



Nutritional status of HIV-seropositive subjects in an AIDS clinic in Paris

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Objective: To measure the prevalence and analyse the characteristics of malnutrition among subjects attending an AIDS outpatient clinic and a day care center, to improve the nutritional management of HIV-infected subjects.

Design: Prospective cross-sectional study.

Setting: AIDS clinic in a University Hospital in Paris.

Subjects: 124 HIV-seropositive adults attending the clinic.

Main outcome measures: Evaluation of nutritional status using anthropometry, impedancemetry, plasma albumin and pre-albumin assays. Degree of malnutrition, defined by the percentage of body weight loss (BWL), calculated by reference to the usual body weight.

Results: Among the 124 subjects recruited (M:F sex ratio: 3.3, mean age: 36.3 ± 7.2 y), 77 (62.1%, 95%CI: 53.9–70.3) had normal nutritional status ($BWL \leq 5\%$), 16 (12.9%, 95%CI: 7.0–18.2) moderate malnutrition ($5\% < BWL \leq 10\%$), 21 (16.9%, 95%CI: 10.3–23.5) intermediate malnutrition ($10\% < BWL \leq 20\%$), and 10 (8.1%, 95%CI: 3.3–12.9) severe malnutrition ($BWL > 20\%$). BWL was related to the CDC class (variance analysis, $P < 9 \times 10^{-5}$) and CD4 cell count ($P < 3 \times 10^{-5}$). Malnutrition was observed even among CDC class A subjects (14.9%). BWL was also related to the body mass index ($P < 3 \times 10^{-6}$), lean body mass ($P < 3 \times 10^{-5}$), body fat ($P < 7 \times 10^{-6}$) and, as assessed by impedancemetry, body cell mass ($P < 10^{-5}$) and the extra/intra cellular water ratio ($P < 2 \times 10^{-4}$). The decrease in lean body mass was related to the decrease in body cell mass.

Conclusions: Given its high frequency, malnutrition should be prevented, detected, monitored and treated from the early stages of HIV infection among patients attending AIDS clinics in order to improve survival and quality of life.

Descriptors: human immunodeficiency virus; AIDS; malnutrition; nutritional assessment; body composition.

Introduction

Described since the outset of the AIDS pandemic (Serwadda *et al*, 1985), malnutrition is frequent and a marker for poor prognosis among HIV-infected subjects (Guenter *et al*, 1993; Kotler *et al*, 1989; Sütman *et al*, 1995). HIV-related malnutrition has several causes (Macallan *et al*, 1995b), including but not limited to a decrease in food intake, the effects of opportunistic infections (OI), metabolic inefficiencies due to cytokine activity and diarrhea. Malnutrition itself can induce immunodepression (Chandra, 1983) and worsen HIV-related immunodepression (Raiter, 1991).

Despite its importance for daily patient management, the prevalence and characteristics of malnutrition among HIV-infected subjects has mostly been investigated among inpatients (O'Sullivan *et al*, 1985; Ysseldyke, 1991).

With the general aim of improving the management of HIV-seropositive subjects, we assessed the nutritional status of HIV-infected outpatients attending an AIDS clinic in Paris.

Methods

This prospective study was performed in the AIDS clinic of the Department of Infectious Diseases of Bichat-Claude Bernard Hospital, a University Hospital located in Paris. The clinic includes an outpatient department and a day care center.

HIV serodiagnosis was performed using ELISA (Diagnostic Pasteur, Marnes la Coquette, France) followed, when positive, by Western blot (New LAV Blot, Diagnostic Pasteur).

The study population was selected among HIV-seropositive subjects attending the outpatient clinic or the day care center from February 15 to June 15, 1995, with their informed consent. The study was performed two days a week, the days being selected from a table of random numbers. Among the 4–5 physicians on duty in the outpatient department on these selected days, two were selected according to the same procedure and the patients they cared for were recruited for the study. Patients requiring hospitalisation were excluded. Each patient was recruited once only, on his or her first visit during the study period.

