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Original Article

Serum Zinc and Albumin Levels in Pulmonary Tuberculosis Patients with and without HIV

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SUMMARY: Limited data are available on the relationship between nutritional status and pulmonary tuberculosis (PTB). Zinc plays a vital role in the immune status of the individual. The present study was carried out to estimate serum zinc and albumin levels in newly detected adult active PTB patients with (n = 20) and without (n = 20) HIV, and to compare them with the levels in controls (healthy family members; n = 20) who satisfied rigid selection criteria. Standard methods were adopted to collect an early morning fasting blood sample for zinc (by Atomic Absorption Spectrometer) and albumin (estimated by the bromocresol green method). The mean ± SD for BMI, zinc and albumin among the controls, HIV positive and HIV negative patients were 19.6 ± 0.6, 18 ± 0.4 and 18.5 ± 0.6 kg/m^2; 117.13 ± 4.2, 53.9 ± 8 and 65.5 ± 9.8 μg/dL; and 4.1 ± 0.6, 2.9 ± 0.4 and 3.6 ± 0.7 g/dL, respectively. All three parameters were significantly low in active PTB patients irrespective of HIV status, but more so in HIV-positive individuals. These changes may be attributable to nutritional factors, enteropathy and acute phase reactant proteins. Hence, the National AIDS Control Organization (NACO) in India is providing nutritional supplements to those HIV-infected cases inducted for antiretroviral therapy and nutritional counseling for others as a part of a national policy.

INTRODUCTION

Almost one-third of the world's population is infected with *Mycobacterium tuberculosis*, and the majority of these individuals live in less developed countries where human immunodeficiency virus (HIV) infection is spreading rapidly. Weight loss is one of the fundamental signs both in HIV-positive and HIV-negative tuberculosis (TB) patients (1). Malnutrition and wasting are associated with TB and HIV infection. Coinfection with one may potentially exacerbate the wasting that occurs in the other (2). Micronutrient deficiencies, such as zinc deficiency, lead to impaired immunity and thereby increase susceptibility to infections such as TB (3,4).

Zinc deficiency affects host defense by decreasing phogocytosis and reducing the number of circulating T cells (5). Also, zinc deficiency has been observed in HIV infection at various stages of the disease (6) and may be a cofactor for the progression of the disease (7). Thus, coinfection with HIV and TB results in a number of micronutrient deficiencies that may increase vulnerability to immune dysfunction (8). Zinc in our body is involved in various activities, such as metabolic functions, immunity and wound healing. Because of the limited data on the serum level of zinc in patients with adult pulmonary tuberculosis (PTB) with and without HIV coinfection, it was decided to study the serum zinc and albumin levels in such patients and compare them with the levels in healthy controls.

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PATIENTS AND METHODS

Patients and selection: A cross-sectional study was designed to study serum zinc and albumin levels in adults with newly detected, untreated active PTB attending the Government Rajaji Hospital in Madurai, India. Selection of cases was based on positive microscopy for acid-fast bacillus in at least two sputum samples. Exclusion criteria were as follows: previous antiretroviral treatment (ART), pregnancy, lactation, other active inflammatory conditions, moderate-to-severe injury or surgery during the last month, acute or chronic liver, renal or cardiac diseases, diabetes mellitus (as measured by elevated fasting blood glucose levels) and neoplasm (as determined by clinical examination) and use of corticosteroids or supplements containing zinc during the previous month. All subjects were free from alcoholism. Controls (n = 20) were healthy adult family members of the cases matched for age with no history of PTB or any overt illnesses.

Data collection: Potential cases and controls were interviewed using a structured questionnaire requesting information related to the inclusion and exclusion criteria. Those who appeared to be eligible were then screened clinically, including by chest X-ray. Cases were offered HIV testing after counseling and were screened for HIV antibodies using an ELISA test established by two different kits, i.e., Innotest™ HIV_1/HIV_2 by Innogenetics (Antwerp, Belgium) and Lab systems (Helsinki, Finland).

Standard procedures were used to determine height (cm) and weight (kg). Body mass index (BMI) was calculated as body weight divided by the height in meters squared (kg/m^2). Cases and controls were regarded as being malnourished (9) if their BMI was below 18.5.

Blood samples were collected in two vacutainers from fasting subjects via venepuncture for estimation of serum

albumin by the bromocresol green method and serum zinc by atomic absorption spectrometry at the Department of Biotechnology, Lady Doak College, Madurai with values of a quality control analyzed with each set of determinations within 3% of certified values.

Ethical considerations: The study was approved by the Institutional Ethical Committee, Goverment Rajaji Hospital and Madurai Medical College, Madurai, Tamilnadu. Informed consent was obtained from cases and controls before the start of the study.

Statistical analysis: A one-sample Kolmogorov-Smirnov test was used to check whether data were normally distributed. The mean and standard deviation (SD) were used for reporting normally distributed data. An independent sample t test was used to assess the differences in normally distributed parameters between cases and controls. The SPSS software package (Windows version 14, SPSS, Chicago, Ill., USA) was used for all statistical analyses and a *P*-value of <0.05 was considered significant.

