent deficiencies in serum zinc concentration in HIV-positive individuals; in Iran, Khalili H et al (42) also noted that serum zinc and selenium levels in individuals infected with human immunodeficiency virus were significantly lower compared to healthy individuals.

The results of all these high publications have confirmed our study which demonstrates that HIV infection induces both inflammation and oxidative stress, the result of which is the degradation of the quality of life of the infected person and status remains despite effective antiretroviral therapy. Probiotic yogurt supplementation provides both ingredients that reduce inflammation because fermented foods may also have improved nutritional and functional properties due to the transformation of substrates and the formation of bioactive or bio-available end products ( 43) that have significant anti-inflammatory effects (44) that lower the indirect markers of bacterial translocation and T-cell activation, and induce an improvement in thymic production and improvement of soluble CD14 inflammatory biomarkers and C-reactive protein with high sensitivity (45). This is particularly the case of the Lin PP (46) team demonstrated by the administration of probiotics orally fermented in rats and observed a suppression of the inflammatory pathway related to TLR-4 which is the same pathway. Bacterial cell wall LPS fixation via soluble and membrane-bound CD14 and MD2 factors, and improves the antioxidant level of patients by the proteolytic activity of probiotics that release bioactive peptides, animate acids, antioxidant enzymes and other compounds (47) and the protein fraction contains antioxidant activity, in particular casein, antioxidant enzymes; lactoferrin; conjugated linoleic acid; Coenzyme Q10; vitamins C, E, A and D3; equol; Uric acid; carotenoids; and mineral activators of antioxidant enzymes (48). In addition, fermentation leads to an increase in the capacity and bioavailability of antioxidants (49) (50) (51); also, the survival rate of ferments during digestion would play a role in bioavailability of antioxidants (52). And the highest antioxidant activity shows that Lactobacillus acidophilus has an antioxidant capacity measured at 54.86% neutralization of free radicals and that of Streptococcus thermophillus at 45.17% (53). And these bacteria are those isolated from the probiotic yogurts used in our series.

## 4. Conclusion

Inflammation and oxidative stress induced by HIV infection are two major problems that prevent optimal progression of patients on antiretroviral therapy. They maintain a low level of CD4, very remarkable increase in biomarkers of inflammation (sCD14, sCD163 and HsCRP) and a permanent oxidative stress by collapse of the main antioxidant system defenses enzymes (superoxide dismuthase and glutathione peroxidase) anis Zinc cofactor, the deficiency of which also has systemic inflammation.

Probiotic yoghurt supplementation with Lactobacillus acidiphilus and streptococcus bulgaricus resulted in improved levels of CD4 and enzymes in the antioxidant system, significantly reducing biomarkers of inflammation. Only the Zinc concentration remained at sub-normal values regardless of the intervention.

## References

[1] K. Banki, E. Hutter, N. J. Gonchoroff, and A. Perl, "Molecular ordering in HIV-induced apoptosis. Oxidative stress, activation of caspases, and cell survival are regulated by transaldolase," The Journal of Biological Chemistry, vol. 273, no. 19, pp. 11944–11953, 1998. View at Publisher · View at Google Scholar · View at Scopus

[2] S. L. Deshmane, R. Mukerjee, S. Fan et al., "Activation of the oxidative stress pathway by HIV-1 Vpr leads to induction of hypoxia-inducible factor 1α expression," The Journal of Biological Chemistry, vol. 284, no. 17, pp. 11364–11373, 2009. View at Publisher · View at Google Scholar · View at Scopus

[3] X. Wang, H. Chai, P. H. Lin, Q. Yao, and C. Chen, "Roles and mechanisms of human immunodeficiency virus protease inhibitor ritonavir and other anti-human immunodeficiency virus drugs in endothelial dysfunction of porcine pulmonary arteries and human pulmonary artery endothelial cells," The American Journal of Pathology, vol. 174, no. 3, pp. 771–781, 2009. View at Publisher · View at Google Scholar · View at Scopus

