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Serum albumin levels and depression in people living with Human Immunodeficiency Virus infection: a cross-sectional study

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ABSTRACT

Background: Lower serum albumin levels and depression are common among HIV-infected persons. High serum albumin levels may provide protection against depression through its defensive role in inflammation and infection. We tested the hypothesis of an independent relationship between serum albumin levels and depressive symptoms in a cohort of HIV-infected persons.

Methods: A cross-sectional survey was conducted among 310 HIV-infected persons (176 men and 134 women) aged 20–60 years residing in the Kathmandu Valley, Nepal. The bromocresol green method was used to measure serum albumin levels and the Beck Depression Inventory method was used to measure depressive symptoms, with a cut off score of 20 or higher indicating likely depression. The relationship between serum albumin levels and depressive symptoms was assessed using both multiple linear regression analysis and multiple logistic regression analysis, with adjustment for sociodemographic, cardiovascular, life-style, and HIV-related clinical and treatment confounding factors.

Results: Serum albumin levels were inversely associated with depressive symptoms scores (beta for 1 unit change in serum albumin levels: $\beta = -3.91$; $p = 0.001$) for the total participant sample. This inverse association was significant in both men ($\beta = -3.93$; $p = 0.009$) and women ($\beta = -4.47$; $p = 0.03$). A significantly decreased risk of depression was observed among participants with the highest serum albumin levels, with odds ratio and 95% CI for those with > 5.0 g/dL versus < 4.0 g/dL of 0.22 (0.06–0.80) ($p = 0.01$).

Conclusion: Serum albumin levels were inversely associated with depressive symptoms scores in HIV-infected persons.

1. Introduction

Human Immunodeficiency Virus (HIV) infection is a chronic inflammatory disease [1] due to the chronic activation of both the adaptive and innate immune systems [2–4]. HIV infection may increase inflammation directly by viral replication and indirectly by adverse effects caused by virus replication in the gut mucosa [2–4]. The virus rapidly spreads throughout the gut-associated lymphoid tissue leading to the loss of CD4 + T cells directly and indirectly to epithelial injury [5–7]. The loss of mucosal integrity exposes the gut mucosa to proinflammatory microbial products such as lipopolysaccharides, which also drive inflammation [8]. HIV-mediated mucosal damage also passes translocated microbial products on to the liver, contributing to hepatic damage, impaired microbial clearance, and impaired protein synthesis that enhances inflammation [9–11].

One of the important bioactive molecules that may capture the dynamic process of inflammation in HIV-infection is albumin. Albumin is a negative acute phase response protein synthesized in the liver [12] and is an important marker of inflammation. Under inflammatory conditions, the transcapillary escape rate of albumin may increase several-fold [13]. An increase leakage of albumin during an inflammatory response could be one of the important reasons for hypoalbuminaemia in a chronic inflammatory condition [14]. In addition, HIV infection might lower albumin levels through a different mechanism. For instance, the transcapillary escape rate of albumin may increase due to the disruption of barrier function of the endothelium by the HIV-1 Tat-1 protein [15]. The serum albumin levels in HIV-infected persons are lower than in healthy individuals [16]. Studies suggest that low serum albumin levels are associated with higher risk of cardiovascular disease in HIV-infected persons [16,17]. Thus, serum albumin could have an important prognostic

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value in HIV-infected persons, as it is an important predictor of survival [16,17]. More importantly, serum albumin has special significance in developing countries because it is an inexpensive and widely available measurement.

Depression is a highly prevalent co-morbid condition occurring in all stages of HIV infection [18]. The prevalence rate of depression is at least two to three times higher for HIV-infected persons [18] compared to the general population [19]. Depression and low serum albumin levels are frequently reported among HIV-infected persons however, the role of serum albumin levels in depression has not been studied in this population. A growing body of evidence suggests [20–22] that low serum albumin levels are associated with various mental health problems in populations other than HIV-infected persons. Low serum albumin levels associated with clinical depression are probably related to increase catabolism of albumin due to inflammation [23].

In this context, we considered that an investigation in an HIV-infected population might provide useful information about the association of serum albumin levels with depressive symptoms among immune-deficient persons with chronic inflammation. Thus, this study aimed to assess the association between serum albumin levels and depressive symptoms in HIV-infected persons, while accounting for important confounding variables including anti-retroviral therapy (ART) and serum C-reactive protein (CRP) and zinc concentrations. As albumin plays an important role in immune and inflammatory mechanisms [12,24] and reduces risk of depression [23,25,26], we hypothesized that increased concentrations of serum albumin levels would be associated with decreased symptoms of depression in HIV-infected persons. Our study would add new information on correlates of depression among HIV-infected population, apart from previous studies' findings on socio-demographic, psychological, and social risk factors of depression [27–30].

