

Plasma vitamin A and zinc levels in HIV-infected adults in Cape Town, South Africa

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A cross-sectional study of 132 adults attending an HIV clinic in Cape Town, South Africa, was conducted to determine predictors of low plasma vitamin A and Zn levels. No patients were on antiretroviral therapy. The possible confounding effect of the acute-phase response was controlled by including C-reactive protein levels in multivariate analysis and by excluding active opportunistic infections. Retinol levels were low ($<1.05 \mu\text{mol/l}$) in 39 % of patients with early disease (WHO clinical stages I and II) compared with 48 and 79 % of patients with WHO stage III and IV respectively ($P < 0.01$). Plasma Zn levels were low ($<10.7 \mu\text{mol/l}$) in 20 % of patients with early disease *v.* 36 and 45 % with stage III and IV disease respectively ($P < 0.05$). C-reactive protein levels were normal in 63 % of subjects. Weak, positive associations were found between CD4+ lymphocyte count and plasma levels of retinol (r 0.27; 95 % CI 0.1, 0.43) and Zn (r 0.31; 95 % CI 0.25, 0.46). Multivariate analysis showed the following independent predictors of low retinol levels: WHO stage IV (odds ratio 3.4; 95 % CI 2.1, 5.7) and body weight (odds ratio per 5 kg decrease 1.15; 95 % CI, 1.08, 1.25), while only body weight was significantly associated with low Zn levels (OR per 5 kg decrease 1.19; 95 % CI 1.09, 1.30). CD4+ lymphocyte count $<200/\mu\text{l}$ was not significantly associated with either low retinol or Zn levels. In resource-poor settings, simple clinical features (advanced disease and/or weight loss) are associated with lowered blood concentrations of vitamin A and/or Zn. The clinical significance of low plasma retinol and/or Zn levels is unclear and more research is required to establish the role of multiple micronutrient intervention strategies in HIV disease.

HIV infection: Vitamin A: Zinc: C-Reactive Protein: Africa

HIV infection continues to increase worldwide, and an estimated 28.5 million adults and children are infected in sub-Saharan Africa alone (Joint United Nations Programme on HIV/AIDS (UNAIDS) 2002). Most studies investigating the micronutrient status of HIV-infected populations have reported low serum or plasma levels of micronutrients such as vitamins A, E, B₆, B₁₂, C and carotenoids, as well as trace elements such as Zn and Se. However, limited results exist for developing countries (Semba & Tang, 1999).

Vitamin A plays a central role in the growth and function of T and B cells, antibody responses and maintenance of mucosal epithelia (Semba, 1994). Low blood levels of vitamin A are associated with accelerated disease progression and increased mortality in HIV-infected adults (Semba *et al.* 1993, 1995; Baum *et al.* 1995, 1997; Tang *et al.* 1997). In addition, low concentrations of

vitamin A may be associated with increased mother-to-child transmission of HIV, higher infant mortality and child growth failure (Semba *et al.* 1994, 1997a,b; Greenberg *et al.* 1997).

In Africa, low blood vitamin A concentrations ($<1.05 \mu\text{mol/l}$) have been reported in 50–63 % of HIV-infected pregnant women (Semba, 1997; Moodley *et al.* 1998). Approximately one-third of seropositive adults attending an outpatient clinic in Uganda, had lowered serum vitamin A levels (Semba, 1997). Another study, conducted among in-patients co-infected with tuberculosis in Rwanda, showed that 29 % of patients presented with low blood vitamin A levels (Rwangabwoba *et al.* 1998). A recent clinical trial among HIV-infected adults with persistent diarrhoea showed that 63 % of patients had vitamin A concentrations consistent with a deficiency state ($<0.7 \mu\text{mol/l}$) (Kelly *et al.* 1999).