The investigation was performed by a single physician (TN). Demographic data and information on risk factors for HIV infection and malnutrition were collected using a standardised questionnaire. Diarrhea was defined as five or more liquid stools per day. Prolonged fever was defined

as a temperature higher than 38.5°C for more than three weeks.

Height (H) was measured with the patient standing erect and weight (W) measured on a standing scale. These measurements were used to calculate the body mass index (BMI) using the formula $BMI = W/H^2$. Self-reports of usual body weight (UBW) and weight measurements taken during the physical examination were used to define body weight loss (BWL) as a percentage of UBW according to the formula: $BWL = 100 - (\text{current body weight}/\text{UBW} \times 100)$.

Other anthropometric measurements were performed according to Heymsfield & Williams (1988). Skinfold thickness was measured using a Lange skinfold calliper. Each measurement was taken three times with the patient standing in a relaxed position. The mean of the three measurements was used in the analysis.

Body fat (BF) was calculated using anthropometric measurements according to Durnin & Womersley (1974). Lean body mass (LBM) was calculated as: $LBM = \text{weight} - \text{BF}$.

In addition, LBM and components of LBM (intracellular water (ICW) and extracellular water (ECW) as well as body cell mass (BCM)) were calculated by tetrapolar bioelectrical impedance analysis (BIA) using 5 kHz and 100 kHz frequencies (Analycor^R, Eugedia, Paris) according to a method described by Boulier *et al* (1991). This method has been validated in HIV-seropositive patients (Sluys *et al*, 1993).

Total and CD4+ lymphocyte counts were measured using a flow cytometer (FACScan^R, Becton Dickinson, San Jose, California). Plasma albumin and pre-albumin were measured by laser immunonephelometry.

Statistical analysis was performed using the Chi-square test and analysis of variance (EPI INFO and BMDP softwares). Differences were considered significant if $P < 0.05$.

Results

As shown in Table 1, 124 patients were recruited (mean age: 36.3 ± 7.2 y, M:F sex ratio: 3.3). The presumed mode of HIV infection was homo- or bisexual in 53 (42.7%), heterosexual in 38 (30.7%), IV drug use in 14 (11.3%), transfusional in 1 (0.8%) and unknown in 18 (14.5%). One patient was infected by HIV2. Forty-seven patients (37.9%) belonged to CDC class A, 22 (17.7%) to class B and 55 (44.4%) to class C (AIDS).

According to the usual criteria (Morgan *et al*, 1980; O'Sullivan *et al*, 1985; Ysseldyke, 1991), patients were categorised into four classes according to the percentage of body weight loss (BWL), calculated by reference to the usual body weight (UBW), as follows:

- (1) $BWL \leq 5\%$ (no malnutrition)
- (2) $5\% < BWL \leq 10\%$ (moderate malnutrition)
- (3) $10\% < BWL \leq 20\%$ (intermediate malnutrition)
- (4) $BWL > 20\%$ (severe malnutrition).

The nutritional status of 77 out of 124 patients was normal (62.1%, 95% Confidence Interval: 53.9–70.3). Moderate malnutrition was observed in 16 patients (12.9%, 95%CI: 7.0–18.2), intermediate malnutrition in 21 (16.9%, 95%CI: 10.3–23.5) and severe malnutrition in 10 (8.1%, 95%CI: 3.3–12.9).

BWL was related to the CDC class ($P < 9 \times 10^{-5}$) and the CD4 cell count ($P < 3 \times 10^{-5}$) (Table 1). Malnutrition was observed even among CDC class A subjects (14.9%). 34 of the 55 class C patients (61.8%) had malnutrition.

Malnutrition was associated with several risk factors: loss of appetite was reported by 10.4% (8 out of 77) of subjects with no malnutrition vs 47.8% (22 out of 47) of subjects with malnutrition ($P = 4 \times 10^{-6}$); nausea: 7.8% (6 out of 77) vs 34.0% (16 out of 47) ($P = 3 \times 10^{-4}$); oropharyngeal pain: 2.6% (2 out of 77) vs 14.9% (7 out of 47) ($P = 2 \times 10^{-2}$); dysphagia: 0 out of 77 vs 12.8% (6 out of 47) ($P = 5 \times 10^{-3}$); diarrhea: 6.5% (5 out of 77) vs 21.3% (10 out of 47) ($P = 2 \times 10^{-2}$); prolonged fever: 1.3% (1 out of 77) vs 19.1% (9 out of 47) ($P = 8 \times 10^{-4}$) and depressive syndrome: 14.3% (11 out of 77) vs 38.3% (18 out of 47) ($P = 3 \times 10^{-3}$).

