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Research Article

CD4 CORRELATION WITHMICRONUTRIENT DEFICIENCY AMONG HIV PATIENTS – A CROSS SECTIONAL STUDY

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A B S T R A C T

Background: The ill effects of malnutrition like disease progression, increased morbidity and reduced survival have been well documented among HIV patients. However, the exact pattern of malnutrition or the individual micronutrient deficiencies responsible for clinical worsening have not been elucidated in much detail earlier.
Aim: To study the pattern of micronutrient deficiency among HIV patients and find out possible correlation with disease progression.
Methods: Cross Sectional study of 144 HIV positive cases with a recently done CD4 count. After getting informed consent, venous sample was collected for estimation of micro & macronutrients in fully automated analyzer. Statistical Analysis Plan: Student independent 't'test using SPSS software11.5
Result: A total of 144 PLHIV were recruited. The CD4 count ranged from 62 to 1564 [mean 502.2]. Only 3 parameters showed significant decrease correlating well with CD4 counts. These included Serum magnesium 1.44 ± 0.60[Mean± SD], Serum Zinc 53.5± 15.4[Mean± SD] andBMI 21.78± 3.41 [Mean± SD]. The Body Mass Index [BMI],serum magnesium and zinc weresignificantly low in advanced disease than in those with CD4 counts >500 [p <0.05].
Conclusion: Malnutrition is a forerunner of disease progression in PLHIV. Our study identified the micronutrient deficiencies which hallmark disease worsening. Lowering of BMI, low Serum Magnesium and Zinc levels significantly predict a downhill course and can be used as potential markers and therapeutic targets to arrest the relentless progression of HIV.

INTRODUCTION

According to WHO 2017 Global Epidemic data totally 36.7 million people are infected by HIV. Every year about 1.8 million people are newly diagnosed as HIV positive. UNAIDS 2017 data portrays the Indian scenario as 2.1 million people living with HIV, 80,000 newly diagnosed cases and 62,000 deaths because of HIV, annually[1].

HIV is a retrovirus, but differs from other retroviruses such as human T cell lymphotrophic (HTLV) 1 and 2 in that the reverse transcriptase of HIV is highly error prone[2]. HIV is transmitted sexually, in blood or blood products and pre-natally. Those most at risk of acquiring HIV infection are homosexuals, injecting drug misusers and those with bisexual orientation. Others include individuals receiving unscreened blood or blood products and infants born of infected women [2].

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HIV in humans originated from cross-species infections by simian viruses in rural Africa, probably due to direct human contact with infected primate blood [3].

Course of Disease

The duration between primary infection and progression to clinical disease averages about 10 years[2]. An immune response to HIV occurs 1 week to 3 months after infection, thereafter plasma viremia drops, and level of CD4 cells rebound[4]. However, the immune response is unable to clear the infection completely and HIV-infected cells persist in the lymph nodes and reticuloendothelial system[4].

Three main body systems usually affected by AIDS are the respiratory system, the gastrointestinal tract and the central nervous system. Most of these conditions are due to the reactivation of latent organisms in the patient or exposure to the numerous microbial flora in the environment. The overall management of AIDS involves the continuous monitoring and treatment of these conditions with drugs that may cause some serious adverse effects[5]. The CD4 T lymphocytes are major targets responsible for virus production, which appears to have

similar high turnover rates, it is estimated that every nucleotide of the HIV genome probably mutates on a daily basis[3]. HIV infection has been associated with renal disease which is characterized by nephrotic range proteinuria (>3.5 g/dl), azotaemia, hypoabluminaemia and occasionally hypocalcemia[4-6]. HIV patients are at a higher risk for hypercalcemia, however a few cases of hypocalcemia may be due to hypoalbunemia[7]. It was reported that these trace elements of interest, when they are reduced, could lead to malabsorption of the intestinal mucosa and osteomalacia[7]. Osteomalacious patients' laboratory abnormalities showed low calcium and phosphorus levels [7].

