

Systematic Review

Effectiveness of nutritional intervention on immunity among people living with HIV/AIDS: a systematic review

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Received: 08 June 2024

Revised: 21 September 2024

Accepted: 23 September 2024

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ABSTRACT

A huge progress is made in the treatment modality of human immunodeficiency virus and acquired immunodeficiency syndrome (HIV/AIDS). To develop cure or enhance immunity of people living with HIV/AIDS (PLHIV), major researches are being conducted across the globe. Nutritional interventions are experimented widely over a period of time in improving immunity among PLHIV but concrete evidence in this regard is doubted still. This study aimed to assess the effectiveness of selected nutritional interventions (zinc) on immunity among PLHIV. The search methods and selection criteria include randomized controlled trial on nutritional interventions, specifically; effect of zinc on immune status of PLHIV was conducted. An extensive search from databases like ProQuest, PubMed, Cochrane and Science Direct was conducted from 28/04/2022 to 28/05/2022, a total of 05 studies were included after screening with PEDro scale and preferred reporting items for systematic reviews and meta-analyses (PRISMA) reporting to derive at a consensus on effect of zinc on immune status of PLHIV. Three reviewers independently screened and selected the trials for inclusion. The cumulative sample size from all the studies was 1329. As studies included were diverse meta-analysis was not possible. Four studies revealed that zinc supplementation was not effective in enhancing immune system of PLHIV whereas another 1 study showed that zinc supplementation is effective in boosting immune level among PLHIV. Zinc supplementation is beneficial and safe among PLHIV as it boosts immunity but further investigation is needed to generalize the findings.

Keywords: HIV, AIDS, PLHIV, Zinc, Immunity, CD4 cell count, Nutrition

INTRODUCTION

A huge progress is made in the treatment modality of HIV/AIDS. Initially, in 1980s when this global pandemic appeared on the face of the world, it had no answer to it but today we are having life saving drugs to control this syndrome.¹

Now is the time to take a step further by treating it completely as curable disease or preventable syndrome by the means of apt health interventions. In this regard, major attempts and researches are being conducted across the globe. Nutritional interventions are also experimented

widely over a period of time in improving immune status among PLHIV but concrete evidence in this regard is doubted still. Nutritional factors play an important role in enhancing immunity and their deficiency had contributed towards compromised immunity in the PLHIV and in particularly with zinc.²

Zinc being a trace element is still an immune booster. The most effective way to deal with HIV/AIDS is by complementing anti-retroviral therapy with zinc. In this regard to investigate the effectiveness of zinc, this study was conducted.³

METHODS

The objective of the study was to assess the effectiveness

of selected nutritional intervention (zinc) on immunity among PLHIV. Following is the population, intervention, comparison and outcome (PICO) description.

Table 1: PICO description.

Population	Intervention	Comparison	Outcome
PLHIV	Nutritional intervention	Standard care/usual care/routine care/placebo	Primary: Immunity Secondary: Viral load, CD ₄ cell count, serum zinc level, mortality, morbidity and nutritional status

Criteria for selection of studies

The literature search and review were conducted from 28/04/2022 to 28/05/2022 and PEDro scale was used to determine the quality of the study. Following are details.

Table 2: Criteria for selection of studies.

Particular	Description
Types of studies	This review considered any randomized control trial (RCT) that evaluates the effectiveness of nutritional intervention (zinc) on immunity among PLHIV.
Types of participants	The study included all the studies in which the PLHIV who received any nutritional intervention in their therapy.
Types of interventions	The study included all the studies in which the following interventions were mentioned-nutrients, micro nutrients, trace elements, diet therapy, zinc, minerals, nutrition therapy, nutritional support, nutritional counselling
Outcome measures: measure and time	The outcome constitutes following aspects- Primary outcome: Immune status Secondary outcome: Viral load, CD ₄ Cell count, serum zinc level, mortality, morbidity and opportunistic infection

Search methods for identification of studies

An extensive search was carried out, the most was from the electronic data base, and the various search strategies were adapted which included: Online databases like PubMed central, Science Direct and ProQuest. The Cochrane library-Cochrane database of systematic reviews and Cochrane central register of controlled trials (central).