Zn is essential for the maturation and differentiation of T lymphocytes and the functioning of cells mediating non-specific immunity such as neutrophils and natural killer cells (Shankar & Prasad, 1998). According to a recent review, no results have yet been reported regarding the prevalence of Zn deficiency, as measured by plasma levels, in HIV-infected patients in Africa (Piwoz & Preble, 2000). However, low Zn levels ($<10.7 \mu\text{mol/l}$) have previously been reported in 25–29 % of HIV-infected adults in the USA (Beach *et al.* 1992; Koch *et al.* 1996; Baum *et al.* 1997). Such low concentrations of Zn have been shown to be predictive of HIV disease progression and mortality (Graham *et al.* 1991; Baum *et al.* 1997).

In a search for more cost-effective interventions to reduce morbidity and mortality in HIV-disease, the identification and correction of micronutrient deficiencies such as vitamin A and Zn, may take on increasing importance. A cross-sectional study was therefore conducted to determine the plasma vitamin A and Zn levels of HIV-infected adults in South Africa and to investigate their relationships with clinical stage, controlling for the acute-phase response.

Methods

The study population consisted of a sample of HIV-infected adults who attended the Groote Schuur Hospital (Cape Town) outpatient clinic consecutively between October 1995 and October 1996 and in whom routine blood tests were requested by the attending medical practitioner. HIV-seropositivity was confirmed according to the WHO antibody-testing strategy, namely by means of three positive enzyme immunoassays (Martin *et al.* 1995a). Exclusion criteria included anti-retroviral therapy, current use of vitamin supplements, pregnancy and a clinical diagnosis of liver disease. Patients with pyrexia ($>38^\circ\text{C}$), those who were receiving treatment for an acute opportunistic infection, as well as patients on therapy for tuberculosis for <12 weeks, were also excluded. The study was approved by the Research and Ethics Committee at the University of Cape Town.

After written informed consent was obtained, subjects were interviewed to obtain socio-demographic information such as educational level, current employment, type of housing and the availability of electricity or a refrigerator. The clinical stage of each patient was assessed by a medical practitioner according to the WHO clinical staging system (World Health Organization International Collaborating Group for the Study of the World Health Organization Staging System, 1993). Body weight was measured to the nearest 0.1 kg with a beam-balance scale, which was calibrated at monthly intervals. Subjects were required to remove heavy clothing and shoes. Height was determined with a stadiometer to the nearest 1 mm. BMI (kg/m^2) was calculated for each subject.

Venous blood for the determination of plasma retinol, Zn and C-reactive protein (CRP) was collected between 13.30 and 15.30 hours and subjects were therefore in a fed state. The puncture site was cleaned with trace-element free alcohol to avoid contamination. All specimens were promptly transported to the laboratory, protected from light and stored at -20°C after centrifugation, until analysis.

Plasma retinol levels were determined by the fluorometric method (Underwood, 1990a,b). Duplicate retinol (Sigma Co., Johannesburg, South Africa) reference standards were prepared in ethanol for the spectrofluorophotometer (E% value: 1835 at 325 nm) for each batch of specimens. Plasma CRP levels were determined by nephelometry using an international reference standard for plasma proteins (Behringwerke AG, Marburg, Germany). CRP levels $\geq 10 \text{ mg/l}$ were considered to be elevated. Plasma levels of Zn were measured by atomic absorption spectrophotometry (Tietzman, 1987). CD4+ and CD8+ T lymphocyte counts were measured by a Coulter flow cytometer (EPICS Profile II, FL, USA).

We estimated that approximately 30 % of our study population had low plasma retinol levels. To estimate such a proportion with a precision of 7.5 %, 143 patients were needed. Clinic records showed that patient attendance was evenly distributed across clinical strata. Assuming a difference between strata proportions of $\leq 10\%$, this would lead to a χ^2 test for trend with significance $<5\%$.