PLHA patients are prone for micronutrient deficiency due to many reasons. Some of them are given below:

- Chronic gastroenteritis, alteration in gut barrier function.
- Inflammatory mediators will reduce the appetite
- Nausea,vomiting,diarrhoea secondary to ART ,HIV infection
- Increased resting metabolic rate.
- Poor socioecnomic status
- Psychosocial problem

Thus, the aim of this study is to investigate the correlation of these trace elements such as Calcium, Magnesium and Phosphorus in relation to the level of viral replication and other metabolic process in human. We also aimed to determine their clinical significance with regards to possible reduction of the circulating CD4T lymphocytes counts in HIV/AIDS patients,

MATERIAL AND METHODS

Inclusion Criteria

All patients of age >18, whotested positive for HIV as per NACO guidelines

Exclusion criteria

- HIV indeterminate.
- PLHIV patients on oral and/or parenteral nutritional support.

Study Design

This is a Cross Sectional study done between July 2016 and May 2017 in theDept of Biochemistry & Department of Internal Medicine (ART centre) at Govt .Theni Medical College, Theni,Tamilnadu. A total of144 patients were selected for the study. After getting written, informed consent patients were included into the study. Patients were subjected to a detailed clinical examination including anthropometric measurements. Special focus was directed towards nutritional assessment.5 ml of venous sample was collected, which was used for estimation of micronutrients in fully automated analyzer.

Statistical analysis

Since the data follow a normal distribution, Pearson's Correlation Coefficient was used to test the correlation between CD4 count and other variables.p value <0.05 was considered as statistically significant. Software used is SPSS version 20.

RESULTS

A total of 144 PLHIV were recruited. The CD4 count ranged from 62 to 1564 [mean 502.2]. A total of 8 parameters were assessed which included Serum Calcium[8.75+/-0.89], Serum Magnesium[1.44+/-0.60], Serum Copper[146.7+/- 33.5], Total proteins[7.23+/-0.69], Serum Albumin[4.11+/-0.45], Serum Zinc[53.5+/-15.4], Serum Iron[91.2+/-30.4], Serum Phosphate[4.89+/-1.08] and BMI[21.78+/-3.41] [Table 1 &2].

Table 1 Descriptive statistics of Anthropometric measurements (N=144)

Measures	Weight (kg)	Height(cms)	BMI(Kg/m^2)
Mean	53.71	156.9	21.78
SD	9.95	11.16	3.41
Range	19 - 85	108 - 183	13.67 - 30.18

Table 2 Descriptive statistics of Biochemical parameters (N=144).

Measures	CD4 count	Total Protein (g/dL)	Total Albumin (mg/dl)	Serum Mg (mg/dl)	Serum Fe (mg/dl)	Serum Cu (mg/dl)	Serum Zn (mg/dl)	Serum Ca (mg/dl)	Serum PO_4 (mg/dl)
Mean	502.2	7.23	4.11	1.44	91.2	146.7	53.5	8.75	4.89
SD	243.6	0.69	0.45	0.60	30.4	33.5	15.4	0.89	1.08
Range	62 - 1564	5.8 -8.5	3.0 -5.2	0.75 - 3.93	43.7 - 167.0	64.1 - 226.0	15.25 - 104.1	7.2 - 11.0	2.5 -7.3

Only 3 parameters showed significant decrease correlating well with CD4 counts. These included Serum magnesium 1.44 ± 0.60[Mean± SD], Serum Zinc 53.5± 15.4[Mean± SD] andBMI 21.78± 3.41 [Mean± SD]. The Body Mass Index [BMI],serum magnesium and zinc weresignificantly low in advanced disease than in those with CD4 counts >500 [p <0.05].