[4] M. Weiß, B. Kost, I. Renner-Müller, E. Wolf, I. Mylonas, and A. Brüning, "Efavirenz causes oxidative stress, endoplasmic reticulum stress, and autophagy in endothelial cells," Cardiovascular Toxicology, vol. 16, no. 1, pp. 90–99, 2016. View at Publisher · View at Google Scholar · View at Scopus

[5] González-Hernández LA, Jave-Suarez LF, Fafutis-Morris M, Montes-Salcedo KE, and Valle-Gutierrez LG .Synbiotic therapy decreases microbial translocation and inflammation and improves immunological status in HIV-infected patients: a double-blind randomized controlled pilot trial. Nutr J. 2012 Oct 29; 11:90. doi: 10.1186/1475-2891-11-90

[6] Marchetti G, Tincati C, Silvestri G.Microbial translocation in the pathogenesis of HIV infection and AIDS. Clin Microbiol Rev. 2013 Jan; 26(1):2-18. doi: 10.1128/CMR.00050-12

[7] Dimala CA, Bechem NN, Aroke D, Kadia BM ,Motives for change of first-line antiretroviral therapy regimens in an unselected cohort of HIV/AIDS patients at a major referral centre in South-west Cameroon.BMC Res Notes. 2017 Nov 28;10(1):623. doi: 10.1186/s13104-017-2948-3.

[8] Woldemedhin B1, Wabe NT The Reason for Regimen Change Among HIV/AIDS Patients Initiated on First Line Highly Active Antiretroviral Therapy in Southern Ethiopia.N Am J Med Sci. 2012 Jan;4(1):19-23. doi: 10.4103/1947-2714.92898

[9] Abo Y1, Minga A, Menan H, Danel C, Ouassa T, Dohoun L, Bomisso G, Tanoh A, Messou E, Eholié S, Lewden C, Anglaret X.Incidence of serious morbidity in HIV-infected adults on antiretroviral therapy in a West African care centre, 2003-2008.BMC Infect Dis. 2013 Dec 27;13:607. doi: 10.1186/1471-2334-13-607.

[10] Farahani M, Mulinder H, Farahani A, Marlink R.Prevalence and distribution of non-AIDS causes of death among HIV-infected individuals receiving antiretroviral therapy: a systematic review and meta-analysis.Int J STD AIDS. 2017 Jun;28(7):636-650. doi: 10.1177/0956462416632428. Epub 2016 Feb 10.

[11] Onyango, DO , Yuen CM , Cain KP , Ngari F , Masini EO , Borgdorff MW 3 Reduction of HIV-associated excess mortality by antiretroviral treatment among tuberculosis patients in Kenya.. PLoS One. 16 novembre 2017: 12 (11): e0188235. doi: 10.1371 / journal.pone.0188235. eCollection 2017.

[12] Roul H, Mary-Krause M, Ghosn J, Delaugerre C, Pialoux G, Cuzin L, Launay O, Lacombe JM, Menard A, De Truchis P, Delfraissy JF, Weiss L, Costagliola D; FHDH-ANRS CO.CD4+ cell count recovery after combined antiretroviral therapy in the modern combined antiretroviral therapy era.AIDS. 2018 Nov 13; 32(17):2605-2614. doi: 10.1097/QAD.0000000000002010

[13] Kroeze S, Ondoa P, Kityo CM, Siwale M, Akanmu S, Wellington M, de Jager M, Ive P, Mandaliya K, Stevens W, Boender TS, de Pundert ME, Sigaloff KCE, Reiss P, Wit FWNM, Rinke de Wit TF, Hamers RL1Suboptimal immune recovery during antiretroviral therapy with sustained HIV suppression in sub-Saharan Africa.AIDS. 2018 May 15; 32(8):1043-1051. doi: 10.1097/QAD.0000000000001801

[14] Irvine SL, Hummelen R, Hekmat S, Looman CW, Habbema JD, Reid G. Probiotic yogurt consumption is associated with an increase of CD4 count among people living with HIV/AIDS.. J Clin Gastroenterol. 2010 Oct; 44(9):e201-5. doi: 10.1097/MCG.0b013e3181d8fba8