Statistical analysis

Statistical analysis was performed using Epi-info (version 6; CDC, Atlanta, GA, USA) and SAS Statistical package, (version 6.03; SAS Institute Inc., Cary, NC, USA). Continuous variables were assessed across clinical stage categories by the Kruskal–Wallis test due to the non-normality of the data. Differences in continuous variables between male and female subjects were assessed by the Wilcoxon rank-sum test. The relationship between categorical variables and clinical stage was assessed by the χ^2 test for trend. Univariate associations between continuous variables were performed using the Spearman correlation coefficient. Multivariate logistic regression was performed using a stepwise approach, with plasma retinol ($<1.05 \mu\text{mol/l}$) and Zn ($<10.7 \mu\text{mol/l}$) as binary outcome variables. Independent variables such as clinical stage, body weight, CD4+ cell count, haemoglobin, packed cell volume and CRP levels were examined. The presence of collinearity ($r \geq 0.8$) was assessed in order to prevent the inclusion of strongly correlated variables into the multivariate models.

Results

A total number of 247 HIV-infected patients attended the clinic during the specified time period; however, routine blood tests were not requested in thirty-eight patients. Furthermore, seventy-six patients were also excluded according to the following criteria: <18 years old ($n 1$); the presence of active opportunistic infection at the time of the clinic visit ($n 10$); on current drug therapy for tuberculosis for <12 weeks ($n 32$); clinical diagnosis of liver disease ($n 3$); use of multivitamin supplements at the time or during the preceding 6 months ($n 17$); pregnancy ($n 9$); prisoners ($n 1$); problems with venous access ($n 3$). One patient refused to participate in the study. None of our subjects were receiving anti-retroviral therapy at the time or prior to study enrolment.

Results are therefore presented on a total number of 132 patients (Table 1). It has previously been demonstrated

that patients with WHO stage I and II HIV infection display similar survival curves (Post *et al.* 1996). Therefore, these patients were grouped together during data analysis, representing early HIV disease. The initial AIDS-defining illness of stage IV patients and the time period between the latter and study enrolment, is listed in Table 2. The mode of transmission for all subjects was heterosexual. No differences were noted between subjects in the different clinical stage categories in terms of the different demographic variables measured. However, only 13 and 14% of subjects with stage III and IV disease respectively, were employed at the time of the study, compared with 43% of subjects with early disease ($P < 0.05$).

Table 1 shows that the number of patients with low plasma levels of retinol ($< 1.05 \mu\text{mol/l}$) (Pilch, 1987) and Zn ($< 10.7 \mu\text{mol/l}$) (Tietzman, 1987), was significantly ($P < 0.001$ and $P < 0.01$ respectively) higher among those with stage III and IV disease, compared with patients with early disease. The median retinol level for patients with early disease was 1.19 (interquartile range (IQR) 0.85–1.50) $\mu\text{mol/l}$, compared with 1.07 (IQR 0.86–1.32) and 0.83 (IQR 0.59–0.99) $\mu\text{mol/l}$ for those with stage III and IV disease, respectively ($P < 0.01$). In terms of plasma Zn, the median level for patients with early disease was 12.9 (IQR 11.0–15.3) $\mu\text{mol/l}$, compared with 11.9 $\mu\text{mol/l}$ (IQR 9.8–14.1) and 11.0 (IQR 9.2–13.8) $\mu\text{mol/l}$ for those with stage III and IV disease respectively ($P < 0.01$).

The median body weight for patients with early disease was 66.0 (IQR 56.5–78.0) kg, compared with 60.5 (IQR 55.0–66.1) kg and 58.0 (IQR 46.0–65.7) kg for those with stage III and IV disease respectively ($P < 0.02$).

No sex differences in terms of body weight within the three clinical staging categories were demonstrated. Due to incompleteness of data, BMI was determined in 116 patients. Only seven of twenty-nine patients with stage IV disease had a BMI $< 18.5 \text{ kg/m}^2$ and could therefore be categorised as having chronic energy deficiency (James *et al.* 1988) (Table 1).

