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Role of Dietary Antioxidants in the Management of Human Immunodeficiency Virus

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ABSTRACT

Acquired Immunodeficiency Syndrome (AIDS) caused by Human Immunodeficiency Virus (HIV) is currently the sixth-biggest cause of death world-wide, accounting for 2.9%. There is also increased hidden hunger among the AIDS patients and a high percentage with unsuppressed viral load despite the various interventions put in place to suppress the virus. Dietary antioxidants including Vitamin A, Vitamin C, Vitamin E, Vitamin K, Zinc and selenium have recently received significant attention as therapeutic agents for the treatment of several immune compromised conditions. This is attributed to their ability to scavenging excess Reactive Oxygen Species (ROS) to maintain normal physiological conditions. This study therefore, seek to find out if dietary antioxidants could be used along with ARVs to suppress HIV viral load. Two scientific databases (PubMed, Scopus) were searched between 1st – 28th February, 2021 using Dietary antioxidants, HIV and AIDS as the key words. Articles published in highly refereed and peer reviewed journals were selected. In total 15 articles were retrieved however, 7 Articles were rejected since they did not discuss the dietary antioxidant in relation to treatment of HIV, or statistical analysis used were not suitable, or the article was a review of other publications. The articles reviewed indicated that AIDS patients have a deficiency of micronutrients contributing to hidden hunger and supplementation of the micronutrients contributes to reduced morbidity and mortality among the patients. Studies indicate that Vitamin A, Vitamin E and zinc are important dietary antioxidants in boosting immunity. In conclusion, Dietary antioxidants are a safe and effective way to scale down morbidity and mortality related to AIDs and therefore, they should be given a significant consideration as a potential strategy for suppressing the viral load alongside antiretroviral therapy.

Keywords: Dietary antioxidants, HIV, AIDS

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I. INTRODUCTION

Human Immunodeficiency Virus (HIV) was first documented in 1981, when the first cases of a typical skin lesions and an aggressive disease of Kaposi's sarcoma appeared in homosexual men (Hymes et al., 1981). In a period of twenty years, HIV became a global epidemic; approximate 20 million people died, and an additional 36 million people were living with the virus with a large majority of those infected living in non-industrialized countries with inadequate financial support to handle the pandemic (Gayle & Hill, 2001). Global Health Estimates show that HIV and AIDS is currently the sixth-biggest cause of death world-wide, accounting for 2.9% (WHO, 2015). Sub-Saharan Africa carries a disproportionate burden of HIV, accounting for more than 70% of the global burden of infection thus the success in HIV management and prevention in sub-Saharan Africa has the potential to impact on the global burden of HIV (Kharsany & Karim, 2016).

The standard of care in HIV/AIDS management requires the suppression of HIV viral load and currently the treatment is by use of antiretroviral therapy (ART) (MOH (NASCOP), 2011). In Kenya, ART treatment is currently at 74% with a viral suppression of 68% of all people living with HIV (UNAIDS, 2020). Other interventions in the management of HIV include Fortified Blended Flours (FBF), Ready to Use Supplementary Foods (RUSF) and Ready to Use Therapeutic Foods (RUTF) (Kenya Ministry of Health, 2014). However, these nutrition supplements aid in weight gain but not necessarily suppressing viral load (Mallewa et al., 2018). Regardless of all these interventions, HIV/AIDS prevalence is still rising in Kenya with increased hidden hunger as well as a high percentage of patients with unsuppressed viral load. If left unattended, HIV/AIDS has potential to upsurge morbidity and mortality rate fourteen (14) times higher than that of HIV/AIDS free persons of the same sex and age group (Aldaz et al., 2011). This situation accentuates the need to map out other alternatives including dietary antioxidants as an effective way to suppress viral load among patients.

Dietary antioxidants including Vitamin A, Vitamin C, Vitamin E, Vitamin K, Zinc and selenium have recently received significant attention in boosting the body immunity. This is attributed to the fact that the immune system is highly reliant on accurate cell-cell communication for optimal function, and any damage to the signaling systems involved will result in an impaired immune responsiveness. This signaling is usually affected by the reactive oxygen species which the body produce as part of its defense against infection. Therefore, adequate amount of neutralizing antioxidants are required to prevent damage to the immune cells. Numerous epidemiological studies have found strong associations between diets rich in antioxidant nutrients and a reduced incidence of cancer, and other chronic diseases. Although more striking effects of antioxidants have been observed in other chronic conditions, there is also evidence that oxidative stress has been observed in HIV pathology. It might therefore, be essential to have an adequate intake of antioxidant nutrients in order to help prevent the pathogenesis of HIV. Therefore, this review was to establish if dietary antioxidants could be used in suppressing HIV viral load.