[15] Anukam KC, Osazuwa EO, Osadolor HB, Bruce AW, Reid G.Yogurt containing probiotic Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 helps resolve moderate diarrhea and increases CD4 count in HIV/AIDS patients.J Clin Gastroenterol. 2008 Mar;42(3):239-43. doi: 10.1097/MCG.0b013e31802c7465

[16] Macatangay BJ, Yang M, Sun X, Morton J, De Gruttola V, Little S, Hogan C, Rinaldo CR; A5217 Team Brief Report: Changes in Levels of Inflammation After Antiretroviral Treatment During Early HIV Infection in AIDS Clinical Trials Group Study A5217.J Acquir Immune Defic Syndr. 2017 May 1;75(1):137-141. doi: 10.1097/QAI.0000000000001320.

[17] Sereti I, Krebs SJ, Phanuphak N, Fletcher JL, Slike B, Pinyakorn S, O'Connell RJ, Rupert A, Chomont N, Valcour V, Kim JH, Robb ML, Michael NL, Douek DC, Ananworanich J, Utay NS10; RV/SEARCH , RV/SEARCH and SEARCH protocol teamsPersistent, Albeit Reduced, Chronic Inflammation in Persons Starting Antiretroviral Therapy in Acute HIV Infection.. Clin Infect Dis. 2017 Jan 15;64(2):124-131. doi: 10.1093/cid/ciw683. Epub 2016 Oct 12.

[18] Negi N1, Singh R2, Sharma A3, Das BK4, Vajpayee M5Comparative evaluation of microbial translocation

products (LPS, sCD14, IgM Endocab) in HIV-1 infected Indian individuals.Microb Pathog. 2017 Oct; 111:331-337. doi: 10.1016/j.micpath.2017.08.004. Epub 2017 Aug 9

[19] Pei R, DiMarco DM, Putt KK, Martin DA, Chitchumroonchokchai C, Bruno RS, Bolling BW Premeal Low-Fat Yogurt Consumption Reduces Postprandial Inflammation and Markers of Endotoxin Exposure in Healthy Premenopausal Women in a Randomized Controlled Trial.J Nutr. 2018 Jun 1; 148(6):910-916. doi: 10.1093/jn/nxy046. Erratum in: J Nutr. 2018 Oct 1; 148(10):1698.

[20] Kong LC, Holmes BA, Cotillard A, Habi-Rachedi F, Brazeilles R, Gougis S, Gausserès N, Cani PD, Fellahi S, Bastard JP, Kennedy SP, Doré J, Ehrlich SD, Zucker JD, Rizkalla SW, Clément K Dietary patterns differently associate with inflammation and gut microbiota in overweight and obese subjects.PLoS One. 2014 Oct 20; 9(10):e109434. doi: 10.1371/journal.pone.0109434. eCollection 2014.PMID: 25330000

[21] Castley A, Berry C, French M, Fernandez S, Krueger R, Nolan D.Elevated plasma soluble CD14 and skewed CD16+ monocyte distribution persist despite normalisation of soluble CD163 and CXCL10 by effective HIV therapy: a changing paradigm for routine HIV laboratory monitoring?PLoS One. 2014 Dec 29;9(12):e115226. doi: 10.1371/journal.pone.0115226. Collection 2014

[22] Burdo TH, Lentz MR, Autissier P, Krishnan A, Halpern E, Letendre S, Rosenberg ES, Ellis RJ, Williams KC.Soluble CD163 made by monocyte/macrophages is a novel marker of HIV activity in early and chronic infection prior to and after anti-retroviral therapy.J Infect Dis. 2011 Jul 1; 204(1):154-63. doi: 10.1093/infdis/jir214.