The majority of our patients did not have elevated plasma CRP levels ($\geq 10 \text{ mg/l}$), although a significant difference was noted across clinical stage categories (Table 1). Only one patient with stage III disease presented with a CRP level $> 100 \text{ mg/l}$. This observation was not excluded.

We demonstrated weak, positive associations between CD4+ lymphocyte levels and plasma levels of retinol (r 0.27; 95% CI 0.10, 0.43) and Zn (r 0.31; 95% CI 0.25, 0.46), using the Spearman correlation coefficient. Similar associations were noted between the CD4+ : CD8+ lymphocyte ratio and plasma retinol and Zn levels.

Multivariate analysis demonstrated that stage IV disease was independently associated with a threefold increased risk of low plasma retinol levels ($< 1.05 \mu\text{mol/l}$) after adjusting for CD4+ lymphocyte count, haemoglobin levels and body weight (Table 3). Low haemoglobin levels ($< 120 \text{ g/l}$) and a decrease in body weight were both independent predictors of low retinol levels. The CD4+ lymphocyte count ($< 200 \text{ cells}/\mu\text{l}$) and CD4+ : CD8+ lymphocyte ratio (< 0.15) were only significantly associated during univariate analysis. Plasma Zn and CRP levels did not contribute significantly to the model, nor did it change the adjusted odds ratios of any of the covariates.

Table 1. Characteristics of HIV-infected adults according to World Health Organization clinical staging of HIV-infection*

	WHO stage I and II		WHO stage III		WHO stage IV		Statistical significance of effect: P
	n	%	n	%	n	%	
Age (years)							
< 30	21	41	22	46	16	49	
≥ 30	30	59	26	54	17	51	
Sex							
Male	15	29	17	35	15	45	
Female	36	71	31	65	18	55	
CD4+ lymphocyte count (cells/ μl)							
< 200	9	19	26	55	22	69	0.001
≥ 200	38	81	21	45	10	31	
BMI							
< 18.5	2	4	3	7	7	24	0.01
18.5–24.9	22	49	28	66	14	48	
≥ 25	21	47	11	27	8	28	
Plasma C-reactive protein (mg/l)							
< 10	39	77	25	52	19	58	0.05
10–40	11	23	19	40	12	36	
> 40	1	2	4	8	2	6	
Plasma retinol ($\mu\text{mol/l}$)							
< 1.05	20	39	23	48	26	79	0.001
≥ 1.05	31	61	25	52	7	21	
Plasma zinc ($\mu\text{mol/l}$)							
< 10.7	10	20	17	36	15	45	0.01
≥ 10.7	40	80	30	64	16	55	

* For details of classification, see World Health Organization International Collaborating Group for the study of the World Health Organization Staging System (1993).

Table 2. Initial AIDS-defining illnesses of World Health Organization clinical stage IV patients*†
(Mean values and standard deviations for twenty-three subjects)

AIDS-defining illness	<i>n</i>	Time period between AIDS-defining illness and study enrolment (months)	SD
Extrapulmonary tuberculosis	20	11.2	10.7
Pneumocystis carinii pneumonia	2	3.0	1.4
Cryptococcosis	1	3.0	
Toxoplasmosis	1	1.0	
Herpes simplex virus	1	0.0	
Kaposi's sarcoma	3	7.3	10.2
Oesophageal candidiasis	3	1.7	2.9
HIV-wasting syndrome	2	0.0	

* For details of subjects, see Table 1.

† For details of classification, see World Health Organization International Collaborating Group for the study of the World Health Organization Staging System (1993).

Table 4 demonstrates that a decrease in body weight was the only significant independent predictor of low plasma Zn levels. During univariate analysis, stage IV disease and a low CD4+ lymphocyte count (<200 cells/ μ l), were almost significant. As earlier, the inclusion of CRP levels did not contribute significantly to the model.