II. METHODS

Published materials which covered supplementation of the following dietary antioxidants; vitamin A, Vitamin C, Vitamin E, Zinc and selenium were searched on two scientific databases (PubMed & Scopus) and gathered from 1st – 28th February 2021. Articles were reviewed to establish whether there is any significant association between the micronutrient supplementation and Health of HIV patients. Literature search was done using the following key words; 'Vitamin A and HIV', 'Vitamin C and CD4 count', 'Vitamin E and HIV viral load', 'Zinc supplementation and HIV', 'Selenium supplementation and HIV', and 'Dietary antioxidants and HIV'. Eligibility criteria included English language; articles published in peer- reviewed journals with preference given to articles published in the last 10 years. From the search criteria, 16 articles were retrieved and screened using the study selection criteria to ensure they were relevant to the study.

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However, 7 Articles were rejected since they did not discuss the dietary antioxidant in relation to treatment of HIV, or statistical analysis used were not suitable, or the article was a review of other publications. Consequently, nine (9) publications met the article selection criteria and were synthesized to provide this reviews' findings.

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III. RESULTS

Table 1 shows key information obtained from the studies that were reviewed. This included; the title of the article, Findings and the reference

S.No	Title	Study Group	Findings	Reference
1.	Lipid-soluble vitamins A, D, and E in HIV-infected pregnant women in Tanzania	1078 HIV-infected pregnant women	- Maternal vitamin A deficiency in HIV/AIDS-infected women has been shown to increase risks of maternal morbidity and mortality - low serum vitamin A levels have an increased risk of mother-to child transmission	(Mehta et al., 2010)
2.	Analysis of serum and supplemented vitamin C and oxidative stress in HIV-infected children and adolescents	54 children and adolescents	HIV-infected individuals experience low levels of vitamin C associated with an increase in oxidative stress, which is evidenced by increased C-Reactive Protein	(De Oliveira et al., 2011)
3.	Effect of vitamin A and vitamin C supplementation on oxidative stress in HIV and HIV-TB co-infection at Lagos University Teaching Hospital (LUTH) Nigeria	40 HIV/TB co-infected and 50 HIV mono-infected patients	Vitamin C and A supplementation have no role on oxidative stress indices in HIV mono-infected and HIV-TB co-infected patients	(Makinde et al., 2017)
4.	Effects of vitamin E and C supplementation on oxidative stress and viral load in HIV-infected subjects	Forty-nine HIV-positive patients	Supplements of vitamin E and C reduce oxidative stress in HIV and produce a trend towards a reduction in viral load.	(Allard et al., 1998)
5.	Vitamin E concentrations in adults with HIV/AIDS on highly active antiretroviral therapy	182 HIV-infected men and women ranging in age from 20 to 59 years and with CD4 T lymphocyte counts ≥200 cells/mm3	HIV/AIDS patients will probably benefit from vitamin E supplementation	(Kaio et al., 2014)
6.	Effect of Haart on Vitamin E Level of HIV Seropositive Women in Nigeria	100 seropositive and 50 seronegative women	Vitamin E plays a very vital role in the maintenance of the immune system and slows down progression to AIDS in HIV-infected patients	(Okungbowa & Odjadjare, 2016)
7.	Brief Report: Zinc supplementation and Inflammation in Treated HIV	52 participants	zinc supplementation is effective in impacting a biological signature in People Living with HIV and modulating biomarkers associated with clinical comorbidities	(Dirajlal-Fargo et al., 2019)
8.	Randomized, controlled clinical trial of zinc supplementation to prevent immunological failure in HIV-infected adults	231 HIV-infected adults	zinc supple- mentation can be used as an adjunct therapy for HIV-infected adult cohorts with poor viral control	(Baum et al., 2010)
9.	Role and effects of zinc supplementation in HIV-infected patients with immunovirological	80 patients	- Zinc supplementation in immune-virological discordance (IVD) patients has no significant difference in CD4 levels	(Silva et al., 2021)

	discordance: A randomized, double blind, case control study		- Zinc supplementation would be more effective on patients with successful immune recovery.	

IV. DISCUSSION

Success in HIV management and prevention has the potential to impact on the global burden of mortality and in comorbidities related to HIV infection. Currently the treatment or suppression of HIV viral load is by use of antiretroviral therapy (ART). However, studies have attributed dietary interventions including use of dietary antioxidants as a way of scaling up suppression of viral load and reducing adverse side effects associated with HIV and ART (Kalebic et al., 1991; Kashou & Agarwal, 2011) thus improving the life of people living with HIV. According to Kaio et al. HIV/AIDS patients will probably benefit from vitamin E supplementation (Kaio et al., 2014) since HIV+ patients experience Vitamin E deficiency and an increased oxidative stress (Dror & Allen, 2011; Kaio et al., 2014; S. Mehta et al., 2010; Saeidnia & Abdollahi, 2014). Vitamin E is a lipid-soluble vitamin with antioxidant properties. This study is in agreement with studies by Saeidnia & Abdollahi, 2014 and Okungbowa & Odjadjare, 2016 who documented that Vitamin E can prevent lipid peroxidation and also decrease free radicals which result in oxidative stress and also play a very vital role in the maintenance of the immune system thus slow down progression to AIDS in HIV infected patients (Okungbowa & Odjadjare, 2016; Saeidnia & Abdollahi, 2014). This set of finding is strong enough to warrant use of Vitamin E supplementation along with ART treatment in the management of HIV/AIDs**.**

