

## Assessment of body hydration in subjects with schistosomiasis

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**Summary.** Total body water (TBW) was measured by deuterium oxide dilution ( $D_2O$ ) and predicted by bioelectric impedance analysis (BIA) (Deurenberg, Schouten, Andreoli and De Lorenzo 1993) in 21 subjects with *Schistosoma mansoni* infection and 17 healthy controls of similar age ( $32.8 \pm 13.7$  years,  $n = 38$ ). Patients were selected to have no visible fluid retention and no cardiac or renal abnormalities. Body hydration (TBW per kg of body weight) was significantly higher in patients with schistosomiasis than in controls ( $62.9 \pm 3.6$  vs  $57.4 \pm 4.3\%$ ,  $p < 0.0005$ ). A significant correlation was found between albumin levels and TBW% on the pooled sample ( $n = 38$ ;  $r = 0.660$ ,  $p < 0.0001$ ). This relationship was not influenced by the presence of disease, as determined by ANCOVA. Values of TBW predicted by BIA were highly correlated and not significantly different ( $p = n.s.$ , ANOVA) from those measured by  $D_2O$  in both controls and patients ( $r = 0.854$ ,  $p < 0.001$ ,  $SEE = 2.3$  l,  $CV = 5.9\%$  and  $r = 0.848$ ,  $p < 0.001$ ,  $SEE = 4.0$  l,  $CV = 9.3\%$ , respectively). The bias (TBW by BIA - TBW by  $D_2O$ ) was of  $0.9 \pm 3.7$  l in controls and of  $-1.3 \pm 4.2$  l in patients. This bias was significantly correlated to TBW% in patients ( $r = 0.575$ ,  $p < 0.05$ ) but not in controls ( $p = n.s.$ ). It is concluded that subjects with schistosomiasis show an apparent subclinical increase in body hydration which could affect the prediction of TBW from BIA.

### 1. Introduction

Schistosomiasis is a parasitic disease which affects more than 200 million individuals worldwide (WHO 1993). Infection with any of three species of *Schistosoma* (*S. haematobium*, *S. japonicum* and *S. mansoni*) commonly results in human disease. Infection takes place when cercariae, released by snail intermediate hosts, penetrate the skin of an individual exposed to contaminated water (Strickland and Abdel-Wahab 1991).

Alterations of nutritional status are common in patients with schistosomiasis and may be partly responsible for the morbidity of the underlying disease (Latham 1982, Warren 1982, Stephenson 1993, WHO 1993). Thus, assessment of nutritional status should be regarded as an essential part of the clinical evaluation of these patients.

Body composition reflects nutritional status, and its regular assessment has the potential to improve the clinical management of patients with schistosomiasis. In particular, 'bedside' body composition techniques, such as the assessment of body fat from skinfolds and the prediction of total body water (TBW) from bioelectric impedance, may allow a simple and inexpensive assessment of body composition in these patients. However, these techniques have been calibrated on healthy individuals and may not work properly in ill subjects whose body composition differs significantly from that of the reference individuals.

Body hydration is frequently increased in a variety of acute and chronic infections (Beisel 1995). Oedema and ascites are common in the advanced stages of schistosomiasis and their presence is known to affect the prediction of TBW from BIA (Strickland and Abdel-Wahab 1991, Deurenberg 1994). However, subclinical

alterations in body hydration may also render inaccurate the assessment of TBW from BIA by means of predictive algorithms developed on healthy subjects (Bedogni, Merlini, Ballestrazzi, Severi and Battistini 1996a, Bedogni, Polito, Severi, Strano, Manzieri, Alessio, Iovene and Battistini 1996b).

The aims of the present study were: (a) to investigate whether body hydration is altered in subjects with schistosomiasis in the absence of clinically evident fluid retention, and (b) to evaluate the potential of BIA for predicting TBW in these patients.