Discussion

The overall prevalence of low plasma retinol concentrations in our study population was 52%, which is comparable with results among infected adults from developing countries (Semba, 1997; Rwangabwoba *et al.* 1998). To our knowledge, this is the first study reporting the prevalence of low plasma Zn levels among HIV-infected adults in Africa. Although the proportion of asymptomatic patients who presented with low blood Zn levels was comparable with previously reported results, a significantly larger number of patients with advanced disease were deficient in Zn ($P < 0.05$). A limitation of the present study is that plasma levels of vitamin A and Zn were not measured in sero-negative individuals. However, Kafwembe *et al.* (2001) demonstrated that HIV-infected individuals in Zambia were 6.3-times more likely to present with low vitamin A concentrations, when compared with sero-negative individuals.

It is likely that several factors contributed to the development of micronutrient deficiencies, such as vitamin A and Zn, in our present study population. Patients with advanced disease were more likely to be unemployed and therefore, although we did not assess the dietary intake of vitamin A and Zn, it is likely that socio-economic factors contributed

to a poorer micronutrient intake in those patients. Rwangabwoba *et al.* (1998) demonstrated that among a group of HIV-infected patients who were co-infected with tuberculosis, patients who presented with weight loss had significantly lower vitamin A levels. Only a small number of our patients were suffering from chronic energy deficiency (BMI < 18.5 kg/m²) at study entry. However, multivariate analysis demonstrated that a higher body weight has a significant protective effect in terms of the development of a deficiency in vitamin A and Zn (Tables 3 and 4).

Although we excluded patients with active infections at the time of study entry, it is likely that previous episodes of infection may have contributed to the depletion of micronutrient stores, such as retinol (Semba, 1997). During infections, plasma retinol levels may decrease due to a poor food intake, an increased utilisation of retinol by target tissues or via increased urinary losses of vitamin A (Campos *et al.* 1987; Stephenson *et al.* 1994). In addition, serum concentrations of several nutrients decline during the acute-phase response, either because they are re-distributed in the body or because they are bound to acute-phase proteins. The precise effect of the acute-phase response on the metabolism of vitamin A is unclear, but it is well documented that infections result in lowered serum retinol levels and hepatic vitamin A stores. During the acute-phase response, plasma Zn and Fe levels also decrease due to hepatic sequestration, whereas Cu levels increase due to an increase in caeruloplasmin. Decreased retinol levels may be caused by a reduced mobilisation of retinol-binding protein from the liver due to hypozincaemia, since retinol-binding protein is a Zn-dependent protein (Fleck, 1989; Raynes, 1994). The serum micronutrient

Table 3. Predictors of plasma retinol levels <1.05 μ mol/l in HIV-infected adults*
(Unadjusted and adjusted odds ratios and 95% confidence intervals)

Variable	OR _{Unadjusted}	95% CI	OR _{Adjusted}	95% CI
WHO clinical stage IV†	4.8	3.0, 7.6	3.4	2.1, 5.7
CD4+ count <200 cells/ μ l	3.6	2.4, 5.6	1.4	0.9, 2.1
Haemoglobin <120 g/l	3.3	2.3, 4.8	2.4	1.6, 3.5
Body weight (per 5 kg decrease)	1.22	1.02, 1.30	1.15	1.08, 1.25

OR, odds ratio.

* For details of subjects and procedures, see Tables 1 and 2.

† For details of classification, see World Health Organization International Collaborating Group for the study of the World Health Organization Staging System (1993).

Table 4. Predictors of plasma zinc levels $<10.7 \mu\text{mol/l}$ in HIV-infected adults* (Unadjusted and adjusted odds ratios and 95% confidence intervals)

Variable	OR _{Unadjusted}	95% CI	OR _{Adjusted}	95% CI
WHO clinical stage IV†	2.2	0.94, 4.90	2.2	0.9, 6.0
CD4+ count $<200 \text{ cells}/\mu\text{l}$	2.2	1.0, 4.8	1.4	0.6, 3.2
Body weight (per 5 kg decrease)	1.19	1.10, 1.28	1.19	1.09, 1.30

OR, odds ratio.