RESULTS

There were 20 healthy controls, and 20 each of HIV-positive and HIV-negative subjects with active PTB. The age of the patients ranged from 29 to 52 years. The mean ± SD ages among the HIV-positive, HIV-negative and control subjects were 34.5 ± 6.5, 35.3 ± 11.3 and 34.5 ± 8.8 years, respectively. There was no statistically significant difference among them.

BMI was below 18.5 in 4 of 20 healthy controls, whereas it was 15 and 6 among PTB patients with and without HIV infection, respectively. The range, median and mean ± SD for BMI among healthy controls were 18 - 20.1, 19.2 and 19.6 ± 0.6 kg/m^2, respectively, whereas those for PTB patients with and without HIV were 17.6 - 18.9, 18.2 and 18 ± 0.4 kg/m^2; and 17.8 - 18.9, 18.4 and 18.5 ± 0.6 kg/m^2, respectively (Table 1). The BMI status was significantly low in PTB patients with HIV coinfection when compared to controls ($P < 0.004$) and with HIV-negative PTB patients ($P < 0.005$). A positive correlation was observed between BMI and albumin as well as between BMI and zinc. Micronutrient zinc deficiency was greater in those with low BMI. Moreover serum zinc and albumin were positively correlated (Pearson correlation r = 0.583, $P < 0.0001$).

Table 1. BMI, albumin and zinc among categories

Category	BMI (kg/m^2)	Serum zinc (μg/dL)	Serum albumin (g/dL)
Control			
Range	18 - 20.1	79 - 120	3.2
Median	19.2	116	4.0
Mean ±	19.6 ± 0.6	117.13 ± 4.2	4.1 ± 0.6
HIV-positive PTB			
Range	17.6 - 18.9	49 - 56	2.1 - 3
Median	18.2	52	2.8
Mean ±	18 ± 0.4*	53.9 ± 8	2.9 ± 0.4
HIV-negative PTB			
Range	17.8 - 18.9	60 - 77	3.0- 3.9
Median	18.4	64	3.6
Mean ±	18.5 ± 0.6**	65.53 ± 9.8	3.6 ± 0.7
P	*< 0.004 **< 0.005	< 0.001	< 0.002

BMI, body mass index; PTB, pulmonary tuberculosis.

Table 1 shows the serum zinc and albumin levels for the controls and PTB patients. Compared with the control group, the concentrations of zinc and albumin were significantly lower ($P < 0.001$) in PTB patients. Among the PTB patients, serum zinc and albumin levels were significantly lower in those with HIV coinfection than in those without. The *P* values for zinc and albumin were $P < 0.001$ and $P < 0.002$, respectively.

DISCUSSION

Infection induces a reduction in serum zinc and albumin levels in human beings as well as experimental animals. In the present study serum zinc and albumin zinc levels were significantly reduced in patients with PTB irrespective of their HIV status compared to healthy controls. The possible causes for the low serum zinc and albumin in PTB patients were considered to be nutritional factors, enteropathy and acute phase reactant proteins (3,8). The hepatic synthesis of acute phase reactant proteins is induced by cytokines such as interleukin-6 and tumor necrosis factor-α (10,11), which inhibit the production of serum albumin and cause dramatic shifts in the plasma concentration of certain essential micronutrients and albumin.

The level of serum zinc observed among TB patients was significantly lower than that of controls, in agreement with a study in Indonesia (3). Also, this was likely due to the redistribution of zinc from plasma to other tissues, or a reduction of the hepatic production of the zinc-carrier protein α_2-macroglobulin and to a rise in the production of metallothionin, a protein that transports zinc to the liver (11).

BMI was significantly lower in patients with active PTB compared with healthy controls, which is in concurrence with a recent report from southern India (2). The low BMI among patients with PTB may be due to poor dietary intake, anorexia, impaired absorption of nutrients or increased catabolism (12). The present observations are in concurrence with studies done in Indonesia (3) and Malawi (1). Low BMI is a known risk factor for mortality (13).

Since HIV-infected adults with PTB had significantly low zinc, albumin and BMI, this subgroup may potentially benefit from nutritional interventions. Several studies (14-16) have revealed that micronutrient supplementation to patients with active TB and HIV improves their health by increasing CD4+ count (14), increasing their weight (15), and improving the efficacy of their drug treatment (15), in addition to decreasing opportunistic infections (16). Interestingly, intake of zinc beyond a certain level was associated with increased relative risk for disease progression (17), although another previous study failed to replicate this finding (18).

To conclude, the nutritional status of patients with active PTB is poor when compared with healthy controls. Reductions in the concentration of plasma zinc and albumin as well as wasting were significantly greater in PTB patients with HIV infection than in non-HIV PTB patients. The study thus indicates the need for therapeutic supplementation of zinc and proteins to patients with active TB irrespective of HIV status. Currently the National AIDS Control Organization (NACO) in India is providing nutritional supplements to those enrolled in the ART Program, while counseling on nutrition in provided for other HIV-infected cases as part of a national policy.

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