LETTER TO EDITOR

CAN IONIC IMBALANCE IN HIV DISEASE BE ATTRIBUTED TO CERTAIN UNDERLYING OPPORTUNISTIC INFECTIONS?

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Dear Editor,

Electrolyte disturbance can be associated with numerous morbid conditions especially among HIV-infected individuals receiving highly active antiretroviral therapy (HAART) (1- 4). Electrolyte imbalance is described to be the prime cause of death due to myriad infectious ailments involving the gastrointestinal tract, exemplified by Asiatic cholera, rota virus infection, shigellosis, salmonellosis, leptospirosis, malaria and parasitic diarrhoea. Unless restored, electrolyte imbalance can be serious and might interfere with a patient's immune response. Terminal HIV disease is characterized by the onset of numerous opportunistic infections (OI) and neoplasms and individuals in terminal AIDS are vulnerable to numerous intracellular infections, where the corresponding aetiological agents reportedly use the intracellular elements (e.g. iron) and metabolites to survive and replicate, which likely alters the events related to cellular metabolism (5). This could subsequently lead to a plethora of functional sabotage events in cellular and immune functions (5). Maintenance of an optimum amount of electrolyte (ionic homeostasis) in the intracellular as well as the extracellular compartment (blood, interstitial fluid etc.) is paramount to healthy living. Electrolyte imbalance could be attributed to numerous factors both from the host as well as from the parasite point of view and principally reflects a disturbance in the host's cellular metabolic pathways possibly after establishment of an infection.

In the post-HAART era, information of the prevalence of electrolyte imbalance is limited both in developed world as well as in resource-limited settings and has never been adequately investigated. One study has identified abnormally low bicarbonate levels (1) and another documented HIV-associated nephropathy (2) among HAART-treated HIV positive persons. Few others have documented that HIV-infected individual with underlying OIs treated with HAART regimens developed biological abnormalities including hyponatraemia, hyperkalaemia or hypokalaemia and acidosis (3, 4). Besides, sodium and potassium imbalances are believed to be associated with a plethora of chronic ailments, such as malnutrition, alcoholism, diabetes mellitus and other infectious causes especially in AIDS. A detailed literature survey revealed the availability of very limited past data on the prevalence of electrolyte imbalances in HIV infected individuals. Further, the underlying risk factors for biological abnormalities are poorly defined. Hence in a cross-sectional study we investigated the proportion of HIV infected persons with abnormal serum electrolytes and identified the possible co-factors of these biological abnormalities among persons attending YR Gaitonde Centre for AIDS Research and Education (YRG CARE), a tertiary referral centre in Southern India, between January 2004 and July 2006. Data were collected with the approval of YRG CARE's freestanding institutional review board.

YRG CARE, since 1993, has provided medical and psychosocial care and support to over 12,000 HIV-infected persons in the south of India. The study was approved by the Institutional Review Board (IRB) of YRG CARE. Written informed consent was obtained from all the participants. We investigated 464 HIV-infected persons who were either HAART naïve or HAART experienced. Demographics, clinical characteristics and co-factors (age, gender, hepatitis B and C status and exposure to HAART) were included in the analysis. Laboratory investigations such as electrolytes (sodium, potassium, chloride and bicarbonate) and absolute CD₄

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T-cell counts were performed. Serum electrolyte levels were analysed using AVL 9180 Ion Selective Electrode (Roche Diagnostics, USA). Absolute CD₄ count was determined by using the Guava Personal CellAnalyser (Guava Technologies Inc., Hayward, CA, USA).

Persons were classified as having normal or abnormal values based on the established reference interval (6). Whole blood was collected in a serum separator gel tube (SST) vacutainer (Becton and Dickinson, Franklin Lakes, NJ, USA) and centrifuged at 3500 rpm for 10 - 15 minutes, serum was separated and processed within 1 hour from the time of separation. Univariate and multivariate analyses were used to analyze the co-factors associated with abnormal electrolyte levels. Statistical data was generated using the SPSS software (SPSS version 13.0, Chicago, IL). P value <0.05 was considered statistically significant. Data were collected with the approval of YRG CARE's freestanding institutional review board.