* For details of subjects and procedures, see Tables 1 and 2.

† For details of classification, see World Health Organization International Collaborating Group for the Study of the World Health Organization Staging System (1993).

status of HIV-infected individuals with acute infections should therefore always be interpreted with caution due to potential misclassification (Fawzi & Hunter, 1998).

In our present study, CRP was measured as a marker of the acute-phase response. CRP is a non-specific marker of inflammation or infection and very high plasma CRP concentrations ($>100 \text{ mg/l}$) are more likely to be associated with bacterial than viral infections (Young *et al.* 1991). Interleukin 6 is thought to be the main mediator of CRP production (Castell *et al.* 1990). HIV-infection *per se* is known to stimulate macrophages resulting in increased interleukin 6 levels, even in asymptomatic HIV-positive patients (Breen *et al.* 1990). It has been suggested that interleukin 6 levels increase with the progression of HIV-infection (Honda *et al.* 1990). In our present study, a significant number of patients with advanced disease had mildly elevated plasma CRP levels (10–40 mg/l), which may be attributable to a direct effect of HIV stage I activity (Table 1). This is consistent with the findings of Tang *et al.* (1997) who showed that 55% of their HIV-infected cohort, of whom 81% were asymptomatic, had elevated serum CRP levels ($\geq 8 \text{ mg/l}$). Melchior *et al.* (1999) recently demonstrated that CRP was an independent predictor of survival in a group of HIV-infected patients, who were free of opportunistic infections at the time of study entry. They suggested that elevated CRP concentrations may be related to the rate of virus replication; however, they did not measure viral load. Serum retinol levels are negatively associated with elevated CRP levels in adults undergoing orthopaedic surgery and in schoolchildren with schistosomiasis (Louw *et al.* 1992; Friis *et al.* 1996). It has been suggested that low plasma Zn levels are reflective of the acute-phase response due to HIV-viral activity (Graham *et al.* 1991). However, multivariate analysis demonstrated that CRP was not an independent predictor of low levels of vitamin A or Zn in our present study.

Lower CD4+ cell counts are associated with low retinol levels among HIV-infected individuals, while the normalization of retinol and Zn levels have been associated with higher counts (Semba *et al.* 1993; Baum *et al.* 1995). Our present findings confirmed weak, positive associations between CD4+ lymphocyte counts and plasma levels of retinol and Zn. The potential confounding effect of tuberculosis on CD4+ counts was controlled for by restricting our present sample to patients who had received drug treatment for at least 12 weeks. A significant rise in CD4+ counts after that period of time has been demonstrated (Martin *et al.* 1995b). Retinoids are known to enhance cellular differentiation of haemopoietic cells and the lineage of other cells

(Nugent & Clark, 1985). Thus, retinol status may be important for the differentiation of CD4+ cells. In human subjects, Zn deficiency results in rapid and marked atrophy of the thymus, lymphopaenia and a reduction of primary and secondary antibody responses, particularly for those antigens that require T cell help (Shankar & Prasad, 1998).

Our present findings demonstrate that patients with WHO stage IV disease had a threefold risk of having plasma retinol levels $<1.05 \mu\text{mol/l}$, after adjusting for CD4+ lymphocyte count, body weight and haemoglobin levels (Table 3). On the other hand, a decrease in body weight was the only significant predictor of low Zn levels in our present study (Table 4). CD4+ lymphocyte count and the CD4+:CD8+ lymphocyte ratio were not independent predictors of a low retinol status in the present study, after adjusting for clinical stage. Reduced haemoglobin and packed cell volume levels have been associated with low serum retinol levels in HIV-infected patients (Semba *et al.* 1993, 1995). Haemoglobin may be an intermediate variable in the relationship between vitamin A and AIDS, since haematopoiesis is vitamin A-dependent. It appears that vitamin A-deficient children are prone to the development of a mild Fe-deficiency anaemia and that vitamin A supplementation may improve haematopoiesis in children who are vitamin A deficient. Vitamin A may therefore be involved in the regulation of Fe release from hepatic stores (Meijia & Chew, 1988; Semba *et al.* 1992).