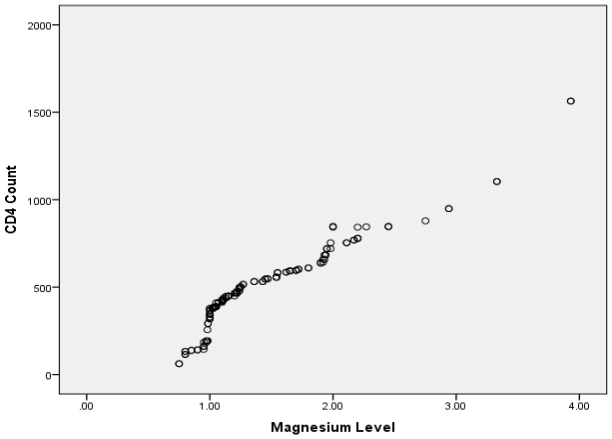

Figure 1 Scatter Diagram showing Correlation between CD4 count and Serum Magnesium

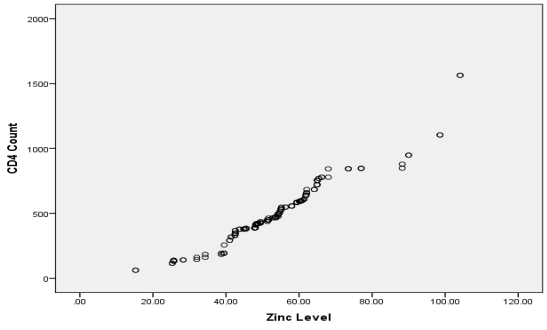

Figure 2 Scatter Diagram showing Correlation between CD4 count and Serum Zinc

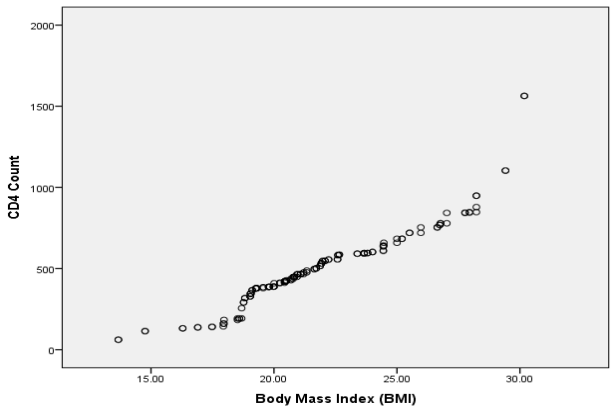

Figure 3 Scatter Diagram showing Correlation between CD4 count and BMI

DISCUSSION

It is interesting to note that an association between acute phase response to infection and alteration in dynamics of many trace elements, particularly iron, zinc and copper, has been recognized for many decades[9](Scrimshaw *et al*., 1968). The fall in serum iron and zinc, and rise in serum copper, are brought about by changes in the concentration of specific tissue proteins such as C-reactive protein (CRP) that are controlled by cytokines .10 The role of micronutrients is crucial in protein synthesis, cell growth, reproduction via DNA, RNA syn (Po4,Zn,Mg), bone formation, vasomotor tone, blood pressure(Ca, K), hormone secretion (thyroid, insulin) (Zn, Mg, I), maintenance of Vitamins function (Zn,Fe,Po4,Co) and the immunologicsystem (Zn, Mg).Calcium has critical roles in intracellular signalling at the plasma membrane and control of function of extra cellular proteins, such as those in the coagulation cascade[8]. The aim of this study was to investigate the correlation of these trace elements such as Calcium, Magnesium and Phosphorus in relation to the level of viral replication and other metabolic process in human. We also aimed to determine their clinical significance with regards to possible reduction of the circulating CD4T lymphocytes counts which had a positive correlation with HIV disease progression in HIV/AIDS patients. In our study the calcium levels were not significantly altered among PLHIV and there was no correlation with CD4 counts.

Magnesium is a cofactor for more than 300 enzymes, required for enzyme substrate formation (e.g. ATP) and an allosteric activator of many enzymes. Reducing the serum magnesium concentration results in increased neuromuscular excitability because magnesium comparatively inhibits the entry of calcium into neurons[8]. We found in our research that serum Magnesium levels were significantly reduced [1.44 ± 0.60[Mean± SD], among patients whose CD4 counts were on the lowest level[Figure 1].This association reflected strongly the earlier hypothesis that low Magnesium levels were amongst the most important contributors towards HIV neuropathy, myelopathy[15].