## 2. Materials and methods

### 2.1. Subjects

Twenty-one male Egyptian subjects with *S. mansoni* infection were consecutively enrolled into the study at the Medical Research Institute of Alexandria University (Egypt). Seventeen healthy male Egyptian subjects of similar age, weight and height served as controls. Informed consent was obtained from all subjects participating in the study. The study protocol had been approved from the Ethical Committee at the University of Tor Vergata (Rome, Italy).

Diagnosis of schistosomiasis was based on the finding of *S. mansoni*'s characteristic ova in the faeces (Strickland and Abdel-Wahab 1991). Three stages of schistosomiasis were distinguished, according to the degree of hepatic involvement: stage 1 (S1, early hepatic involvement): patients were asymptomatic and the liver and spleen could not be palpated; stage 2 (S2, intermediate hepatic involvement): the liver and spleen could be palpated easily; stage 3 (S3, advanced hepatic involvement): the liver was markedly fibrotic and shrunken, as detected by ultrasonography. Besides clinically evident fluid retention, the study protocol required that patients had no evidence of cardiac or renal involvement from the underlying disease, and no sign of malabsorption. Some patients were taking praziquantel, an antihelminthic drug with no influence on water and electrolyte metabolism. All subjects were on a free diet.

### 2.2. Anthropometry

Body weight (Wt), height (Ht), arm circumference (AC) and skinfolds [triceps (TSF), biceps (BSF), subscapular (SSF), suprailiac (SISF), abdominal (ASF), anterior and posterior thigh (ATHSF, PTHSF)] were measured following the Anthropometric Standardization Reference Manual (Lohman, Roche and Martorell 1988). Body mass index (BMI) was calculated as  $Wt \text{ (kg)}/Ht^2 \text{ (m)}$ . Arm fat area (AFA) and arm muscle area (AMA) were calculated from AC and TSF as described by Frisancho (1990).

### 2.3. TBW assessment

TBW was measured by deuterium oxide ( $D_2O$ ) dilution. A preliminary study aimed at establishing the equilibration time of  $D_2O$  was performed on the plasma of three unselected patients. In all cases  $D_2O$  reached the equilibrium within 3.0 h after its administration, a time similar to that observed in patients with non-ascitic liver disease (Borghi, Bedogni, Rocchi, Severi, Farina and Battistini 1996). Subjects had fasted for at least 8 h before receiving orally a precisely weighed solution made up of 10 g of  $D_2O$  and 40 g of drinkable water. Plasma samples were collected before and 3.5 h after the administration of this solution, as described in detail elsewhere (Battistini, Severi, Brambilla, Virgili, Manzoni, Beccaria and Chiumello 1995b).  $D_2O$  concentration in plasma samples was measured by FT-IR spectrophotometry

(Lukaski and Johnson 1985). TBW was calculated as deuterium dilution space  $\times$  0.95, taking into account non-aqueous distribution of D<sub>2</sub>O (Heymsfield and Waki 1991). Body hydration (TBW%) was calculated as [TBW (l)/Wt (kg)]  $\times$  100.

#### 2.4. BIA

The determination of bioelectric impedance ( $Z$ ) was made with a tetrapolar impedance plethysmograph (Human IM Scan, Dietosystem, Milano, Italy) at multiple frequencies. The equation of Deurenberg *et al.* (1993) was used to predict TBW from the impedance index at 100 kHz [ $ZI_{100} = \text{height}^2 (\text{cm}^2)/Z_{100} (\Omega)$ ]. We preferred these equations to others available in the literature because they were developed using the same impedance plethysmograph employed in the present study, and because we had already evaluated their accuracy on external groups of healthy and ill subjects (Battistini, Facchini, Bedogni, Severi, Fiori and Pettener 1995a; Borghi *et al.* 1996).

#### 2.5. Statistics

Descriptive statistics, ANOVA, ANCOVA and regressions were performed on an Apple Macintosh computer using the Statview 4.5 and SuperAnova 1.1 software packages (Abacus Concepts, Berkeley, California, USA). The significance level was set to a value of  $p < 0.05$ . Values are presented as mean  $\pm$  SD.