Table 2 shows the values of nutritional indicators according to the nutritional categories defined above. BWL was related to lean body mass ($P < 3 \times 10^{-5}$) and body fat ($P < 7 \times 10^{-6}$), as measured by anthropometry. This was consistent with the results of these two variables obtained by impedancemetry.

In addition, the analysis taking into account the results of impedancemetry (Table 2) showed that BWL was also related to body cell mass ($P < 10^{-5}$) but not to the volume of extracellular water ($P = 0.31$, NS). A relation was found between BWL and the extra/intracellular water ratio ($P < 2 \times 10^{-4}$), which increased as nutritional status worsened. This pattern reflects extracellular hyperhydration.

Table 1 Nutritional status as measured by weight loss according to age and disease characteristics

	Total population <i>n</i> = 124	No malnutrition <i>n</i> = 77 (62.1%) ^d	Moderate malnutrition <i>n</i> = 16 (12.9%)	Intermediate malnutrition <i>n</i> = 21 (16.9%)	Severe malnutrition <i>n</i> = 10 (8.1%)	<i>P</i>
Age (y) ^c	36.3 ± 7	36.1 ± 7	37.2 ± 7	37.2 ± 7	34.4 ± 5	NS ^a
CDC class						
A	47	40 (85.1) ^d	6 (12.8)	1 (2.1)	0	< 9 × 10 ^{-5b}
B	22	16 (72.7)	3 (13.6)	2 (9.1)	1 (4.6)	
C	55	21 (38.2)	7 (12.7)	18 (32.7)	9 (16.4)	
CD4/mm ^{3c}	78 ± 207	231 ± 208	198 ± 2692	45 ± 47	22 ± 25	< 3 × 10 ^{-5a}
> 500	10	8 (80.0)	2 (20.0)	0	0	< 9 × 10 ^{-5b}
200–500	29	27 (93.1)	2 (6.9)	0	0	
< 200	85	42 (49.4)	12 (14.1)	21 (24.7)	10 (11.8)	

^aVariance analysis.

^bChi square test.

^cMean/standard error.

^d*n* (% calculated on line).

Table 2 Relationship between nutritional status and other nutritional indicators

	Total population n = 124	No malnutrition n = 77	Moderate malnutrition n = 16	Intermediate malnutrition n = 21	Severe malnutrition n = 10	P
Anthropom						
weight (kg) ^c	63.7 ± 13.0	67.8 ± 11.6	64.7 ± 14.1	55.4 ± 9.7	47.9 ± 7.2	< 3 × 10 ^{-6a}
BMI	21.4 ± 3.7	22.8 ± 2.9	21.7 ± 4.3	18.5 ± 2.3	16.0 ± 1.9	< 3 × 10 ^{-6a}
LBM (kg)	47.0 ± 11.2	49.7 ± 10.8	49.0 ± 11.1	41.2 ± 8.9	34.8 ± 6.1	< 3 × 10 ^{-5a}
BF (kg)	16.3 ± 4.1	17.4 ± 4.2	15.7 ± 4.0	14.2 ± 2.5	13.2 ± 3.3	< 7 × 10 ^{-6a}
Impedance						
BCM (kg)	36.4 ± 7.9	38.2 ± 5.6	38.2 ± 4.3	32.7 ± 3.2	28.7 ± 4.1	< 10 ^{-5b}
ECW (l)	16.2 ± 2.3	16.4 ± 2.2	16.7 ± 2.0	15.8 ± 2.5	14.5 ± 2.4	NS ^a
ECW/ICW	0.84 ± 0.09	0.81 ± 0.08	0.83 ± 0.08	0.88 ± 0.09	0.96 ± 0.11	< 2 × 10 ^{-4a}
Plasmatic markers (g/l)						
albumin	41.4 ± 6.2	44.4 ± 6.0	40.5 ± 6.4	35.4 ± 7.2	32.8 ± 5.5	< 10 ^{-4a}
pre-albumin	0.27 ± 0.11	0.28 ± 0.08	0.26 ± 0.07	0.30 ± 0.27	0.16 ± 0.09	< 0.02 ^b

BMI = body mass index; LBM = lean body mass; BF = body fat; BCM = body cellular mass; ECW = extra cellular water; ICW = intra cellular water.