2. Methods

2.1. Study design and setting

We conducted a cross-sectional study among HIV-infected persons living in the Kathmandu, Lalitpur, and Bhaktapur districts (Kathmandu Valley) of Nepal. Nepal has faced a concentrated epidemic of HIV with a high prevalence of infection in specific groups, such as injecting drug users (6.3%), female sex workers (4.2%), men who have sex with men (3.8%), and labor migrants to India (1.8%) [31,32]. About 50,200 people aged 15–49 years are living with HIV, with a prevalence of 0.3% in the general population. The ART coverage was only 26.5% as of 2014 [33] despite having free ART services in Nepal since 2004.

2.2. Study participants

The study procedures have been reported in detail elsewhere [34,35]. Briefly, we recruited 322 HIV-infected persons aged between 18 and 60 years into a prospective study through networking five non-governmental organizations working with HIV-infected persons in the Kathmandu Valley. Our study protocol was approved by the Ethics Committees of the Nepal Health Research Council, Kathmandu, Nepal; National Center for Global Health and Medicine, Japan; and Waseda University, Tokyo, Japan. The Institutional Review Board of the University of Massachusetts, Amherst, USA also approved the study procedures.

2.3. Data collection

We used a structured pre-tested Nepali language questionnaire to interview participants. Trained interviewers conducted a face-to-face interview in a private setting with approximately 45–60 min for each interview. A prepared information sheet was used to inform all participants about the study procedures. Participants provided written informed consent prior to being interviewed. We assured participants that their names would not be used in any documents to ensure confidentiality.

We collected information on depressive symptoms, socio-demographics, cardiovascular risk factors, smoking, alcohol intake, physical exercise, ART, and history of chronic diseases adopting instruments used in previous studies in Nepal [36]. Depressive symptoms over the prior two weeks were measured using the Nepali version of the 21-item Beck Depression Inventory (BDI)-I [37]. A four-point Likert scale was used to score each item, with a total range for the instrument between 0 and 62. The scale was validated for use in Nepal [37] with clinical Diagnostic and Statistical Manual of Mental Disorder (DSM-IV) diagnoses [38] of major depressive disorder (sensitivity 0.73, specificity 0.91; area under the curve 0.92). According to the validation study, symptom scores of 20 and higher are consistent with moderate to severe depression [37]. ART type and adherence were measured based on current use of medication at the time of the survey. The measurement of other socio-demographic variables was described elsewhere [34,35].

2.4. Physical examination

We measured each participant's body weight (in light clothing and without shoes) using digital scales in kilograms. Body height was measured in centimeters using a stadiometer. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. We measured blood pressure using an Omron Automatic Blood Pressure Monitor after participants had been at rest for at least 10 min beforehand. All anthropometric measurements were repeated to estimate mean values for these parameters. The mean values were used as the final score.

2.5. Blood collection and laboratory methods

We took fasting blood samples from 322 participants after an overnight fast during the survey period. Laboratory technicians at the government hospital drew about ten milliliters of venous blood into an evacuated tube and centrifuged immediately for 15 min to separate serum from other blood components. Serum samples were then transported to a local laboratory in Kathmandu in a cooler box with dry ice and were stored in the same laboratory during fieldwork. We then transported samples in a dry ice to a research laboratory in Tokyo, Japan where they were stored at − 80 °C until analysis. Serum samples were sent to an external laboratory (Mitsubishi Chemical Medience Corporation, Tokyo, Japan) for testing, where serum albumin levels were measured by bromocresol green (BCG) method. The intra assay coefficient of variation of serum albumin levels ranged from 0.4 to 0.9%. The high-sensitive serum CRP and zinc concentrations were measured by the latex agglutination nephelometry method and atomic absorption method, respectively. The intra assay coefficient of variation of serum zinc and CRP concentrations ranged from 2.9 to 6.4% and 0.1 to 0.9%, respectively. We measured $CD4^+$ T-cell counts using a specific monoclonal antibody and fluorescence-activated cell sorter (FACS) analysis. Viral loads measurements were not done due to lack of resources.

2.6. Statistical analyses

We excluded 12 participants with missing information (e.g. serum albumin levels or depressive symptoms score or body weight or body height) from the present analysis, resulting in a final study sample of 310 participants (176 men and 134 women). A BDI cut-off score of 20 or higher was used to identify depressed participants from those who were not depressed. The serum albumin levels were categorized by median cut off value of 4.6 g/dL into high (albumin > 4.6 g/dL) and not high (albumin ≤ 4.6 g/dL). We used the median value of 4.6 g/dL to divide participants into two groups with equal sample sizes. Equal sample size in each subgroup of the total sample size gives more power