[23] Generoso M, Álvarez P, Kravietz A, Mwamzuka M, Marshed F, Ahmed A, Khaitan A. High soluble CD163 levels correlate with disease progression and inflammation in kenyan children with perinatal hiv-infection.AIDS. 2019 Sep 26. doi: 10.1097/QAD.0000000000002378. [Epub ahead of print]

[24] Ticona E, Bull ME, Soria J, Tapia K, Legard J, Styrchak SM, Williams C, Mitchell C, La Rosa A, Rosa AL, Coombs RW, Frenkel LM.Biomarkers of inflammation in HIV-infected Peruvian men and women before and during suppressive antiretroviral therapy.AIDS. 2015 Aug 24; 29(13):1617-22. doi: 10.1097/QAD.0000000000000758. Erratum in: AIDS. 2015 Sep 24; 29(15):2065. Rosa, Alberto L A [corrected to La Rosa, Alberto].PMID: 26372272

[25] Knudsen TB, Ertner G, Petersen J, Møller HJ, Moestrup SK, Eugen-Olsen J, Kronborg G, Benfield T.Plasma Soluble CD163 Level Independently Predicts All-Cause Mortality in HIV-1-Infected Individuals.J Infect Dis. 2016 Oct 15;214(8):1198-204. doi: 10.1093/infdis/jiw263. Epub 2016 Jun 28.PMID: 2735436

[26] Borato DC1, Parabocz GC, Ribas SR, Kalva-Filho CA, Borba LM, Ito CA, Bail L, dos Santos FA, Vellosa JC. Changes of metabolic and inflammatory markers in HIV infection: glucose, lipids, serum Hs-CRP and myeloperoxidase.Metabolism. 2012 Oct;61(10):1353-60. doi: 10.1016/j.metabol.2012.03.003. Epub 2012 Apr 3.

[27] Muswe R , Oktedalen O , Zhou DT , Zinyando E , Shawarira-Bote S , Stray-Pedersen B , Siziba A , Gomo ZAR. Marqueurs inflammatoires et lipides plasmatiques chez les patients VIH : Une étude d'analyse de corrélation. Open Biochem J. 2017 28 déc. 11: 105-118. Doi: 10.2174 / 1874091X01711010105. eCollection 2017.

[28] Kozić Dokmanović S, Kolovrat K, Laškaj R, Jukić V, Vrkić N, Begovac J.Effect of Extra Virgin Olive Oil on Biomarkers of Inflammation in HIV-Infected Patients: A Randomized, Crossover, Controlled Clinical Trial.Med Sci Monit. 2015 Aug 16; 21:2406-13. doi: 10.12659/MSM.893881

[29] Hattab S, Guihot A, Guiguet M, Fourati S, Carcelain G, Caby F, Marcelin AG, Autran B, Costagliola D, Katlama C Comparative impact of antiretroviral drugs on markers of inflammation and immune activation during the first two years of effective therapy for HIV-1 infection: an observational study.BMC Infect Dis. 2014 Mar 4; 14:122. doi: 10.1186/1471-2334-14-122.

[30] NAOMI TUPPER, New Molecule from Olive Antioxidant Could Reduce HIV..https://www.oliveoiltimes.com › olive-oil-health-news. 23 juillet 2012

[31] Oluwamayowa Makinde,1 Kunle Rotimi, Victor Ikumawoyi, Titilope Adeyemo and Sunday Olayemi.Effect of vitamin A and vitamin C supplementation on oxidative stress in HIV and HIV-TB co-infection at Lagos University Teaching Hospital (LUTH) NigeriaAfr Health Sci. 2017 Jun; 17(2): 308–314.doi: 10.4314/ahs.v17i2.3PMCID: PMC5637014PMID: 29062324

[32] Suresh DR, Annam V, Pratibha K, Prasad BV.Total antioxidant capacity--a novel early bio-chemical marker of oxidative stress in HIV infected individuals.J Biomed Sci. 2009 Jul 7; 16:61. doi: 10.1186/1423-0127-16-61.