### 3. Results

The main characteristics of controls and patients are given in table 1. Of the enrolled patients, five had S1, 10 had S2, and six had S3 schistosomiasis.

Table 1. Main characteristics of controls and patients with schistosomiasis.

	Controls ( $n = 17$ )	Patients with schistosomiasis ( $n = 21$ )
Age (years)	31.1 $\pm$ 14.3	32.5 $\pm$ 13.8
Weight (kg)	69.2 $\pm$ 11.7	68.5 $\pm$ 10.9
Height (cm)	170.3 $\pm$ 8.5	172.2 $\pm$ 5.3
BMI (kg/m <sup>2</sup> )	23.9 $\pm$ 3.1	23.1 $\pm$ 3.4
BSF (mm)	4.2 $\pm$ 1.0	3.3 $\pm$ 0.7*
TSF (mm)	7.7 $\pm$ 2.4	6.2 $\pm$ 2.8
SSF (mm)	11.3 $\pm$ 2.8	9.1 $\pm$ 2.6
SISF (mm)	13.4 $\pm$ 7.0	10.4 $\pm$ 6.3
ASF (mm)	13.6 $\pm$ 6.5	12.3 $\pm$ 8.4
ATHSF (mm)	13.4 $\pm$ 4.9	9.8 $\pm$ 5.2*
PTHSF (mm)	9.8 $\pm$ 3.4	8.9 $\pm$ 5.0
AFA (cm <sup>2</sup> )	8.5 $\pm$ 2.1	6.8 $\pm$ 3.1
AMA (cm <sup>2</sup> )	57.5 $\pm$ 17.2	57.4 $\pm$ 9.8
TBW (l)	39.3 $\pm$ 4.4	43.1 $\pm$ 7.4
TBW% (%)	57.4 $\pm$ 4.3	62.9 $\pm$ 3.6**
Z <sub>100</sub> ( $\Omega$ )	439 $\pm$ 50	465 $\pm$ 55
Albumin (g/dl)	4.3 $\pm$ 0.6	3.1 $\pm$ 0.6***

\*  $p < 0.05$ , \*\*  $p < 0.0005$  and \*\*\*  $p < 0.0001$  vs controls at ANOVA.

BMI = body mass index; BSF = biceps skinfold; TSF = triceps skinfold; SSF = subscapular skinfold; SISF = suprailiac skinfold; ASF = abdominal skinfold; ATHSF = anterior thigh skinfold; PTHSF = posterior thigh skinfold; AFA = arm fat area; AMA = arm muscle area; TBW = total body water; TBW% = TBW per kg of body weight; Z<sub>100</sub> = body impedance at 100 kHz.

Wt, Ht and BMI were not significantly different in controls and patients ( $p = \text{n.s.}$ , ANOVA). AMA was similar in controls and patients while AFA was 20% lower in the latter ( $p = \text{n.s.}$  for both, ANOVA). Of the skinfolds, BSF and ATHSF were significantly lower in patients than in controls ( $p < 0.05$ , ANOVA).

TBW was higher in patients than in controls but the difference did not reach statistical significance ( $p = \text{n.s.}$ , ANOVA). However, TBW% was significantly higher in patients than in controls ( $p < 0.0005$ , ANOVA).

Surprisingly,  $Z_{100}$  was higher in patients than in controls despite their increased TBW%. This paradoxical finding was explained by the unusually high values of  $Z$  of two subjects with schistosomiasis. The analysis of their clinical charts did not reveal any violation to the study protocol, so that they were maintained in the data sheet. In every case the difference in  $Z_{100}$  between groups did not reach statistical significance ( $p = \text{n.s.}$ , ANOVA).