^aVariance analysis.

^bKruskal Wallis test.

^cMean/standard error.

Albuminemia but not pre-albuminemia was related to BWL. A fall in pre-albumin levels was observed only in severe malnutrition.

Discussion

This study of a representative sample of patients attending an AIDS outpatient clinic and day care center shows the high frequency of malnutrition (37.9% of the overall study population) and its occurrence even in asymptomatic CDC class A HIV-infected subjects (14.9%).

One originality of our study is the fact that patients were randomly selected, giving a more accurate evaluation of nutritional status than in most other studies, which involved non-random samples (Cheblowski *et al*, 1989; Chelluri & Jostremski, 1989; Graham *et al*, 1993; Kotler *et al*, 1991; O'Sullivan *et al*, 1985; Sharkey *et al*, 1992; Schwenk *et al*, 1993; Ysseldyke, 1991). Our results are thus more relevant to clinical practice and confirm that malnutrition is an important issue in the management of HIV-infected subjects.

The initial nutritional classification was based on weight loss, a criterion commonly used in previous studies (Morgan *et al*, 1980; O'Sullivan *et al*, 1985; Ysseldyke, 1991). Although differences in sampling methods make comparisons with previously published studies difficult, the prevalence rate of malnutrition was relatively low in the subgroup of AIDS patients (61.8%). But, compared with the patients at earlier stages of HIV infection, the AIDS patients we investigated were also most severely malnourished. Ysseldyke (1991) reported that 87% of patients with *Pneumocystis carinii* pneumonia had lost more than 10% of their usual body weight. In the study by O'Sullivan *et al* (1985), 62% of the AIDS in-patients had lost more than 10% of their usual weight. The differences with our results might be related to the fact that our patients were ambulatory and were therefore not seen during an ongoing opportunistic infection.

We confirmed the link between malnutrition in HIV-seropositive subjects and dysphagia, nausea, diarrhea, etc. (Macallan *et al*, 1995b; Sharkey *et al*, 1992; Kotler *et al*, 1991). Special attention should be paid to depressive syndromes, that affected 23% of our patients and are known to be associated with malnutrition in HIV-infected

subjects, through decreased food intake (Macallan *et al*, 1995a).

As demonstrated by anthropometry among subjects with moderate malnutrition, weight loss was related to a decrease in body fat, with preservation of lean body mass. This is similar to the situation observed in healthy subjects with decreased food intake (Shizgal, 1981). Among the subjects with moderate or severe malnutrition, weight loss was due to a loss of both body fat and lean body mass. These changes may be related to decreased food intake, increased whole-body protein turnover (Macallan *et al*, 1995b), and the release of cytokines and stress hormones (Evans *et al*, 1989; Grunfeld & Feingold, 1992; Salehian *et al*, 1993).

50 kHz unifrequency BIA is the most commonly used BIA method and has been validated in HIV-infected patients (Kotler *et al*, 1996). Using this method, Ott *et al* (1993) observed, as in this study, a decrease in lean body mass and an increase in total body water during the early stages of HIV infection. However, 50 kHz unifrequency BIA does not allow intra and extra cellular water to be measured contrary to 5 kHz and 100 kHz bifrequency BIA. These variables are relevant to HIV infection, as the present study using bifrequency BIA showed that the decrease in lean body mass (also demonstrated by anthropometry) was related to a decrease in the body cell mass associated with extracellular hyperhydration. Taken together, these results suggest that both BIA methods are useful for the clinical evaluation of nutritional status in HIV-infected patients.