The search strategy included the key words and the mesh terms related to PICO of the intended work, like- "Humans" "viruses" "HIV", "retroviridae"

"HIVinfections""sexually transmitted diseases", "communicable diseases" "acquired immunodeficiency syndrome" "sarcoma, kaposi", "muscular atrophy" "HIV wasting syndrome" "nutrients", "micro nutrients" "trace elements" "minerals", "zinc" "nutritional support" "nutrition therapy", "diet therapy" "nutritional status" "nutritional sciences", "immunity" "immune system" "antigens", "HIV antibodies" "cd4-positive t-lymphocytes" viral load" and "adaptive immunity "immunity, humoral."

All the acquired studies through this search were subjected to quality check by using PEDro scale in an intention to identify potential studies that could be considered for inclusion. PEDro scale included 11 items (yes/no). a score on PEDro scale <4 was considered to be weak, 5-6 was considered to be fair, 6-8 was considered as good and 08-10 was considered as optimal Out of 213 studies only 06 manuscripts were taken for recommendation as per the inclusion criteria.⁵

The details of PRISMA are given below.⁶

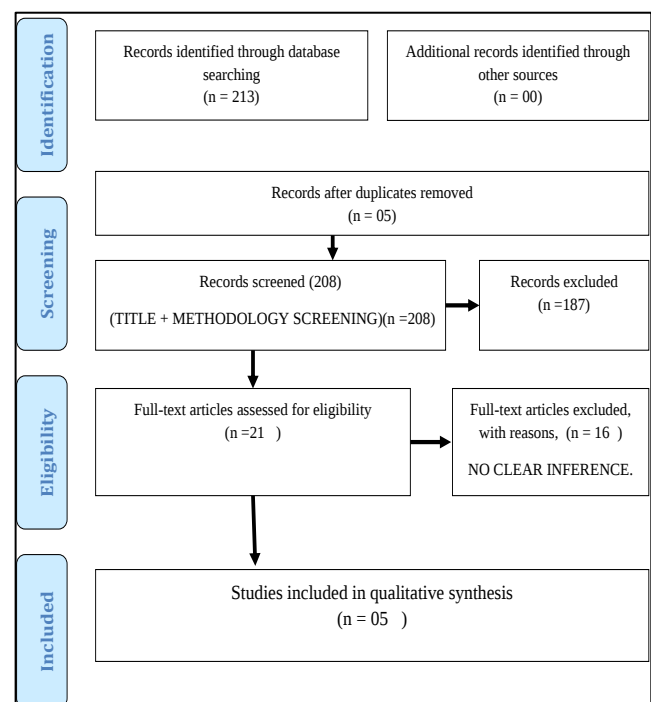


Figure 1: Prisma flow diagram.

Table 3: Studies included in this systematic review.

Name of author	Title of study	Journal name and year of public	Sample size and setting	Interventions		Outcome		Results
				Expt group	Ctrl group	Primary	Secondary	
Freiberg et al⁷	Effect of zinc supplementation vs placebo on mortality risk and HIV disease progression among HIV-positive adults with heavy alcohol use: a randomized clinical trial	JAMA network open	254 and St Petersburg, Russia	Pharmacy-grade zinc gluconate supplementation (15 mg for men and 12 mg for women, taken daily by mouth for 18 months).	Placebo	The zinc trial's primary outcome was a change in VACS index score	secondary outcomes: (1) CVD risk (2) HIV disease progression (3) biomarker levels of inflammation	Zinc supplementation did not reduce mortality risk, CD4 cell counts, CVD risk, and levels of inflammation or microbial translocation in people with heavy alcohol use who are living with HIV/AIDS.
Dirajlal et al⁸	Zinc supplementation and inflammation in treated HIV	Journal of acquire immune deficiency syndrome, 2019	52 and rainbow babies and children hospital	Zinc capsules 45 mg low dose 90 mg high dose daily for 16 weeks.	Placebo	Novel findings that zinc can affect biological marker in PLHIV and modulate clinical markers in comorbidities	Zinc is effective in increasing circulating zinc levels	Zinc is effective in increasing immunity levels of PLHIV.
Ndeezi et al⁹	Effect of multiple micronutrient supplementation on survival of HIV-infected children in Uganda: a randomized, controlled trial	Journal of the international AIDS society, 2010	847 and the pediatric HIV clinics of the national referral hospital (Mulago)	14 micronutrients as the intervention arm (vitamins A, B1, B2, niacin, B6, B12, C, D and E, folate, zinc, copper, iodine and selenium);	Standard recommended dietary allowance of 6 multi vitamins (A, D2, B1, B2, C and niacin)	Twice recommended dietary allowance of 14 micronutrients compared	A standard recommended dietary allowance of six	Multivitamins and micro nutrients for 6 months was well tolerated, but it did not significantly alter mortality, growth or CD4 counts. Future intervention studies should carefully consider: composition and dosing of supplements.
Silva et al¹⁰	Role and effects of zinc supplementation in HIV-infected patients with immune virological discordance: A randomized, double blind, case control study	PLoS One, 2021	80 and university of Chile school of medicine	Patients with IVD were randomized to receive zinc (15 mg daily)	Placebo.	Within group of immune recovery of patients with hypo zincemia was analyzed and compared to those with normozincemia; no statistical difference identified	-	Patients with IVD have plasma zinc levels similar to those who achieve adequate immune recovery. Zinc supplementation in IVD patients showed a statistically non-significant difference in CD4 levels between cases and controls.
Raziya et al¹¹	Safety and efficacy of zinc supplementation for children with HIV-1 infection in south Africa-a randomized double blind placebo-controlled trial.	The Lancet	96 and Grey's Hospital in Pietermaritzburg, South Africa.	10 mg of elemental zinc among PLHIV	Placebo	Plasma HIV-1 viral load.	-	Zinc supplementation of HIV-1-infected children does not result in an increase in plasma HIV-1 viral load and could reduce morbidity caused by diarrhoea.