Albumin levels were significantly lower in patients than in controls ( $p < 0.0001$ , ANOVA). Anthropometric characteristics, TBW%,  $Z_{100}$  and albumin levels were similar between S1, S2 and S3 patients ( $p = \text{n.s.}$ , ANOVA; data not shown). For this reason all the patients were included in a single sample ( $n = 21$ ) for further analysis.

To test whether TBW% was influenced by albumin levels, a linear model was constructed using TBW% as the dependent variable and albumin as the independent (predictor) variable. Schistosomiasis status (0 for controls and 1 for patients) was entered in the model as a covariate, and comparison of intercepts and regression coefficients of the regression lines was used to test whether the relationship between TBW% and albumin was influenced by disease (Norgan 1995). Since schistosomiasis status had no effect on the prediction ( $p = \text{n.s.}$ , ANCOVA), it was removed from the model. According to the final model, albumin explained 44% ( $r^2 = 0.436$ ) of the variance of TBW% on all the subjects ( $n = 38$ ,  $r = 0.660$ ,  $p < 0.0001$ ; figure 1).

Values of TBW predicted by BIA were highly correlated and not significantly different ( $p = \text{n.s.}$ , ANOVA) from those measured by  $D_2O$  dilution in both controls and patients ( $r = 0.854$ ,  $p < 0.001$ ,  $\text{SEE} = 2.3$ ,  $\text{CV} = 5.9\%$  and  $r = 0.848$ ,

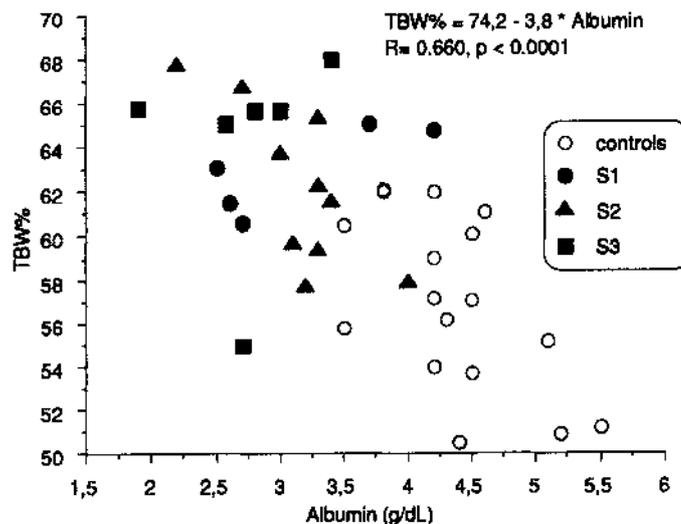


Figure 1. Relationship between serum albumin and body hydration (TBW%) in patients with schistosomiasis [stages (S) 1, 2 and 3] and controls.

$p < 0.001$ , SEE = 4.0 l, CV = 9.3%, respectively). The bias associated to the prediction of TBW from BIA (TBW by BIA - TBW by D<sub>2</sub>O) was of  $0.9 \pm 3.7$  l in controls and of  $-1.3 \pm 4.2$  l in patients. Interestingly, this bias was significantly correlated to TBW% in patients ( $r = 0.575$ ,  $p < 0.05$ ) but not in controls ( $p = \text{n.s.}$ ).

#### 4. Discussion

Body hydration is frequently increased in a variety of acute and chronic infections (Beisel 1995). The increase in body hydration is more evident when organs with a key role in water homeostasis—such as the heart, kidney and liver—are involved from the underlying disease (Rose 1994). It is therefore not surprising that fluid retention is so common among patients with advanced stages of schistosomiasis (Strickland and Abdel-Wahab 1991). With this degree of water retention, indirect methods for the assessment of body composition cannot be used safely. However, in about 80% of patients schistosomiasis is diagnosed at earlier stages, where these alterations in body hydration are not evident (WHO 1993).

In this study, patients with schistosomiasis were selected to have no visible fluid-retention and no cardiac or renal abnormalities from the underlying disease. While these patients were apparently similar to controls in their anthropometric characteristics, their TBW% was significantly higher. Our study therefore suggests that sub-clinical alterations in body hydration may occur in subjects with schistosomiasis.