Severe malnutrition has long been known as an independent risk factor for infections (Kotler *et al*, 1989; Pelletier *et al*, 1995; Van den Broeck *et al*, 1993), including opportunistic infections in HIV-seropositive subjects (Guenter *et al*, 1993). The life expectancy of HIV-infected patients is related, among other parameters, to their nutritional status (Kotler *et al*, 1989; Graham *et al*, 1993). Standardised evaluation of nutritional status should thus be made regularly. In addition to anthropometry (including the measure of BWL), impedancemetry and serum albumin assay will provide baseline data on which to base the diagnosis, treatment and follow up of malnutrition before it becomes severe (Ott *et al*, 1993). Even if extracellular hyperhydration contributes, by a dilution effect, to the decrease in albumin level, the latter remains a parameter

of major significance to assess the severity of malnutrition.

Curable causes of malnutrition such as candidiasis-related oropharyngeal pain and dysphagia should be treated and patients should be maintained in satisfactory nutritional status to help them handle nutritional disorders related to episodes of opportunistic infections. During and after opportunistic infections, food intake should be adapted to obtain positive calorie and protein balances.

The mode of feeding is based on the patient's clinical status. First-line treatment is with oral nutritional supplementation and standard dietary counseling. Progression to tube feeding—or total parenteral nutrition should be based on gastrointestinal intolerance and treatment decisions involving the patient's own opinion.

Given its high frequency among patients attending AIDS clinics, malnutrition should be prevented, detected, monitored and treated from the early stages of HIV infection, using standardised procedures, as these simple measures may improve both survival and quality of life.