CD4+ lymphocyte counts are a standard laboratory marker of disease progression in HIV infection, but expense precludes their use in many resource-poor settings in Africa. We demonstrated that WHO clinical stage IV HIV disease was a stronger predictor of low plasma concentrations of micronutrients, such as vitamin A, than CD4+ cell counts in our present study population. It could thus be argued that these patients might be targeted for micronutrient supplementation by practitioners at a primary-care level. However, it must be noted that our cross-sectional study design precludes any causal inferences about the association between plasma vitamin A and Zn status and the progression of HIV disease.

High-dose vitamin A supplementation has been shown to reduce diarrhoeal disease morbidity and AIDS-related mortality in HIV-infected children, and improve the CD4+ cell counts of children with AIDS (Coutsoudis *et al.* 1995; Hussey *et al.* 1996; Fawzi *et al.* 1999). In contrast, the short-term administration of high doses of vitamin A in HIV-infected adults did not increase CD4+ counts. The HIV viral load remained unchanged. However, only a small number of adults in two of the three studies cited

had plasma vitamin A levels that were consistent with deficiency (Coutsoudis, 1997; Semba *et al.* 1998; Humphrey *et al.* 1999). High circulating HIV viral load has been shown to be a risk factor for HIV progression (Ferre *et al.* 1995). It has been suggested that vitamin A deficiency and viral load may be independent risk factors for the progression of HIV disease (Semba, 1997). Several clinical trials have documented the lack of a beneficial effect of vitamin A supplementation on reducing the mother-to-child transmission of HIV. In view of these findings, it has been suggested that serum retinol concentrations may be merely markers of HIV-disease severity, which is an important predictor of vertical transmission (Semba, 1997; Coutsooudis *et al.* 1999; Fawzi *et al.* 2000). However, other potential biological mechanisms still remain, whereby vitamin A supplementation may be beneficial in reducing morbidity and mortality in HIV disease.

Zn supplementation has been demonstrated to increase the efficiency of the immune system in a number of study populations, including marasmic infants (Castillo-Duran *et al.* 1987), and children recovering from malnutrition (Golden & Golden, 1981). A recent meta-analysis showed that Zn has a major role to play in the primary prevention of diarrhoeal disease and acute lower respiratory tract infections in children from developing countries. (Zinc Investigators' Collaborative Group, 1999). Few Zn supplementation studies have been conducted in HIV-AIDS patients. Supplementation for 1 month of adults with AIDS on zidovudine therapy resulted in the stabilisation of body weight, as well as increases in CD4+ cell count and plasma levels of Zn-bound thymulin. A marked reduction in opportunistic infections in the Zn-treated group was also demonstrated (Mocchegiani *et al.* 1995).

Conclusion

Our present findings suggest that low plasma concentrations of vitamin A and Zn are common among HIV-infected adults attending an outpatient health facility in South Africa. We showed that patients with advanced disease and/or weight loss were more likely to present with low plasma levels, even in the absence of any opportunistic infection, especially in the case of plasma retinol levels.

At present, it is not known whether low serum or plasma levels merely reflect disease progression or whether they indicate true micronutrient deficiencies. Clinical trials are needed to evaluate the safety and effectiveness of micronutrient supplements such as vitamin A and Zn on the progression of HIV disease in developing countries, where the majority of HIV-infected individuals are likely to have a marginal micronutrient status. In sub-Saharan Africa, where antiretroviral therapies are prohibitively expensive, the optimisation of micronutrient status may be among the affordable strategies available to improve the morbidity and mortality of HIV-infected adults and children.

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