A decrease in fat mass may be responsible for an increase in the hydration of body weight and of the fat-free mass (Shetty 1995). AFA was 20% lower in patients than in controls, so the possibility exists that the former had a decreased fat mass. This may have at least partially contributed to their increased TBW%.

Hypoalbuminaemia is a well-known cause of oedema. In the absence of other factors favouring fluid retention, albumin levels  $< 1.5$ – $2.0$  g/dl are needed to have a clinically detectable increase in ECW relative to TBW (ECW%) (Rose 1994). In this study the lowest albumin level was one of 1.9 g/dl, which was seen in a S3 patient. Even with albumin levels of 1.9 g/dl and higher, and in the absence of oedema, albuminaemia was significantly linked to TBW% in our study population. Moreover, this relationship was not influenced by disease. Although we did not measure ECW in our subjects, the observed relationship between TBW% and albumin suggests that the difference in TBW% between patients and controls could be accounted for by an expansion of ECW% (Rose 1994). However, as we have recently shown in patients with liver disease and minimal changes in TBW%, the possibility of an increase in intracellular water (ICW) relative to TBW should not be completely excluded (Borghi *et al.* 1996). Nevertheless, our data suggest that albumin plays a major role in controlling body water homeostasis in conditions of normal and subclinically altered body hydration. Further studies are needed to ascertain if this relationship is peculiar to the study population, or can be extended to other populations.

BIA is a simple, portable and low-cost technique for the assessment of TBW and of its distribution between ECW and ICW (Heitmann 1994). Owing to these characteristics, BIA has a great potential to be employed for bedside assessment of hydration status. However, BIA is known to be sensitive to changes in TBW% and in the ECW:ICW ratio (Deurenberg, van der Kooy, Leenen and Schouten 1989, Bedogni *et al.* 1996a,b). In this study a formula developed on healthy European subjects allowed a reasonably good prediction of TBW from BIA in healthy African subjects. The SEE and the bias associated with the use of this

formula in healthy African subjects are comparable to those reported for its utilization in external groups of European and Asiatic subjects (Battistini *et al.* 1995a). This formula, however, gave a less accurate prediction of TBW in patients with schistosomiasis, and its bias was clearly influenced by their altered TBW%. Thus, it appears that the subclinical increase in TBW% shown by patients with schistosomiasis can affect the prediction of their TBW from BIA. It should nonetheless be noted that the employed formula gave an accurate prediction of TBW in cirrhotic patients without significant changes in TBW% and with minimal changes in the ECW:ICW ratio with respect to controls (Borghini *et al.* 1996).

In conclusion, our study shows that body hydration may be increased in patients with schistosomiasis also in the absence of clinically evident fluid retention, and that this affects the prediction of TBW with BIA. Further studies are needed to determine the pathophysiological bases of the altered body-water homeostasis in schistosomiasis, and to establish if adjustments of traditional body composition models are needed to give an accurate prediction of body composition in these patients, owing to their altered body hydration.