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References

- Boulier A, Fricker J, Thomasset AL & Apfelbaum M (1990): Fat-free mass estimation by the two-electrode impedance method. *Am. J. Clin. Nutr.* **52**, 581–585.
- Chandra RK (1983): Nutrition, immunity and infection: present knowledge and future directions. *Lancet* **1**, 688–691.
- Chlebowski RT, Grosvenor MB, Bernhard NH, Morales LS & Bulcavage LM (1989): Nutritional status, gastrointestinal dysfunction, and survival in patients with AIDS. *Am. J. Gastroenterol.* **84**, 1288–1293.
- Chelluri L & Jostremski MS (1989): Incidence of malnutrition in patients with acquired immunodeficiency syndrome. *Nutr. Clin. Pract.* **4**, 16–18.
- Durnin JV & Womersely J (1974): Body fat assessed from total density estimation from skinfold thickness: measurements on 418 men and women aged from 16 to 72 years. *Br. J. Nutr.* **32**, 77–97.
- Evans RD, Argiles JM & Williamson DH (1989): Metabolic effects of tumor necrosis factor- α (cachectin) and interleukin 1. *Clin. Sci.* **37**, 357–364.
- Graham NMH, Munoz A, Bacellar H, Kingsley LA, Visscher BR & Phair JP (1993): Clinical Factors associated with weight loss related to infection with human immunodeficiency virus type 1 in the Multicenter AIDS Cohort Study. *Am. J. Epidemiol.* **137**, 439–446.
- Grunfeld C & Feingold KR (1992): The role of the cytokines, interferon α and tumor necrosis factor in the hypertriglyceridemia and wasting of AIDS. *J. Nutr.* **122**, 749–753.
- Guenther P, Muurahainen M, Simons G, Kosok A, Cohan GR, Rudenstein R & Turner JL (1993): Relationships among nutritional status, disease progression, and survival in HIV infection. *J. Acquir. Immune. Defic. Syndr.* **6**, 1130–1138.
- Heymsfield SB & Williams PJ (1988): Nutritional assessment by clinical and biochemical methods. In *Modern Nutrition in Health and Disease*, 7th edn, eds ME Shils & VR Young, pp 817–860. Philadelphia: Williams and Wilkins.
- Kotler DP, Tierney AR, Ferrano R, Cuff P, Wang J, Pierson RN & Heymsfield SB (1991): Enteral alimentation and repletion of body cell mass in malnourished patients with acquired immunodeficiency syndrome. *Am. J. Clin. Nutr.* **53**, 149–154.
- Kotler DP, Tierney AR, Wang J & Pierson RN (1989): Magnitude of body-cell-mass depletion and timing of death from wasting in AIDS. *Am. J. Clin. Nutr.* **50**, 444–447.
- Kotler DP, Burastero S, Wang J & Pierson RN (1996): Prediction of body cell mass, fat free mass and total body water using bioimpedance analysis: effects of race, gender and disease. *Am. J. Clin. Nutr.* **64**, 489S–499S.
- Macallan DC, McNurlan MA, Milne E, Calder AG, Garlick PJ & Griffin GE (1995a): Whole-body protein turnover from leucine kinetics and the response to nutrition in human immunodeficiency virus infection. *Am. J. Clin. Nutr.* **61**, 818–826.
- Macallan DC, Noble C, Baldwin C, Jeeb SA, Prentice AM, Coward WA, Sawyer MB, McManus TJ & Griffin GE (1995b): Energy expenditure and wasting in human immunodeficiency virus infection. *N. Engl. J. Med.* **333**, 83–88.
- Morgan DB, Hill GL & Burkinshaw L (1980): The assessment of weight loss from a single measurement of body weight: problems and limitations. *Am. J. Clin. Nutr.* **33**, 2101–2105.
- O'Sullivan P, Linke RA & Dalton S (1985): Evaluation of body weight and nutritional status among AIDS patients. *J. Am. Diet. Assoc.* **85**, 1483–1484.
- Ott M, Lembcke B, Fischer H, Jäger R, Polat H, Geier H, Rech M, Staszewski S, Helm EB & Caspary WF (1993): Early changes of body composition in human immunodeficiency virus-infected patients: tetrapolar body impedance analysis indicates significant malnutrition. *Am. J. Clin. Nutr.* **57**, 15–19.
- Pelletier DL, Frangillo EA, Schroeder DG & Habicht JP (1995): The effects of malnutrition on child mortality in developing countries. *WHO Bull.* **73**, 443–448.
- Raiten DJ (1991): Nutrition and HIV infection: a review and evaluation of the extant knowledge and the relationship between nutrition and HIV infection. *Nutr. Clin. Pract.* **6** Suppl. 1, 1S–94S.
- Salehian D, Salmon D, Niyongabo T, Melchior JC, Rigaud D & Vilde JL (1993): Tumor necrosis factor and resting energy expenditure during AIDS. *Am. J. Clin. Nutr.* **58**, 715–716.
- Schwenk A, Bürger B, Wessel D, Stützer H, Ziegenhagen D, Diehl V & Schrappe M (1993): Clinical risk factors for malnutrition in HIV-1-infected patients. *AIDS* **7**, 1213–1219.
- Serwadda D, Sewankambo NK, Carswell JW, Bayley AC & Tedder RS (1985): Slim disease: a new disease in Uganda and its association with HTLV-III infection. *Lancet* **2**, 849–852.
- Sharkey SJ, Sharkey KA, Sutherland LR, Church DL & GI/HIV Study Group (1992): Nutritional status and food intake in human immunodeficiency virus infection. *J. Acquir. Immune. Defic. Syndr.* **5**, 1091–1098.
- Shizgal HM (1981): The effect of malnutrition on body composition. *Surg. Gynecol. Obstet.* **152**, 22–26.
- Sluys TEM, van der Ende ME, Swart GR, van den Berg JWO & Wilson THP (1993): Body composition in patients with acquired immunodeficiency syndrome: a validation study of bioelectrical impedance analysis. *JPEN* **17**, 404–406.
- Sütman U, Ockenga J, Selberg O, Hoogestraat L, Deicher H & Müller MJ (1995): Incidence and prognostic value of malnutrition and wasting in human immunodeficiency virus-infected outpatients. *J. Acquir. Immune. Defic. Syndr. Hum. Retrovirol.* **8**, 239–246.
- Van den Broeck J, Eeckels R & Vuylsteke J (1993): Influence of nutritional status on child mortality in rural Zaïre. *Lancet* **341**, 1491–1495.
- Ysseldyke LL (1991): Nutritional complications and incidence of malnutrition among AIDS patients. *J. Am. Diet. Assoc.* **91**, 217–218.