[33] Quaye O, Kuleape JA, Bonney EY, Puplampu P, Tagoe EA.Imbalance of antioxidant enzymes activities and trace elements levels in Ghanaian HIV-infected patients. PLoS One. 2019 Jul 24; 14(7):e0220181. doi: 10.1371/journal.pone.0220181. eCollection 2019.PMID: 31339937

[34] Look MP, Rockstroh JK, Rao GS, Kreuzer KA, Barton S, Lemoch H, Sudhop T, Hoch J, Stockinger K, Spengler U, Sauerbruch T Serum selenium, plasma glutathione (GSH) and erythrocyte glutathione peroxidase (GSH-Px)-levels in asymptomatic versus symptomatic human immunodeficiency virus-1 (HIV-1)-infection.Eur J Clin Nutr. 1997 Apr; 51(4):266-72.

[35] Ogunro PS1, Ogungbamigbe TO, Elemie PO, Egbewale BE, Adewole TA Plasma selenium concentration and glutathione peroxidase activity in HIV-1/AIDS infected patients: a correlation with the disease progression.Niger Postgrad Med J. 2006 Mar; 13(1):1-5.

[36] Watanabe LM, Barbosa Júnior F, Jordão AA, Navarro AM. Influence of HIV infection and the use of antiretroviral therapy on selenium and selenomethionine concentrations and antioxidant

protection.Nutrition. 2016 Nov-Dec; 32(11-12):1238-42. doi: 10.1016/j.nut.2016.03.024. Epub 2016 Apr 8.PMID: 27255831

[37] Shivakoti R1, Christian P2, Yang WT3, Gupte N4, Mwelase N5, Kanyama C6, Pillay S7, Samaneka W8, Santos B9, Poongulali S10, Tripathy S11, Riviere C12, Berendes S13, Lama JR14, Cardoso SW15, Sugandhavesa P16, Tang AM17, Semba RD18, Campbell TB19, Gupta A20; NWCS 319 and PEARLS Study TeamPrevalence and risk factors of micronutrient deficiencies pre- and post-antiretroviral therapy (ART) among a diverse multicountry cohort of HIV-infected adults.Clin Nutr. 2016 Feb; 35(1):183-9. doi: 10.1016/j.clnu.2015.02.002. Epub 2015 Feb 10.

[38] Stephensen CB, Marquis GS, Douglas SD, Kruzich LA, Wilson CM.Glutathione, glutathione peroxidase, and selenium status in HIV-positive and HIV-negative adolescents and young adults.Am J Clin Nutr. 2007 Jan; 85(1):173-81.

[39] Poudel KC, Bertone-Johnson ER, Poudel-Tandukar K. Serum Zinc Concentration and C - reactive protein in Individuals with Human Immunodeficiency Virus Infection: the Positive Living with HIV (POLH) Study.Biol Trace Elem Res. 2016 May; 171(1):63-70. doi: 10.1007/s12011-015-0520-3. Epub 2015 Oct

[40] Mburu AS, Thurnham DI, Mwaniki DL, Muniu EM, Alumasa FM The influence of inflammation on plasma zinc concentration in apparently healthy, HIV+ Kenyan adults and zinc responses after a multi-micronutrient supplement.Eur J Clin Nutr. 2010 May; 64(5):510-7. doi: 10.1038/ejcn.2010.33. Epub 2010 Mar 10

[41] Osuna-Padilla I1, Briceño O, Aguilar-Vargas A, Rodríguez-Moguel NC, Villazon-De la Rosa A, Pinto-Cardoso S, Flores-Murrieta FJ, Perichart-Perera O, Tolentino-Dolores M, Vargas-Infante Y, Reyes-Terán G.Zinc and selenium indicators and their relation to immunologic and metabolic parameters in male patients with human immunodeficiency virus.Nutrition. 2019 Sep 13; 70:110585. doi: 10.1016/j.nut.2019.110585.]

[42] Khalili H1, Soudbakhsh A, Hajiabdolbaghi M, Dashti-Khavidaki S, Poorzare A, Saeedi AA, Sharififar R. Nutritional status and serum zinc and selenium levels in Iranian HIV infected individuals.BMC Infect Dis. 2008 Dec 9; 8:165. doi: 10.1186/1471-2334-8-165.