A total of 464 HIV-infected individuals HAART- experienced and HAART- naive were analyzed for abnormalities in potassium, sodium, chloride, and bicarbonate levels. Of these 278 (60%), 312 (67.2%), 319 (68.7%) and 176 (38%) had abnormal potassium, sodium, chloride and bicarbonate levels. The mean age was 36 ± 9.3 and 35 ± 8.3, 35 ± 8.5 and 35 ± 8.8, 35 ± 8.6 and 35 ± 8.8, 35 ± 8.7 and 35 ± 8.8 years for the individuals with normal and abnormal potassium, sodium, chloride and bicarbonate groups respectively. Persons that had abnormal potassium levels were significantly younger than those that revealed normal levels (P=0.03). In this group, 79(28.4%) had AIDS-defining ailments and 149(53.6%) had low absolute CD₄ T cell counts as compared to 62(33.3%) and 149 (53.6%) with normal levels. Furthermore, persons with abnormal sodium levels had relatively lower BMI as compared with normal group (P=0.05). One hundred and ten (35.3%) individuals had underlying AIDS-defining illnesses as compared to 31(20.4%) normal healthy individuals. Similarly, 187(59.9%) individuals had lower absolute CD₄ cell count <200cells/μL as compared to 38.8% normal individuals (p<0.001). In the abnormal chloride group, 102(32%) individuals had some AIDS-defining illness as compared to 39(26.9%) normal individuals. Likewise, 177(55.5%) individuals had low absolute CD₄ T cell count i.e. <200cells/μL as compared to 47.6% normal individuals. In abnormal bicarbonate group we noticed that 88(30.6%) individuals had AIDS-defining illness and 106(60.2%) individuals had a CD₄ count <200cells/μL compared to 53(30.1%) and 140 (48.6%) normal individuals (P=0.03). In the multivariate analysis, we

identified that low absolute CD₄ cell count and male gender were the significant co-factors of abnormal electrolyte levels in HIV disease.

In the present study we documented the association of abnormal electrolytes with multiple OIs, low absolute CD₄ cell counts and male gender among HIV infected individuals. Our finding was supported by a recent African study (7). This study further confirms other similar reports that have shown complications like hyperkalaemia, low serum bicarbonate and hypophosphataemia in HIV-infected patients (8). It is known that during infective episodes, hyperkalemia results from intravascular hemolysis or rhabdomyolysis, and occasionally from decreased activity of Na⁺, K⁺-ATPase. Hyponatremia occurs frequently in infectious conditions, as a result of increased levels of vasopressin, entry of sodium into cells, sodium loss and resetting of osmoreceptors (9). The underlying reason could be because patients who had CD₄<200 cells/μL are likely to have underlying OIs. Persistent diarrhea (dehydration), extensive muscle wasting, loss of proteins in urine and poor nutritional status could be the principal cause for these biological abnormalities. Earlier studies have shown that low CD₄ T cell count (≤ 200 cells/mm³) and nephropathy could be the risk factors for such biological imbalances in HIV infected individuals (10, 11) and are in agreement with our findings. Ionic dysregulation by any means could be harmful and could alter the acid base balances, which in turn could lead to a series of osmo and thermodyregulation events. Measurements of serum electrolytes along with clinical findings could help clinicians to correct the abnormal values of sodium, potassium, chloride and bicarbonate levels, at early stage of disease.

The study has certain limitations that could have strengthened the correlates of electrolyte imbalance namely the nature of OI, the length of infection period etc. Furthermore, due to limited funding some of the other renal parameters like cystatin C, urea, creatinine and uric acid could not be investigated. In conclusion, we found that multiple OIs, absolute CD₄ cell count and male gender have correlated with abnormal electrolyte levels in HIV infected individuals and importantly, there appears to be an association between OIs and abnormal electrolyte levels. Whether or not certain infectious agents are associated with abnormal electrolyte levels remains to be investigated in HIV disease and therefore, more prospective follow-up studies may be required to elucidate our findings.

Key words: Electrolytes, HAART, Co-factor, CD₄ count.

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