Phosphate in inorganic and organic forms is an important and widely distributed element in the human body. Inorganic phosphate is the fraction measured in serum and plasma by clinical laboratories[11]. Phosphate is also an essential element of cyclic nucleotides (such as cyclic Adenosine Monophosphate (AMP) and Nicotinamide Adenine Dinucleotide Phosphate (NADP). It is important for the activity of several enzymes[11-14]. Plasma concentrations <1.5 mg/dl (<0.48 mmol/L) may produce clinical manifestations. In our research study we failed to document any significant alteration in serum phosphate levels which had a positive correlation with HIV disease progression. Thus, the aim of this study is to investigate the correlation of these trace elements such as Calcium, Magnesium and Phosphorus in relation to the level of viral replication and other metabolic process in human. We also aimed to determine their clinical significance with regards to possible reduction of the circulating CD4T lymphocytes counts in HIV/AIDS patients, Significantly lower serum total protein in patients with HIV/AIDS than in diabetics and controls corroborates earlier finding[16].Decrease in serum total protein in HIV infection has been associated with either increased losses and/or catabolism or as a result of reduction in intake and/or absorption due to sores in the mouth, pharynx and/or oesophagus, fatigue, depression and side effects of medications[17]. However, with HIV progression protein loss may be more pronounced as it has been shown that about 0.6-1.2g of protein per kilogram body weight per day are lost in adults due to infection as a result of mobilisation of amino acids from skeletal muscles in response to the release of cytokines such as interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α)[18].Our study however did not reveal a strong correlation between Total Proteins and Serum Albumin levels (Total proteins[7.23+/-0.69], Serum Albumin[4.11+/-0.45]) and low CD4 counts.

Among adults, nutritional assessment includes anthropometric, biochemical, clinical, and dietary pattern evaluation.HIV is the wasting syndrome of this era for more reasons than one. Firstly, the disease per se causes a hypercatabolic status which melts the patient almost on par with neoplastic cachexia. Secondly, frequent opportunistic infections induces severe anorexia and nausea thereby leading to weight loss. Finally, the adverse effects of drugs used in HAART is a significant cause for anorexia, lipodystrophy and hypoproteinemia which reduce the BMI in such patients[19]. In our study, we observed that there was a positive correlation between low BMI and reduced CD4 counts which was statistically significant[21.78+/-3.41] ($p<0.05$) {Figure 3}.

One of the major manifestations of the HIV disease is the diarrhea-wasting syndrome[20].Patients with wasting syndrome were reported to have low levels of plasma micronutrients, including serum level of zinc and copper compared to that in non-wasting patients [21,22]. In the present study, we documented a low Serum Zinc level[53.5+/-15.4mg%] correlated well with low CD 4counts [$p<0.005$]. This is probably explained by the fact that zinc deficiencies predispose patients to diarrhea irrespective of their HIV status. It is worthy to note that serum zinc appears to be a marker of susceptibility to infections in patients with AIDS[22]. The association of low serum Zinc levels with HIV has been the bone of contention for many immunologists. Whether it is a cause or effect of disease progression is still a matter speculation which necessitate further studies to elucidate the exact pathogenic mechanism.

CONCLUSION

Micronutrient deficiency is common in PLHIV.Magnesium and Zinc deficiency appear early in the disease.These micronutrient deficiencies correlate with the CD4 count and worsens with progressive disease. Furthermore, BMI has a strong inverse relationship with disease progression in PLHIV.

Micronutrient supplementation will break the vicious cycle and help prevent Opportunistic Infections.Correction of malnutrition reduces mortality in chronic infections like Tuberculosis and also enhances adherence to ART drugs. It has a direct bearing on the life expectancy / longevity of the PLHA.The quality of life attained by improving the nutritional status is a boon to their misery.

Recommendation

Prevention is better than cure, hence the following recommendations are being put forward:

- Nutritional diet chart for all PLHA.
- Assess the nutritional status(1-2 times per year for asymtomatic patient and 4-6 times per for AIDS related patients)
- Nutrition counseling based on available foodstuffs
- Adding nutritional supplementation, physical exercise regimens.

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