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**Zusammenfassung.** Bei 21 Patienten mit einer *Schistosoma mansoni* Infektion und 17 gesunden Kontrollen ähnlichen Alters ( $32.8 \pm 13.7$  Jahre,  $n = 38$ ) wurde das Gesamtkörperwasser (TBW) zum einen über die Deuteriumoxid Verdünnungsmethode ( $D_2O$ ) gemessen und zum anderen aus der Bioelektrischen Impedanzanalyse (BIA) geschätzt (Deurenburg, Schouten, Andreoli and De Lorenzo 1993). Ausschlusskriterien für die Patienten waren eine sichtbare Flüssigkeitsretention sowie kardiale oder renale Auffälligkeiten. Die Hydratation des Körpers (TBW pro kg Körpergewicht) war bei Patienten mit Schistosomiasis signifikant höher als bei den Kontrollen ( $62.9 \pm 3.6$  vs  $57.4 \pm 4.3\%$ ,  $p < 0.0005$ ). In der Gesamtstichprobe wurde eine signifikante Korrelation zwischen der Albuminkonzentration und dem prozentualen TBW-Anteil gefunden ( $n = 38$ ;  $r = 0.660$ ,  $p < 0.0001$ ). Eine ANCOVA-Analyse zeigte, dass der Krankheitsstatus diese Beziehung nicht beeinflusst. Sowohl bei den Patienten als auch bei den Kontrollen waren die mittels BIA geschätzten TBW-Werte hoch mit den durch  $D_2O$  gemessenen Werten korreliert (ANOVA;  $r = 0.854$ ,  $p < 0.001$ ,  $SEE = 2.31$ ,  $CV = 5.9\%$  bzw.  $r = 0.848$ ,  $p < 0.001$ ,  $SEE = 4.01$ ,  $CV = 9.3\%$ ), und beide Ergebnisse waren nicht signifikant verschieden ( $p = n.s.$ ). Der Bias (TBW-BIA minus TBW- $D_2O$ ) betrug  $0.9 \pm 3.71$  bei den Kontrollen und  $-1.3 \pm 4.21$  bei Patienten. Bei Patienten, nicht aber bei Kontrollen ( $p = n.s.$ ), war der Bias signifikant mit dem prozentualen TBW-Anteil korreliert ( $r = 0.575$ ,  $p < 0.05$ ). Aus den Ergebnissen lässt sich schließen, dass bei Patienten mit Schistosomiasis eine augenscheinliche subklinische Erhöhung der Hydratation vorliegt, welche die Prädiktion des TBW mittels BIA beeinflussen könnte.

**Résumé.** L'eau corporelle totale (ECT) a été mesurée par dilution d'oxyde de deuterium ( $D_2O$ ) et prédite par analyse d'impédance bioélectrique (AIB) (Deurenberg, Schouten, Andreoli and De Lorenzo 1993) chez 21 sujets présentant une infestation à *Schistosoma mansoni* et chez 17 contrôles sains d'âge similaire ( $32.8 \pm 13.7$  ans,  $n = 38$ ). Les patients ont été sélectionnés de telle sorte qu'ils ne présentent ni rétention visible de fluide, ni anomalies cardiaques ou rénales. L'hydratation corporelle (ECT par kg de poids) est significativement plus élevée chez les patients avec schistosomiase que chez les contrôles ( $62.9 \pm 3.6$  contre  $57.4 \pm 4.3\%$   $p < 0.0005$ ). Une corrélation significative a été trouvée entre les niveaux d'albumine et l'ECT% sur l'ensemble des sujets ( $n = 38$ ,  $r = 0.660$ ,  $p < 0.0001$ ). Cette association n'est pas influencée par la présence de la pathologie (ANCOVA). Les valeurs d'ECT prédites par AIB sont fortement corrélées et ne diffèrent pas significativement ( $p = n.s.$  ANOVA) de celles mesurées par  $D_2O$  chez les contrôles et les patients à la fois (respectivement  $r = 0.854$ ,  $p < 0.001$ ,  $SEE = 2.31$ ,  $CV = 5.9\%$  et  $r = 0.848$   $p < 0.0001$ ,  $SEE = 4.01$ ,  $CV = 9.3\%$ ). Le biais (ECT par AIB-ECT par  $D_2O$ ) est de  $0.9 \pm 3.71$  chez les contrôles et  $-1.3 \pm 4.21$  chez les patients. Il est corrélé significativement à l'ECT% chez les patients ( $r = 0.575$ ,  $p < 0.05$ ), mais non chez les contrôles ( $p = n.s.$ ). On en conclut que les sujets ayant une schistosomiase montrent un accroissement sous-clinique de l'hydratation corporelle, qui pourrait affecter les prédictions d'ECT par AIB.