[43] Marco ML, Heeney D, Binda S, Cifelli CJ, Cotter PD, Foligné B, Gänzle M, Kort R, Pasin G, Pihlanto A, Smid EJ, Hutkins R.Health benefits of fermented foods: microbiota and beyond.Curr Opin Biotechnol. 2017 Apr;44:94-102. doi: 10.1016/j.copbio.2016.11.010. Epub 2016 Dec 18.

[44] Lorea Baroja M1, Kirjavainen PV, Hekmat S, Reid G Anti-inflammatory effects of probiotic yogurt in inflammatory bowel disease patients.Clin Exp Immunol. 2007 Sep;149(3):470-9. Epub 2007 Jun 22.

[45] Serrano-Villar S, Vázquez-Castellanos JF, Vallejo A, Latorre A, Sainz T, Ferrando-Martínez S, Rojo D, Martínez-Botas J, Del Romero J, Madrid N1, Leal M, Mosele Jl, Motilva MJ, Barbas C, Ferrer M, Moya A, Moreno S, Gosalbes MJ, Estrada V.The effects of prebiotics on microbial dysbiosis, butyrate production and immunity in HIV-infected subjects.Mucosal Immunol. 2017 Sep;10(5):1279-1293. doi: 10.1038/mi.2016.122. Epub 2016 Dec 21.

[46] Lin PP, Hsieh YM, Kuo WW, Lin YM, Yeh YL, Lin CC, Tsai FJ, Tsai CH, Tsai CC, Huang CY.Suppression of TLR-4-related inflammatory pathway and anti-fibrosis effects of probiotic-fermented purple sweet potato yogurt in hearts of spontaneously hypertensive rats.Chin J Physiol. 2013 Jun 30;56(3):174-83.

[47] Marco Gobbetti Fabio Minervini Carlo G Rizzello. Angiotensin I-converting-enzyme-inhibitory and antimicrobial bioactive peptides. International journal of dairy technology.26 April 2004 https://doi.org/10.1111/j.1471-0307.2004.00139.x

[48] Fardet A, Rock E.In vitro and in vivo antioxidant potential of milks, yoghurts, fermented milks and cheeses: a narrative review of evidence.Nutr Res Rev. 2018 Jun;31(1):52-70. doi: 10.1017/S0954422417000191. Epub 2017 Oct 2.

[49] Alfredo Parrella Emanuela Caterino Margherita Cangiano Emma Criscuolo Chiara Russo Margherita Lavorgna Marina Isidori. Antioxidant properties of different milk fermented with lactic acid bacteria and yeast. International Journal of food science and technology.13 August 2012 https://doi.org/10.1111/j.1365-2621.2012.03127.x

[50] Solieri L, Rutella GS, Tagliazucchi D.Impact of non-starter lactobacilli on release of peptides with angiotensin-converting enzyme inhibitory and antioxidant activities during bovine milk fermentation.Food Microbiol. 2015 Oct; 51:108-16. doi: 10.1016/j.fm.2015.05.012. Epub 2015 May 27.

[51] Virtanen T1, Pihlanto A, Akkanen S, Korhonen H.Development of antioxidant activity in milk whey during fermentation with lactic acid bacteria.J Appl Microbiol. 2007 Jan; 102(1):106-15.

[52] Gagnon M, Savard P, Rivière A, LaPointe G, Roy D. Bioaccessible antioxidants in milk fermented by Bifidobacterium longum subsp. longum strains.Biomed Res Int. 2015; 2015:169381. doi: 10.1155/2015/169381. Epub 2015 Feb 23.

[53] Nikola Gjorgievski, Juliana Tomovska, Gordana Dimitrovska, Borce Makarijoski, Mohammad Ali Shariati .Determination of the antioxidant activity in yogurt.Journal of Hygienic Engineering and Design 8, 88-92. 2014