Vitamin A another fat-soluble compound involved in several physiological pathways connected to several disease causes, is associated with enhancement of both innate and adaptive immune responses and its metabolites are key regulators of epithelial cell differentiation and growth therefore critical in promoting epithelial tissue integrity hence helping to reduce cases of diarrhea among the HIV Positive patients (Ponton & Morimoto, 2019). Studies have demonstrated that vitamin A is essential for proper development and differentiation of colonic $CD169_+$ macrophages which is important for immunity against HIV (Huang et al., 2018; Kim et al., 2015). However, Vitamin A deficiency is common among HIV+ patients (Obuseh et al., 2011). A study by Mauricio in 2019 document that a significant proportion of HIV-1 infected individuals have vitamin A deficiency, which have been associated with lower CD4+ cell counts, increased maternal-fetal transmission, increased mortality from AIDS or infections, and increased risk of progression to AIDS (Mauricio, 2019). This study is in line with S. Mehta et al., 2010 who also documented that most HIV-related deaths and growth failure cases in HIV infected children have been found to be associated with vitamin A deficiency (S. Mehta et al., 2010). In addition, Saurabh Mehta & Fawzi, 2007 observed that Vitamin A therapy in HIV infected children has protective effects against morbidity and mortality by lowering respiratory tract infection and severe diarrhea (Saurabh Mehta & Fawzi, 2007). Other several studies on HIV-infected pregnant women have displayed low serum vitamin A levels with an increased risk of mother-to child transmission (MTCT) (Cs et al., 2011; Justine et al., 2018; S. Mehta et al., 2010). Vitamin A is therefore, essential in immune response of macrophages, which are one of the first cells at the onset of HIV-infection.

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Vitamin A deficiency may thus directly or indirectly, be responsible for the depletion of a large number of CD4+ T-cells and disease progression. Therefore, these observations require further studies to elucidate the pharmacokinetics and pathogenesis of how vitamin A deprivation causes immunodeficiency in HIV-infected patients.

Studies have also shown Vitamin C, a water soluble antioxidant protects the body from free radical damage and boost immune response as well suppress the HIV replication via inhibiting reverse transcriptase activity (Jamshidi-Kia et al., 2020; Saeidnia & Abdollahi, 2014). Supplementation of vitamin C play a key role since HIV-infected individuals experience low levels of vitamin C associated with an increase in oxidative stress, which is evidenced by increased C-Reactive Protein (De Oliveira et al., 2011). Contrarily to these findings, a study by Makinde et al., 2017 gave contradicting findings on the impact of vitamin C and other exogenous anti-oxidant supplementation on controlling oxidative stress in HIV/TB co-infection and HIV mono-infection. The findings showed that there was no beneficial roles in positively modulating the associated oxidative stress (Makinde et al., 2017). However, this study was run for a period of 1 month supplementation and the study did not indicate the treatment phase of the participants. These contradicting findings call for further studies on long-term prospective cohort studies to monitor efficacy of vitamin C in HIV/AIDS patients since the beginning of treatment.

Other dietary antioxidants that play critical role in HIV progression include zinc and selenium. They are essential trace element which play a critical role for immune system and deficiency of these elements affects multiple aspects of innate and adaptive immunity leading to increased susceptibility to infections (Haase & Rink, 2009; Nunnari et al., 2012). Recent studies found out that zinc supplementation was effective in impacting a biological signature in People Living with HIV and modulating biomarkers associated with clinical comorbidities (Baum et al., 2010; Dirajlal-Fargo et al., 2019; Mda et al., 2010). Studies have as well shown that patients living with HIV, have extensively reported zinc and selenium deficiency before and after the introduction of ART which is associated with an increased risk of mortality (Mburu et al., 2010; Nunnari et al., 2012; Saeidnia & Abdollahi, 2014; Sheehan et al., 2012). A study by Silva et al., 2021, demonstrated that Zinc supplementation in immune-virological discordance (IVD) patients showed a statistically non-significant difference in in CD4 levels between cases and controls(Silva et al., 2021). This could mean that zinc supplementation in the diet of HIV infected individuals would be more effective on patients with successful immune recovery.

V. CONCLUSION

Dietary antioxidants which play a critical role in scavenging excess Reactive Oxygen Species (ROS) to maintain normal physiological conditions should be given significant consideration as a potential component in the management of HIV/AIDS alongside antiretroviral therapy.

VI. RECOMENDATIONS

A dietary therapeutic feed from locally available foods should be formulated/considered as a nutrition intervention as it can provide a sustainable, accessible and cost-effective method in the management of HIV/AIDS. However, Future studies should be undertaken to determine the correct dosages and duration of antioxidant treatment necessary to slow down the progression of HIV/AIDS infection.

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