Method of data collection and analysis

The titles and abstracts of the acquired studies were reviewed by the authors. The relevance to the topic was determined; all the related articles were subjected to full text review by the author. On review of full text, the author decided either to include or not to include the study based on inclusion and exclusion criteria.

Inclusion criteria

RCTs on nutritional intervention(zinc) for improving immunity among PLHIV were included.

Exclusion criteria

Pre experimental studies on nutritional interventions for improving immunity among PLHIV, case reports on nutritional interventions for improving immunity among PLHIV. Other non-experimental or qualitative studies on nutritional interventions for improving immunity among PLHIV were excluded.

RESULTS

In the Table 3 finding of the study shows that out of 5 studies 4 studies revealed that zinc supplementation was not effective in enhancing immune system of PLHIV whereas another 1 study showed that zinc supplementation is effective in boosting immune level among PLHIV.

DISCUSSION

In communities with high incidence and prevalence of HIV/AIDS, the mortality and morbidity rate can be seen on high. Anti-retroviral therapy (ART) is found to be effective in bringing down the mortality rate among PLHIV. In combination to ART, a complementary nutrient therapy like administration of micro nutrients and macro nutrients to avoid muscle wasting and strengthen immune system can significantly contribute to elevate the effectiveness of ART. In addition, zinc supplementation, in minimal volume for a longer period of time may improve the immune status in patients with HIV/AIDS.¹²⁻¹⁵

Zinc, despite being a trace element plays a central role in immune system and zinc deficient person has increased susceptibility to pathogens/infections. The immune function of zinc starts with skin barrier and ends up to activation of T-Lymphocytes. It is essential for development and functioning of cells mediating nonspecific immunity like neutrophils. This review explored the biology of zinc in relation to immune system and takes a step further to provided basis to draw a consensus on credibility of immune system in zinc deficiency or zinc supplementation.¹⁶

Our review identified various studies RCTs and other than a RCT those contributed to the evidence base supporting the effectiveness of zinc in enhancing the immunity of and individual but only RCTs were included in this study to maintain homogeneity. Few RCTs showed no conclusive evidence of effectiveness of zinc in enhancing the immunity.¹⁷⁻¹⁹

Therefore, to further explore, we need to investigate effectiveness of zinc in relation to minimum dose and maximum duration. Given the features of zinc, it is indispensable to explore as it is cost effective, minimum side effects and huge upside potential.^{20,21}

CONCLUSION

Zinc appears to have a promising property in complementing and strengthening the ART in treatment of HIV/AIDS. The challenge to the scientific community is that it has to be rigorously tested over a large sample size to generalize the finding.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: John S, Natekar DS. Effectiveness of nutritional intervention on immunity among people living with HIV/AIDS: a systematic review. *Int J Community Med Public Health* 2024;11:4050-4.